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ANALYSIS ON THE CLINICAL DATA OF PULMONARY SPACE-OCCUPYING LESION AND EVALUATION OF THE DIAGNOSTIC EFFICACY OF LUNG CANCER

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Abstract: Objective: Based on the pathological result and inspection data of 44 cases of pulmonary space-occupying lesion, this paper discussed the practical value of CT-guided pathological biopsy and three tumor markers being named CEA, NSE and CYFRA21-1 in the detection of lung cancer. Methods: The results of Pathology, immunohistochemistry, CEA, NSE and CYFRA21-1 in 44 cases of confirmed pulmonary space-occupying lesions were collected. This paper calculated the positive rate from unique and united test of the three tumor markers on the lung cancer group and non-malignant group. Chi square test were used to make the comparison between different groups, and then plotting a ROC curve based on the analysis of specificity and sensitivity. Results: The results show 33 cases in lung cancer group, 11 cases in non-malignant group among the 44 pulmonary space-occupying lesion cases. Immunohistochemistry was carried out to check 16 cases. The positive rate of TTF-1and CK7 in adenocarcinoma group was 57.14% while P40 in squamous cell carcinoma was 60%. The positive rate of lung cancer group, including NSE, CYFRA21-1 and the co-detection of three index, were 48.48 %, 78.78% and 81.81%. Respectively, these rate in non-malignant group was 0%, 27.27%, 36.36%. Chi square test showed $p<0.05$, the differences were statistically significant. The AUC was 0.875 while the sensitivity was 81.8% of tumor markers united test, both higher than the unique test. However, the specificity is 63.3%, lower than the unique test. Besides, the positive rate of CYFRA21-1 among different pathological types of lung cancer showed significantly difference, for the result of chi square test was $p < 0.05$, which was statistically significant. Conclusion: The study demonstrated that the CT-guided percutaneous lung biopsy was beneficial to detect and later treatment of lung cancer. The results of the tumor marker NSE and CYFRA21-1 unique test are ideal, better than the co-detection of three index. We suggested to give priority to the test of NSE and CYFRA21-1 in the follow-up diagnosis and treatment.
Keywords: Pulmonary space-occupying lesion, CEA, NSE, CYFRA21-1, CT-guided percutaneous lung biopsy

1. INTRODUCTION

The proportion of lung cancer is quite high among the confirmed pulmonary space-occupying lesion cases. The incidence rate and death rate of the lung cancer are in high level[1,2], which have become serious problem to human health. The majority of people are in the moderate or far advanced of lung cancer when they become confirmed cases[1], follow-up treatment is difficult and passive. Herein, it is important to detect and confirm the lung cancer as early as possible. Pathologic biopsy is crucial to the early diagnosis and treatment of lung cancer. The commonly used clinical biopsy 6techniques including endoscopes and Percutaneous Transthoracic Needle Biopsy(PTNB). CT has obvious advantages in resolution compared with other guidance methods such as B-ultrasound, and has become the preferred and most commonly used guidance method of PTNB[3]. Serum tumor markers is important and meaningful to the early diagnosis of lung cancer. The CEA, NSE and CYFRA21-1 have close relationship with lung cancer[4]. The results based on the unique test might be insufficient and lacking of accuracy. Therefore, in clinical, it is needed to using united tests to increase the accuracy to diagnose the lung cancer. This paper investigated the efficiency of CT-guided percutaneous lung biopsy and united tests of three tumor markers on detecting the lung cancer by analyzing the clinical data from 44 confirmed pulmonary space-occupying lesion cases.

2. DATA AND METHODS

Clinical Data

This study summarized the clinical data of 44 patients who performed CT-guided percutaneous lung biopsy for pulmonary space-occupying lesion from May, 2019 to October, 2021 in Guangzhou Development District Hospital. The criteria for sample collection: no antitumor treatment were applied before confirmed; the imaging examination suggested pulmonary space-occupying lesion and had indications of CT-guided percutaneous lung biopsy; the blood routine, blood type, coagulation function, hepatitis B, syphilis, HIV, hepatitis- C and ECG were completely before operation; patients had clear consciousness, no rough cough, and were able to collaborate with the doctor to finish CT guided percutaneous lung biopsy. The criteria for exclude samples: enhanced scan indicated the presence of large

vessels in the lesion, which was not suitable for puncture biopsy; coagulation dysfunction, hrombo-cytopenia, bleeding tendency; cardiopulmonary dysfunction could not tolerate operation; the predicted site of puncture had bleeding and infection issues; could not collaborate with the doctor to finish operation.

