

Progress in Serological Markers in Lung Cancer TCM Syndrome Types and Efficacy Evaluation of Chinese Medicine

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Abstract: Lung cancer is the most common lung malignancy, and is the highest incidence rate and mortality rate in cancer. The detection of serum tumor markers or combined detection has a certain reference value for the diagnosis and condition monitoring of lung cancer, and the expression of tumor markers has a certain relationship with TCM syndrome differentiation. Therefore, this paper mainly reviews the etiology and pathogenesis of lung cancer, TCM syndrome types, the correlation between serum markers and TCM syndrome types of lung cancer, and whether serum tumor markers can be used as an evaluation index in the treatment of lung cancer with integrated traditional Chinese and Western medicine.

1. Introduction

2020 global cancer statistics report shows that lung cancer is still the leading cause of death among all cancers. It is estimated that 1.8 million people died of lung cancer, accounting for 18% of all cancer deaths ^[1]. Gender incidence rate incidence rate is higher incidence of male than female ^[2], the main reason of male cancer incidence and mortality is lung cancer, and in women, it is the only third place in breast cancer and colorectal cancer, the incidence rate is only second, and the incidence rate is only second times ^[3]. At present, lung cancer has seriously threatened the life safety of human. Therefore, early diagnosis of lung cancer and improving the prognosis of lung cancer patients are particularly important.

2. Overview of lung cancer

Lung cancer, or primary bronchial cancer or primary bronchial lung cancer, is defined by the World Health Organization (who) as a malignant tumor originating from respiratory epithelial cells (bronchus, bronchioles and alveoli). The clinical symptoms were mostly hidden, with cough, expectoration, hemoptysis and weight loss as the main manifestations. X-ray imaging mainly showed pulmonary nodules and mass shadow. According to anatomical location Lung cancer can be divided

into central lung cancer and peripheral lung cancer; lung cancer can be divided into two categories according to histopathology: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Among them, non-small cell lung cancer is the most common cancer, accounting for about 85%^[4] of lung cancer incidence rate. The etiology of lung cancer is complex. Until now, the etiology of lung cancer has not been fully clarified. Studies have shown that the occurrence of lung cancer is closely related to the causes of long-term massive smoking in patients with lung cancer. The probability of lung cancer in patients with long-term massive smoking history is 10 to 20 times higher than that in patients without smoking history. The longer the smoking age, the greater the probability of lung cancer^[5]. Patients with lung cancer have no typical clinical features in the early stage of lung cancer, and lack of effective early diagnosis methods. Most patients are in the late stage of onset after diagnosis, and most patients are prone to organ metastasis, such as lymph nodes. The effect of surgical treatment is not good and the prognosis is poor. Therefore, effective early diagnosis is of great significance for the diagnosis and prognosis of patients^[6].

3. TCM understanding of lung cancer

3.1 Different views of TCM on TCM syndrome differentiation of lung cancer

The textbook of internal medicine of traditional Chinese medicine divides the TCM syndrome types of lung cancer into four types: blood stasis blocking the lung collaterals, phlegm dampness accumulating the lung, yin deficiency, toxin and heat, and Qi yin deficiency. For the TCM syndrome type of lung cancer, many famous contemporary TCM scholars have discussed it. From the perspective of cancer toxin theory, Zhou Zhongying^[7], a master of Chinese medicine, divided the TCM syndrome types of lung cancer into five types: phlegm turbidity blocking lung syndrome, cancer toxin blocking lung syndrome, Qi and yin deficiency syndrome, qi stagnation and blood stasis syndrome, spleen and stomach weakness syndrome. Professor Liu Jiayang^[8] Based on his rich clinical experience for many years, taking the syndrome differentiation of Qi and blood as the meridian and the syndrome differentiation of viscera as the latitude, and according to the clinical manifestations of lung cancer, he can be divided into four types: Yin deficiency and internal heat, spleen deficiency and phlegm dampness (lung and spleen qi deficiency), Qi and yin deficiency and Yin and yang deficiency. Professor Lin Hongsheng^[9] divided advanced lung cancer into four basic syndrome types according to the authoritative bibliography and combined with many years of clinical observation and treatment experience since: Qi and yin deficiency syndrome, spleen deficiency and phlegm dampness syndrome, yin deficiency and internal heat syndrome, Qi stagnation and blood stasis syndrome. Professor Gu mingsan^[10] divided the TCM syndrome differentiation of lung cancer into four types: lung yin deficiency type, lung dryness and collateral injury type, phlegm heat Yongsheng type and lung spleen deficiency type. Professor Chen Ruishen^[11] often divides lung cancer into four types: lung depression and phlegm stasis type, spleen deficiency and phlegm dampness type, yin deficiency and phlegm heat type, Qi and yin deficiency type. Professor Zhang Daizhao^[12] believes that the syndrome differentiation of lung cancer patients can be divided into the following five types: Yin deficiency and internal heat, spleen deficiency and phlegm dampness, qi stagnation and blood stasis, Qi and yin deficiency, lung and kidney deficiency, and points out that most of them are Qi and yin deficiency. Mako^[13] and others analyzed the collected clinical flow regulation data of 310 patients with primary bronchial lung cancer, and divided the TCM syndrome types of primary bronchial lung cancer into five types: phlegm dampness accumulating lung type, Qi and blood deficiency type, lung yin deficiency type, kidney yang deficiency type and lung spleen Qi deficiency. According to the pre-designed observation table and clinical syndrome diagnosis criteria, Wu Wanyin^[14] and others adopted a retrospective research method to statistically analyze 207 patients with advanced non-small cell lung cancer collected in, and obtained the types of qi deficiency

