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*Original Research*

# Exploration and analysis of the value of tumor-marker joint detection in the pathological type of lung cancer

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**Abstract:** Lung cancer is a disease characterized by the uncontrolled growth of cells in lung tissue. If left untreated, cell growth can spread beyond the lungs to a process called metastasis and reach surrounding tissues or other organs. This experiment was set up to discuss and analyze the research value of joint detection of tumor markers including carcino-embryonic antigen (CEA), cytokeratin 19 fragments (CYFRA21-1) and neuron-specific enolase (NSE) in the diagnosis and pathological type of lung cancer. From November 2016 to February 2018, 378 cases of patients with lung cancer treated in our hospital and 200 cases of people with healthy physical examinations were collected. The electrochemical immunoluminescence method was adopted to detect the CEA, CYFRA21-1 and NSE. The detected positive rate and the concentration of CEA, CYFRA21-1 and NSE of lung cancer group were higher than that of the healthy physical examination group. The differences were of statistical significance *(P<0.05)*; the detected positive rate of CEA and CYFRA21-1 and the concentration of CEA, CYFRA21-1 and NSE of squamous carcinoma group were higher than that of the adenocarcinoma group. The differences were of statistical significance *(P<0.05)*. The CEA, CYFRA21-1 and NSE are related to the pathological type of lung cancer and can be regarded as related indicators to diagnose lung cancer.

***Key words:*** Tumor marker; Carcino-embryonic antigen; Cytokeratin 19 fragments; Neuron-specific enolase.

## Introduction

Lung cancer is one of the most common malignant tumors and its morbidity is gradually on the rise in recent years. Worldwide, this type of cancer is the most common cause of cancer mortality among men and women. Most lung cancers, called primary lung cancers, are carcinomas that originate in the lining tissue. The main types of lung cancer are small-cell lung cancer (SCLC), also known as atmospheric cellular cancer, and non-small cell lung cancer (NSCLC). The most common symptoms are cough (with bloody sputum), weight loss and shortness of breath (1, 2). Early diagnosis and early treatment are important means to treat lung cancer. Common treatments include surgery, chemotherapy, and radiation therapy. Sometimes NSCLC can be treated with surgery, but SCLC usually responds better to chemotherapy and radiation therapy. Symptoms and signs that may indicate lung cancer include respiratory symptoms (cough, bloody sputum, wheezing or shortness of breath), systemic symptoms (weight loss, fever, clubfoot, or weakness) and symptoms of localized pressure (chest pain, bone pain, obstruction of the superior vena cava, difficulty swallowing). If cancer grows on the airway, it may block the flow of air, making it difficult to breathe. This can lead to the accumulation of secretions behind the blockage and will be prone to pneumonia. (2, 3). In addition to the inefficient diagnosis of lung cancer at an early stage, the traditional diagnostic method cannot be widely promoted because of its high cost. As a result, tumor markers play a significant role in the prediction of disease and are widely used in clinical practice. Yet there are various kinds of tumor markers and quantitative indexes are insufficient, resulting in the difficult promotion of clinical application (4, 5). In addition, as the therapeutic schedules for lung cancer of different pathological types are different, early diagnosis of lung cancer is the key to the treatment and prognosis. The detection of a tumor marker can provide an important diagnostic reference value for patients with lung cancer (6,7), but due to relatively low sensitivity and accuracy of single tumor marker, combined detection of multiple tumor markers is adopted clinically to diagnose patients with lung cancer. Rational selection of tumor marker for joint detection can effectively improve the detectable rate of lung cancer, providing a laboratory basis for early clinical diagnosis and treatment. Three tumor markers, carcino-embryonic antigen (CEA), cytokeratin 19 fragments antigen (CYFRA21-1) and neuron-specific enolase (NSE), were selected by the researcher to detect patients with lung cancer and healthy subjects, so as to explore their values in the diagnosis and pathological type of lung cancer.

## Materials and Methods

### General materials

From November 2016 to February 2018, 378 patients with lung cancer including 271 males and 107 females, aged 29 to 91 with a mean age of (60.5±9.9), were confirmed by pathological diagnosis in our hospital and were selected as lung cancer group. There were 313 cases of non-small cell lung cancer including 134 cases of squamous carcinoma, 170 cases of adenocarcinoma, 4 cases of large cell lung carcinoma, 5 cases of adenosquamous carcinoma and 65 cases of small cell lung cancer. A total of 200 healthy subjects in the same period, including 136 males and 64 females, aged 28 to 80 years with an average age of (58.0±13.2), were selected as a healthy control group. The general information such as age, gender, etc. of these two research objects was compared, and the differences showed no statistical significance *(P>0.05)*.