Method

Preoperative preparations and evaluation

Detailed history was collected, the CT and other imaging results were analyzed before operation. Blood test and ECG were applied. Evaluate the function of cardiopulmonary and eliminate contraindications. CT guided percutaneous lung biopsy was singed and agreed by the patient.

Puncture location and biopsy

Siemens 16-slice CT machine and 18G automatic biopsy needle (Bard MC1816) were used for CT guided percutaneous lung biopsy. The specimens was fixed in 10% formaldehyde fixative and sent for pathological examination.

Pathological examination and test of tumor markers

The pathological reports were signed by pathologists. The results of serum tumor markers were obtained from the immunology laboratory of our hospital, and the blood collection and specimen submission procedures of all patients were standardized in accordance with the blood collection and specimen submission procedures in our hospital. Before operation, per 3ml venous blood was taken when patients were fasting, and the detection method was electrochemiluminescence. The instrument was Roche Cobas E602 automatic chemiluminescence analyze, and the original matching kit of Roche Diagnostics. The standards for three markers: CEA<5ng/ml, NSE<16.3ng/ml, CYFRA21-1<3.3ng/ml. If the resulted values were higher than the upper limit of the standard, then the researchers labeled it as positive specimen. In united test, if any measurements showed a positive result, then the specimen would be labelled as positive, otherwise it labelled as negative.

Analysis of the Statistic

Excel and SPSS 26.0 softwares were used to summarize the data, analyzing the positive rate of the test result. Chi square test were carried out to compare each groups , the difference was statistically significant when $P < 0.05$. We plotted the ROC curves and obtain the area under the curve (AUC).

3. RESULTS

The General Situation of the Patient

The researchers selected 44 confirmed cases and listed their basic information including gender, age and pathological group. (Table.1)

Table.1 The basic information of patients [n(%)]

Group		Lung cancer group	Non-malignant group
Gender	male	23(69.69)	8(72.72)
	female	10(30.3)	3(27.27)
Age	<40 years	4(12.12)	1(9.09)
	40~59 years	8(24.24)	7(63.63)
	>60 years	21(63.63)	3(27.27)

Pathological Results of Patients

The pathological results of 44 patients were classified as follows. (Table.2)

Table.2 The result of CT guided percutaneous lung biopsy

Pathological type	Cases	Percentage /%
Malignant lesion	33	75.00
Adenocarcinoma	23	52.27
Squamous cell carcinoma	4	9.09
Small cell lung cancer	2	4.55
Other	4	9.09
Non-malignant tumor	11	25.00
Organizing pneumonia	2	4.55
Pneumonia	3	6.82
Lung tissue	6	13.64
Total	44	100.00

ImmunohistoChemistry Results

16 cases had been used to do the immunohistochemistry. Within the patient of adenocarcinoma, TTF-1, CK7 and NapsinA had positive rate of 57.14%, 57.14% and 21.43%, respectively. By contrast, the positive rate of squamous cell carcinoma patient was 0%, 20% and 0%. For the squamous cell carcinoma patients, the positive rate of CK5/6, P40 and P63 was 20%, 60% and 20%, respectively. Those values were 7.14%, 0% and 14.29% in adenocarcinoma (Table.3).

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Table.3 The expression differences of various immunohistochemical related antibodies

Group	Squamous cell carcinoma			Adenocarcinoma		
	+	-	The positive rate %	+	-	The positive rate %
TTF-1	0	2	0	8	3	57.14
CK7	1	0	20	8	0	57.14
NapsinA	0	0	0	3	2	21.43
CK5/6	1	0	20	1	3	7.14
P40	3	0	60	0	4	0.00
P63	1	0	20	2	4	14.29

The Results of Tumor Marker

Comparison of positive rate of tumor markers between non-malignant group and lung cancer group

Compare the result of CEA from patients, the lung cancer group had 16 positive cases while the non-malignant group had 2 positive cases with P=0.076 so that these groups were not statistically significant. However, the NSE result showed that lung cancer group had 16 positive cases while the non-malignant group all showed negative result with P=0.003. CYFRA21-1 tests showed 26 confirmed positive cases in lung group and 3 cases in non-malignant group with P=0.001. The united tests by three tumor markers showed 27 positive cases in lung group and 4 cases in non-malignant group with P=0.004; The unique and united tests showed difference in statistic. The CYFRA21-1 and NSE tests showed high efficiency. The Chi square test of united tests got P=0.004, which showed less advantages (Table.4).