and phlegm dampness, Qi and yin deficiency and blood stasis And yin deficiency toxin heat syndrome. The distribution of each syndrome is as follows: Qi deficiency and phlegm dampness syndrome is the most, accounting for 76.3%; The second is deficiency of Qi and Yin, accounting for 9.2% of; The proportion of qi stagnation and blood stasis type and yin deficiency and toxin heat type was 5.8%; The feverish heat toxin type has the least distribution, accounting for 2.9%. Therefore, it is concluded that Qi deficiency and phlegm dampness type is the main TCM syndrome type in patients with advanced non-small cell lung cancer (stage IIIB and IV). Zhang Mingping^[15] investigated the TCM Syndromes of 68 patients with NSCLC diagnosed clinically. After analyzing their different histopathological types, clinical stages and the distribution of TCM syndromes before and after chemotherapy, he came to the conclusion: Qi deficiency syndrome, Qi Yin deficiency syndrome, qi stagnation and blood stasis syndrome, yin deficiency and phlegm heat syndrome Qi deficiency and phlegm dampness syndrome are the most common TCM syndromes in patients with advanced non-small cell lung cancer. Han Dan^[16] and others selected 861 patients with complete clinical data from a total of 920 patients with primary non-small cell lung cancer. After using the questionnaire, they focused on the questionnaire according to the unified dialectical standard. After processing data, statistics and analysis, they obtained five TCM Syndrome Types of lung cancer: spleen qi deficiency syndrome, lung yin deficiency syndrome, lung qi deficiency syndrome, dampness trapped spleen and stomach syndrome The proportion of phlegm dampness obstruction of lung syndrome is spleen qi deficiency syndrome, accounting for 55.05%, and the other four types account for 44.72%, 32.40%, 20.67% and 10.10% respectively.

To sum up, Qi and yin deficiency syndrome is the most common in TCM dialectical classification of lung cancer.

3.1.1 Etiology and pathogenesis

There is no record of "bronchial lung cancer" in traditional Chinese medicine. According to its symptom characteristics, it belongs to the category of "lung accumulation" and "asthma syndrome" in traditional Chinese medicine. However the understanding and discussion of etiology and pathogenesis of lung cancer by famous traditional Chinese medicine experts are different. Professor Chao Enxiang^[17], a master of traditional Chinese medicine, combined with his more than years of clinical practice experience, believes that positive deficiency and evil excess are the pathogenesis of lung cancer, the pathological basis and inevitable result of the occurrence and development of lung cancer, and run through the whole course of lung cancer, which is the foundation of the occurrence and development of lung cancer. Professor Zhou daihan^[18] believes that lung cancer is similar to "lung accumulation", "lung carbuncle" "hemoptysis" and other diseases in traditional Chinese medicine. The onset site is in the lung, which is closely related to the spleen and kidney. Its onset lies in the mutual cementation of phlegm, blood stasis, toxin and deficiency. The etiology and pathogenesis are mostly the deficiency of positive Qi, the internal invasion of evil toxin and the cementation of phlegm and blood stasis. Professor Zhang Daizhao^[12] believes that the etiology of lung cancer mainly lies in the deficiency of positive Qi, which runs through the whole course of lung cancer, especially in patients in the middle and late stage of lung cancer. Professor Zhang pointed out that lung cancer is a disease of standard reality and deficiency, in fact, it mostly shows phlegm coagulation, blood stasis, qi stagnation and toxin knot. Deficiency mostly shows the deficiency of both yin and Yang and the deficiency of both qi and blood. Professor Liu Weisheng^[20] pointed out that the key to the pathogenesis of tumor is the lack of healthy qi, and cancer toxin is the direct factor leading to the occurrence of lung cancer. Lung cancer is a kind of disease with deficiency of the whole body and local truth. The deficiency lies in the weakness of viscera function and deficiency of yin and Yang and Qi and blood; The existing mass (or residual cancer cells) and tangible excess evil such as infiltration and compression are standard excess, so the deficiency and excess is the basic pathological basis of the tumor, and the most common pathological changes of lung cancer are