### Instrument and reagent

ADVIA Centaur XP type full-automatic chemiluminescent analyzer and special mating kit of Siemens AG (Germany) were adopted to detect serum CEA. Architect i-2000 type full-automatic chemiluminescent analyzer and special mating kit of Abbott Laboratories (The United States) were used to detect serum CYFRA21-1. MAGLUMI4000 type full-automatic chemiluminescent analyzer and special mating kit of New Industries Biomedical Engineering Co., Ltd. (China) were applied to detect serum NSE. All operations were strictly performed according to the instrument and reagent instructions.

### Methods

All the patients and healthy subjects were extracted 5ml of venous blood under a fasting state in the morning, and the serums were separated after high-speed centrifugation. The electrochemical immunoluminescence method was adopted to detect the conditions of carcino-embryonic antigen (CEA), cytokeratin 19 fragments (CYFRA21-1) and neuron-specific enolase (NSE). All operations were strictly subject to the instruction. Determination criterion of normal value: CEA: 0~5ng /mL, CYFRA21-1: 0.1~3.3 ng/mL and NSE: 0~25 ng/mL. The detection value would be positive when it exceeded the normal value.

### Statistical methods

All collected data were recorded into the database, and SPSS 17.0 statistical software was adopted to process data. The enumeration data were expressed as [n (%)], and tested by chi-square ($\chi^2$). The measuring data was described by ($\chi$±s) and tested by the t-test. If *P<0.05*, the difference was of statistical significance.

## Results

### Comparison of the detected positive rate of tumor markers

The detected positive rate of CEA, CYFRA21-1 and NSE of lung cancer group was higher than that of a healthy subject group. The difference was of statistical significance *(P*<0.05, Table 1).

### Comparison of the detection result of 3 tumor markers in patients with a different histologic type of lung cancer

For different pathological types of lung cancer, the levels of tumor markers were different. The CYFRA21-1 level was the highest one in patients with squamous carcinoma and was markedly higher than that in patients with adenocarcinoma and small cell lung cancer. The difference was of statistical significance *(P<0.05)*; the CEA level was the highest one in patients with adenocarcinoma, and was apparently higher than that in patients with squamous carcinoma and small cell lung cancer. The difference was of statistical significance *(P<0.05)*; the NSE level was the highest in patients with small-cell lung cancer and was evidently higher than that in patients with squamous carcinoma and adenocarcinoma. The difference was of statistical significance *(P*<0.05, Table 2).

### Comparison of the positive rate of 3 tumor markers in patients with a different histologic type of lung cancer

The positive rates of CYFRA21-1 in patients with squamous carcinoma were relatively high (90.30%), and were all markedly higher than that in patients with adenocarcinoma and small cell lung cancer. The difference was of statistical significance *(P<0.05)*; the positive rate of CYFRA21-1 in patients with adenocarcinoma was relatively high (74.71%), followed by CEA

**Table 1.** Comparison of the detected positive rate of tumor marker [n (%)].

| Group | Cases | CEA | CYFRA21-1 | NSE |
|---|---|---|---|---|
| Lung Cancer | 378 | 167 (44.2) | 189 (50.0) | 174 (46.0) |
| Healthy Control | 200 | 6 (3.3) | 0 | 0 |
| $\chi^2$ Value | - | 46.186 | 66.667 | 60.078 |
| P Value | - | 0.000 | 0.000 | 0.000 |

**Table 2.** Comparison of the detection result of 3 tumor markers in patients with different histologic type of lung cancer [M (P25, P75)].

| Histologic Type | n | CEA (ng/mL) | CYFRA21-1 (ng/mL) | NSE (ng/mL) |
|---|---|---|---|---|
| Squamous Carcinoma | 134 | 3.35 (1.79,7.68) | 7.40 (3.21,25.74) | 6.06 (4.51,8.90) |
| Adenocarcinoma | 170 | 9.64 (2.75,9.42)* | 3.84 (2.05,8.76) * | 5.30 (4.05,7.53)* |
| Small Cell Lung Cancer | 65 | 2.99 (1.53,5.90) # | 2.81 (1.90,4.29)*# | 18.37 (10.14,31.98)*# |

Remark: Compared with squamous carcinoma, *P<0.05; Compared with adenocarcinoma, #P<0.05.

**Table 3.** Comparison of the positive rate of 3 tumor markers in patients with different histologic type of lung cancer [n (%)].

| Histologic type | n | CEA (ng/mL) | CYFRA21-1 (ng/mL) | NSE (ng/mL) |
|---|---|---|---|---|
| Squamous Carcinoma | 134 | 49(36.57) | 121(90.30) | 24(17.91) |
| Adenocarcinoma | 170 | 95(55.88)* | 127(74.71)* | 24(14.12) |
| Small Cell Lung Cancer | 65 | 20(30.77)# | 43(66.15)* | 50(76.92)*# |

Remark: Compared with squamous carcinoma, *P<0.05; Compared with adenocarcinoma, #P<0.05.