Table.4 Positive rate of tumor markers and chi square test

Category	Non-malignant tumor	Lung cancer	$\chi 2$	P
Quantity	11	33		
CEA(case, %)	2(18.18)	16(48.48)	3.13	0.076
NSE(case, %)	0(0)	16(48.48)	8.38	0.003
CYFRA21-1(case, %)	3(27.27)	26(78.78)	9.74	0.001
The co-detection of three index(case, %)	4(36.36)	27(81.81)	8.18	0.004

Specificity and sensitivity of tumor markers in the diagnosis of lung cancer

The above discussed tumor marker united tests showed sensitivity for 81.8%. In the unique test, the sensitivity of CEA, NSE and CYFRA21-1 was 48%, 48% and 79%, respectively. The sensitivity of united tests was higher than the unique test. However, the specificity value of united tests was 63.3%, relatively lower than the unique tests. (Table.5)

Table.5 Specificity and sensitivity of tumor markers

Index	Non-malignant tumor (11 cases)	Lung cancer(33 cases)	Sensitivity(%)	Specificity(%)
CEA(+/-)	2/9	16/17	0.48	0.82
NSE(+/-)	0/11	16/17	0.48	1.00
CYFRA21-1 (+/-)	3/8	26/7	0.79	0.73
The co-detection of three index (+/-)	4/7	27/6	0.818	0.636

The ROC curves of tumor markers during lung cancer diagnose

The AUC of the tumor markers test was CEA (0.799), NSE (0.851), CYFRA21-1(0.832), united tests (0.875), the AUC values from united tests were higher than the unique tests, indicated that the united tests showed higher efficiency to diagnose the lung cancer. (Table.6)

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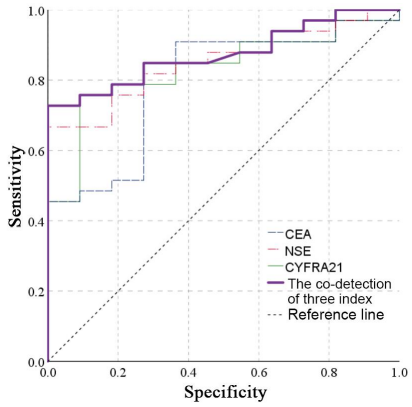

Fig.1 The ROC curve of tumor markers

Table.6 AUC of tumor markers

Item	AUC	95% confidence interval
CEA	0.799	0.652~0.945
NSE	0.851	0.74~0.962
CYFRA21	0.832	0.707~0.956
The co-detection of three index	0.875	0.774~0.975

The comparison of tumor markers between different types of pathological of lung cancer patients

The positive rate showed difference from three tumor markers. CYFRA21-1 value differences were meaningful in statistic (P=0.038). The positive rate difference between CEA and NSE was not valid (P>0.05), neither for the test results from three united tests of different types of lung cancer (P>0.05). (Table.7)

Table.7 The comparison of positive rates

Category		Cases	CEA		NSE		CYFRA21-1		Co-detection of three index	
			Positive rate (Cases, %)	χ2 (P)	Positive rate (Cases, %)	χ2 (P)	Positive rate (Cases, %)	χ2 (P)	Positive rate (Cases, %)	χ2 (P)
Gender	male	23	12(52.17)	0.01 (0.91)	12(52.17)	0.01 (0.91)	6(26.08)	1.07 (0.30)	5(21.73)	0.64 (0.42)
	female	10	5(50)		5(50)		1(10)		1(10)	
Type	Adenocarcinoma	23	13(56.52)	4.36 (0.22)	10(43.47)	2.36 (0.5)	20(86.95)	8.41 (0.04)	20(86.95)	3.69 (0.30)
	Squamous cell carcinoma	4	2(50)		2(50)		3(75)		3(75)	
	Small cell lung cancer	2	1(50)		2(100)		2(100)		2(100)	
	Other	4	0(0)		2(50)		1(25)		2(50)	