"phlegm", "deficiency" "blood stasis" and "poison". Xu Li ^[21] Professor believes that the lack of healthy qi, exogenous evil Qi, eating habits, emotional disorders and improper work and leisure are the main causes of lung cancer. The basic pathological basis is the deficiency of Qi and Yin, the intersection of heat toxin, phlegm turbidity and blood stasis. For a long time, there is cancer toxin in the body and lung mass, leads to lung cancer. Lung cancer is always based on deficiency and marked by excess, which leads to excess, causes disease from excess, and is mixed with deficiency and excess. In the early stage of the disease, the evil Qi is abundant and the healthy qi is not empty, which is mainly based on the standard reality, it has long been an image of the inclusion of this deficiency. The disease is located in the lung, mainly involving the spleen and kidney. To sum up, in the etiology and pathogenesis of lung cancer, the premise of onset is "deficiency". In the early stage, it is mainly deficiency of positive Qi, and in the middle and late stage, it is mostly mixed with deficiency and excess, which reflects the guiding ideology of "positive Qi exists in the body, and evil can not be dried" in traditional Chinese medicine ^[22].

4. Correlation between serum tumor markers and TCM syndrome types

Tissue biopsy is recognized as the gold standard for the diagnosis of lung cancer, but it is limited due to its traumatic nature. Tumor markers refer to the substances that exist specifically in malignant tumor cells or have abnormal production of malignant tumor cells, which reflect the occurrence and development of tumors. In recent years, with the deepening of molecular biology and cellular immunology research, the detection of serum tumor markers has been widely used in the early screening of lung cancer because of its advantages of simple operation, low price and no adverse reaction. At present, there are mainly cytokeratin 19 fragment (CYFRA21-1), carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), gastrin releasing peptide precursor (ProGRP) and squamous cell carcinoma associated antigen (SCC Ag).

Many scholars have had a profound discussion on the relationship between tumor marker and TCM dialectics of lung cancer. Wang Lei ^[23] adopted SPSS13.0 statistical software. The expression levels of five tumor markers: cytokeratin 19 fragment (CYFRA21-1), carcinoembryonic antigen (CEA), carbohydrate antigen 125 (CA125), gastrin releasing peptide precursor (ProGRP) and squamous cell carcinoma associated anti antigen (SCC Ag) in 196 patients with bronchial lung cancer were analyzed by nonparametric test. The results showed that the level of spleen qi deficiency syndrome in patients with lung cancer was higher than that in patients with lung cancer; there was no significant difference between CEA, CA125, ProGRP and SCC Ag levels. CYFRA21-1 is a specific index of non-small cell lung cancer. Dai Sui ^[24] compared four different TCM syndrome types (Qi deficiency and phlegm dampness type The serum levels of carcinoembryonic antigen, cytokeratin 19 fragment and squamous cell antigen of yin deficiency phlegm heat type, lung depression phlegm stasis type and Qi Yin deficiency type) were found: carcinoembryonic antigen, cytokeratin 19 fragment and squamous cell carcinoma antigen have important clinical application value for the early diagnosis of lung cancer and TCM Syndrome differentiation of non-small cell lung cancer. The expression level of carcinoembryonic antigen was different among four different TCM syndrome differentiation types of small cell lung cancer. The serum expression level was significantly increased in Yin deficiency phlegm heat type and Qi Yin deficiency type; Cytokeratin 19 fragment and squamous cell carcinoma antigen increased significantly in Qi deficiency and phlegm dampness type and lung depression and phlegm stasis type, and there was significant difference in expression level compared with Yin deficiency and phlegm heat type and Qi and yin deficiency type. Li Hanmin ^[25] et al. Used multiple tumor markers protein chip monitoring system to measure the serum levels of 12 tumor markers such as CA19-9, NSE and CEA in 32 patients with primary lung cancer including four different TCM syndrome types. The results are as follows: the concentrations of CEA, CA19-9 and