(55.88%), and the positive rate of CEA was higher than that in patients with squamous carcinoma and small cell lung cancer. The difference was statistically significant *(P<0.05)*; the positive rate of NSE in patients with small-cell lung cancer were relatively high (76.92%), and was apparently higher than that in patients with squamous carcinoma and adenocarcinoma. The difference was of statistical significance *(P*<0.05, Table 3).

## Discussion

Over recent years, the incidence of lung cancer in China has ranked first place among all malignant tumors and presented an escalating trend year after year. Most lung cancers in the early phase can be cured, with more than 90% of the cure rate. However, there is still short of effective early diagnostic methods. Most patients with lung cancer are diagnosed at an advanced stage, missing the optimal treatment time (8, 9). The development of research on tumor markers in recent years has provided a new thought for the early diagnosis of lung cancer. A tumor marker is of great significance to the auxiliary diagnosis, the monitoring of the curative effect and the prognosis of tumors (10, 11). However, as a single tumor marker is relatively low in sensitivity and accuracy, combined detection of tumor markers is often used in the auxiliary diagnosis of cancer so as to improve the detection rate of tumors clinically. In this research, the joint detection of CEA, CYFRA21-1 and NSE, three tumor markers, was employed to discuss the clinical value of joint detection in the diagnosis and pathological type of lung cancer.

CEA is an acid glycoprotein. Research has revealed that CEA is expressed in various cancer tissues and is of important significance in the replication and metastasis of cancer cells. As one of the widely used tumor markers to diagnose lung cancer, CEA can be also used to monitor the curative effect of lung cancer treatment (12-15). Due to the non-specificity of the index, it is often jointly applied with other tumor markers in the clinical practice. Most CYFRA21-1 exists in the epithelial cell but the content is low in the healthy people and high in cancer cells. Therefore, CYFRA21-1 is a tumor marker with the high sensibility to non-small cell lung cancer, especially squamous carcinoma (16-19). When the cancer cells are apoptotic, protease will decompose protein into many fragments, and one of the fragments is CYFRA21-1, which enters into blood along with the rupture of cytomembrane (20,21). NSE is neuron-specific enolase existing in the nerve cells and neurogenic cells. It can be used as a marker of neuroblastoma and small-cell lung cancer. However, red blood cells and platelet contain NES, which will easily lead to false-positive after hemolysis. Hence, hemolysis specimens are excluded from this experiment (22,23).

In this research, the detected positive rate of CEA, CYFRA21-1 and NSE of lung cancer group was higher than that of the healthy control group *(P<0.05)*, suggesting that CEA, CYFRA21-1 and NSE were highly expressed in the patients with lung cancer. This conclusion was in accord with the previous report (24). The detected positive rate of CEA and CYFRA21-1 of the squamous carcinoma group was higher than that of the adenocarcinoma group *(P*<0.05). The detected positive rate of NSE of the squamous carcinoma group was lower than that of the adenocarcinoma group *(P<0.05)*. The concentration of CEA, CYFRA21-1 and NSE in squamous carcinoma group was higher than that of the adenocarcinoma group *(P*<0.05). The detected positive rate of squamous carcinoma group was lower than that of the adenocarcinoma group, while the concentration of CEA, CYFRA21-1 and NSE was higher than that of the adenocarcinoma group. It was evident from the result that the expression of tumor markers is different in lung cancer with different pathological types. CEA was highly sensitive to adenocarcinoma, which was 55.88%; the CYFRA21-1 was highly sensitive to squamous carcinoma, which was 90.30%; the NSE was highly sensitive to small cell lung cancer, which was 76.92%. It is suggested that the tumor marker has a certain value for the differential diagnosis of lung cancer of different histologic types. For the situation where squamous carcinoma is slow in proliferation but quick in metastasis, while adenocarcinoma is quick in proliferation but slow in metastasis, it is because the detected positive rate is related to the development course of cancer. The higher the positive rate detected, the quicker cancer proliferates. The higher the concentration of CEA, CYFRA21-1 and NSE, the more unstable the cancer conditions are, and the faster the metastasis is. This conclusion is consistent with the previous report (25).

Many studies have been done on cancer and the effects of genetic and non-genetic factors have been investigated (26-33). They have also looked at several diagnostic methods (34-40). In this experiment, we investigated the value of tumor-marker joint detection in the pathological type of lung cancer.

In conclusion, CEA, CYFRA21-1 and NSE are related to the pathological type of lung cancer and can be used as relevant indicators for the diagnosis of lung cancer. As a result, the monitoring of markers can be adopted to diagnose the conditions of lung cancer to some extent.

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