4. DISCUSSION

The pulmonary space-occupying lesion had become a common phenomenon in clinical diagnose, which could be induced by several reason, including lung cancer, tuberculosis, lung abscess, inflammatory pseudotumor and sarcoidosis, etc. When the imaging suggested malignant lesions, one should confirm the pathology of the pulmonary space-occupying lesion as early as possible. In clinical, widely used methods to diagnose the diseases including surgery, bronchoscope and percutaneous biopsy, etc. Percutaneous biopsy was a safety and high efficient minimally invasive method, which was super important for diagnosing the lung disease[5,6]. percutaneous biopsy showed the advantages of high accuracy and resolution, which had been widely used in clinical could determine the actuate position of intrapulmonary lesions, easy to operation with high safety level and less complications. In the research, 44 cases were successfully punctured with definite diagnosis, match well with the data from previous reports by using CT-guided percutaneous lung biopsy[7-9]. The specimen diagnose rate of puncture biopsy was 100%, which was related to the maturity of puncture technology and the limited number of cases included in this study.

CT-guided percutaneous lung biopsy had a small needle with relative small amount of disease tissue and easily to be destroyed by compression. The tissue morphology of lung cancer cannot be determined by optical microscopy, the immunohistochemistry was super important to the disease diagnose. TTF-1 is also named thyroid transcription factor-1, which was in the family of nuclear transcription factor NKX2, mainly expressed in alveolar epithelial cells and thyroid follicular epithelial cells, which had close relationship with lung cancer and thyroid carcinoma[10]. CK7 mainly expressed in epithelial cells, in our study, the positive rate of TTF-1 and CK7 was 57.14% and 57.14%, respectively. In adenocarcinoma group, which could be used to identify

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the adenocarcinoma and other types of lung cancer. The positive rate was 60% of squamous cell carcinoma group (P40). P40 was one specific type of P63 protein, Enhanced expression in squamous cell carcinoma[11], which was important to diagnose of squamous cell carcinoma[12].

Tumor markers has been widely used in clinical for the applications of tumour diagnose, assessment of treatment and optimization. It is a safety, high efficiency and economic method. In this study, the unique tumour markers tests showed high efficiency on lung cancer diagnose. We performed chi square test on the test results of CYFRA21-1, P = 0.001, and the NSE test result P=0.003, which were ideal tests. However, in united tests, the chi square test result was P=0.004, which did not show significant advantages. CEA is called Carcinoembryonic antigen, which can be demonstrate in several different types of Malignant tumor. NSE is mainly secreted by neurogenic and neuroendocrine cells, and its expression is usually elevated in small cell lung cancer. CYFRA21-1 mainly distribute in Monolayer epithelial cell. When the tumor cell is degradation, a large amount of cell protein 19 Soluble fragment can be tested in the blood. In this study, the positive rate of CEA, NSE and CYFRA21-1 of lung cancer group were higher than the non-malignant tumor group from both unique and united tests. The positive rate of CEA in Adenocarcinoma group was higher than the Squamous cell carcinoma group and Small cell lung cancer group but the difference was not statistically different, which was similar to one previous report[13]. The positive rate of NSE in Small cell lung cancer group was larger than any other types of lung cancer, the difference was not statistically different. The tumor marker united tests showed a AUC of 0.875, sensitivity of 81.8%, higher than the unique tests, match well with one previous report[14]. The tumor marker test could increase the efficiency of lung cancer diagnose, which could act as an important method to confirm the lung cancer in early stage. Literature data showed that tumor marker united tests could increase the efficiency to confirm different types of lung cancer[15]. However, this study could not evaluate the diagnostic efficacy in different pathological types of lung cancer.

In summary, this study demonstrated that the CT-guided percutaneous lung biopsy was beneficial to detect and later treatment of lung cancer. The results of the tumor marker NSE and CYFRA21-1 unique tests were ideal, better than the co-detection of three index. The researchers suggested to give priority to the test of NSE and CYFRA21-1 in the follow-up diagnosis and treatment. However, the number of cases in this study was limited and there were some limitations. At present, it is impossible to evaluate the diagnostic efficacy of tumor markers in different pathological types of lung cancer.

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