CA242 in Qi and blood stasis type, phlegm dampness accumulation lung type and heat toxin excess type are significantly higher than those in Qi and yin deficiency type, But there was no significant difference among the three types of blood stasis, phlegm dampness accumulation in the lung and excessive heat toxin; The concentration of CA125 in phlegm dampness accumulating lung type, Qi and blood stasis type and deficiency of Qi and Yin type was significantly higher than that in hot toxin type. Therefore, it is concluded that the expression level of multiple tumor markers in patients with lung cancer is closely related to the syndrome type of traditional Chinese medicine, which can be used as one of the important indicators of Micro syndrome differentiation. Lv Dan^[26] analyzed the results of four lung cancer tumor markers CYFRA21-1, CEA, CA12-5 and NSE of 342 subjects (including 242 patients in the lung cancer group, 50 patients in the benign lung group and 50 healthy controls), After observing the expression level changes of four tumor markers in different TCM syndrome differentiation types (deficiency of Qi and Yin, deficiency of yin and toxin heat, phlegm blocking lung collaterals and phlegm dampness accumulating lung), it is found that the level of four tumor markers in lung cancer patients is significantly higher than that in the normal group, and there are significant differences in the expression levels of the first three tumor markers in different TCM syndrome types. Therefore, it is concluded that CYFRA21-1 The detection results of CEA, CA12-5 and NSE can be used as reference indexes for early screening, clinical efficacy and prognosis evaluation of patients with lung cancer, and the levels of CYFRA21-1, CA12-5 and CEA have a certain correlation with TCM syndrome differentiation, which can be used as an auxiliary basis for TCM syndrome differentiation of lung cancer. Fu Yanli^[27] analyzed the correlation between the distribution of TCM Syndrome Types and tumor markers in 388 patients with lung cancer according to five main syndrome types (lung yin deficiency syndrome, lung qi deficiency syndrome, spleen qi deficiency syndrome, blood stasis blocking lung collaterals syndrome and lung yin deficiency and fire excess syndrome). The results showed that: in the abnormal expression of CEA, the proportion of lung yin deficiency and fire excess syndrome was significantly higher than that of lung yin deficiency and fire excess syndrome Lung qi deficiency syndrome and blood stasis blocking lung collaterals syndrome; The proportion of spleen qi deficiency syndrome was significantly higher than that of lung yin deficiency syndrome and blood stasis blocking lung collaterals syndrome. In the abnormal expression of NSE, the proportion of elevated in lung yin deficiency and fire hyperactivity syndrome was significantly higher than that in lung qi deficiency syndrome, spleen qi deficiency syndrome and lung yin deficiency syndrome; The increase of blood stasis blocking pulmonary collaterals syndrome was significantly higher than that of lung qi deficiency syndrome. CYFRA21-1 In lung yin deficiency, the proportion of abnormal increase of fire excess syndrome and blood stasis blocking lung collaterals syndrome was significantly higher than that of lung qi deficiency syndrome. Therefore, the abnormal increase of tumor markers CEA, NSE and CYFRA21-1 has a certain correlation with different TCM syndrome types.

5. Serological markers can be used as one of the evaluation indexes of integrated traditional Chinese and Western medicine in the treatment of lung cancer

In the process of integrated traditional Chinese and Western medicine in the treatment of lung cancer, whether the content change of serum tumor markers can be used as one of the evaluation indexes of clinical efficacy, many experiments have studied this problem. Shan Kuizhong^[28] randomly divided 94 patients with advanced non-small cell lung cancer into observation group (treated with integrated traditional Chinese and Western Medicine) and control group (treated with GP chemotherapy only). After three courses (one course every 21 days), the serum tumor markers carcinoembryonic antigen (CEA) and Changes of carbohydrate antigen 199 (CA199) and nerve specific enolase (NSE). The results showed that there was no significant difference in the level of

serum tumor markers between the two groups before treatment; After treatment, the levels of CEA, CA199 and NSE in the two groups decreased, and the levels of CEA, CA199 and NSE in the observation group were lower than those in the control group. Therefore, the treatment of integrated traditional Chinese and Western medicine can reduce the levels of CEA, CA199 and NSE. Cui Yanfei^[29] divided 90 elderly patients with advanced non-small cell lung cancer into two groups. The control group received GP regimen (cisplatin + gemcitabine) chemotherapy, 28 days as a cycle; The observation group was treated with Qingfei Xiaoji formula on the basis of the control group, twice a day, one dose each time, 14 days as a cycle. Both groups were treated continuously for 3 cycles. After three chemotherapy cycles, the levels of carbohydrate antigen 125 (CA125) and carcinoembryonic antigen (CEA) were observed. The results were as follows: compared with before treatment, the levels of CA125 and CEA in the two groups decreased significantly after treatment. After treatment, the levels of CA125 and CEA in the observation group were lower than those in the control group. Chen Yanfeng^[30] randomly divided 90 patients with non-small cell lung cancer who failed molecular targeted therapy into observation group and control group, with 45 cases in each group. The observation group was treated with docetaxel twice, 21 days each time as a cycle; The observation group was treated with self-made Yiqi Yangyin xiao cancer Decoction for 28 days on the basis of the treatment of the control group. The changes of serum tumor markers (CEA, CA125, CYFRA21-1 and NSE) before and after treatment were detected. The results showed that the levels of serum CEA, CA125, NSE and CYFRA21-1 after treatment were significantly lower than those before treatment; And the average of four serum tumor marker water in the observation group was significantly lower than that in the control group.

The above studies show that after the treatment of integrated traditional Chinese and Western medicine, the average level of serum tumor marker water decreases significantly, and the decline of serum tumor marker level reflects the degree of treatment success to a certain extent. Therefore, in the process of integrated traditional Chinese and Western medicine in the treatment of lung cancer, the change of serum tumor marker content is of certain significance for clinical treatment efficacy evaluation and condition monitoring.

6. Conclusion

Many studies have shown that integrated traditional Chinese and Western medicine can effectively improve the treatment effect of lung cancer patients, and can effectively improve the quality of life and survival time of patients. There are significant differences in the expression levels of serum tumor markers in different TCM syndrome types of lung cancer. However, there is still no unified standard for TCM syndrome differentiation of lung cancer so far. Therefore, establishing a unified TCM syndrome type of lung cancer and deeply studying the correlation between serum markers and TCM Syndrome type is of great significance for the diagnosis and treatment of lung cancer with integrated traditional Chinese and Western medicine.

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References

[1] Tian Yantao, Kang Wenzhe. *New progress of global cancer incidence research [J]. Chinese Medicine, 2021, 16(10): 1446-1447.*

- [2] Lu T, Yang X, Huang Y, Zhao M, Li M, Ma K, Yin J, Zhan C, Wang Q. Trends in the incidence, treatment, and survival of patients with lung cancer in the last four decades. *Cancer Manag Res.* 2019Jan 21; 11: 943-953. doi: 10.2147/CMAR.S187317. a
- [3] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin.* 2021 May;71(3):209-249. doi: 10.3322/caac.21660. Epub 2021 Feb 4.
- [4] Ge Junbo, Xu Yongjian. *Internal Medicine [M]. 9th Ed. Beijing: People's Medical Publishing House, 2018.*
- [5] Shao Yun, Guan Jiangfeng. Psychological needs and nursing strategies of lung cancer patients undergoing chemotherapy for the first time [J]. *Health Care Medicine Research and Practice*, 2018, 15(02): 70-72.
- [6] Liu Xia, Wang Yan, Yang Fumeng. Detection of serum β 2-Mg, CEA, CA125, NSE and CyFRA21-1 in early diagnosis of lung cancer [J]. *Jilin Medical Science*, 2021, 42(01): 8-11.
- [7] Cai Yun, Chen Yuanbin, YE Fang, WU Lei, LI Liu, Lin Lin. TCM master Zhou Zhongying's experience in differentiation and treatment of lung cancer from the theory of cancer toxicity [J]. *Chinese Journal of Traditional Chinese Medicine*, 2020, 35(06): 2879-2882.
- [8] Li Hegen. Professor Liu Jiexiang's experience in the treatment of lung cancer by strengthening the normal method [J]. *Sichuan Traditional Chinese Medicine*, 2005(07): 5-6.
- [9] Xue Xin-li. Lin Hong-sheng clinical experience in the treatment of non-small cell lung cancer by invigorating qi and nourishing Yin [J]. *Global Chinese Medicine*, 2015, 8(08): 983-984.
- [10] Guan Tianyu, Gu Yifang. Gu Mingsan's experience in the treatment of advanced lung cancer [J]. *Journal of Internal Medicine of Practical Traditional Chinese Medicine*, 2011, 25(05): 17+19.
- [11] Hu Yan, Tan Kaiji, Chen Zhijian, Cao Yang. Introduction of Professor Chen Ruishen's experience in the treatment of lung cancer [J]. *New Traditional Chinese medicine*, 2008, 40(12): 8-9.
- [12] Cui Huijuan, Zhang Peiyu. Zhang Daizhao's experience in the treatment of lung cancer [J]. *Journal of China-Japan Friendship Hospital*, 2011, 25(01): 57-58.
- [13] Ma Ke, Ma Ling, Shi Zhiming. Study on standardization of TCM syndromes of primary bronchial lung cancer [J]. *Liaoning Journal of Traditional Chinese Medicine*, 2007(04): 421-422.
- [14] Xiao B, Long S Q, Deng H. Distribution characteristics of TCM syndrome types in 207 cases of advanced non-small cell lung cancer [J]. *Journal of Liaoning University of Traditional Chinese Medicine*, 2013, 15(03): 188-190.
- [15] Zhang Ming-ping, Wang Jian-jun, LI Zhi-hong. Clinical observation of TCM syndrome type in advanced non-small cell lung cancer [J]. *World Journal of Integrated Traditional Chinese and Western Medicine*, 2012, 7(08) :706-708.
- [16] Han D, Li W, Fang R. Clinical investigation of TCM syndrome types in 861 cases of primary lung cancer [J]. *Shanxi traditional Chinese medicine*, 2016, 37(12): 1589-1591.
- [17] Xu Yinji, Wang Xinqiu, Chao Enxiang. Chao Enxiang's experience in the treatment of lung cancer [J]. *New Traditional Chinese Medicine*, 2016, 48(08): 228-229.
- [18] Deng Yunzong, Sun Hongxin, Zheng Xijun. Zhou Daihan's experience in the treatment of lung cancer [J]. *Journal of Traditional Chinese Medicine* 2017, 32(03): 318-321.
- [19] Deng Hong, He Wenfeng, Li Liuning, Wu Wanyin, Long Shunqin. Liu Weisheng clinical experience in treatment of lung cancer [J]. *Shi Zhen Chinese medicine*, 2011, 22(09): 2312-2314.
- [20] Jiang Jianhong, Xu Li. Professor Xu Li's experience in the treatment of lung cancer with "three segments and six discriminations" model [J]. *Chinese Medicine Guide*, 2016, 22(18): 31-34.
- [21] Zhang Shuhong, LIU Jian, Rao Zhiguo. Study on the correlation between TCM syndrome types and clinical objective indicators of non-small cell lung cancer [J]. *Chinese Journal of Traditional Chinese Medicine*, 2020, 35(02): 295-298.
- [22] Wang Lei, Ning Xiaoxiao, Li Hegen, Wang Qihua, XU Weijie, Zhou Lei, Xu Ling. Analysis of the relationship between TCM syndromes and histological types, clinical stages and tumor markers in patients with lung cancer [J]. *Laboratory medicine*, 2013, 28(05): 387-390.
- [23] Dai Sui, Zhao Jing, Li Huiqiang. Study on the relationship between TCM syndromes and tumor markers in non-small cell lung cancer [J]. *Shaanxi Traditional Chinese Medicine*, 2014, 35(03): 312-313.
- [24] Yan Xuesheng, Li Hanmin, Peng Yaqin. Study on the correlation between tumor markers and TCM syndrome differentiation of lung cancer [J]. *Hubei Journal of Traditional Chinese Medicine*, 2007(09): 11-12.
- [25] Lv Dan, Wang Baishan, Li Yali, Zhang Cheng, Jin Di. Study on the correlation between tumor markers cyFRA21-1, CEA, CA12-5, NSE and TCM syndrome differentiation in patients with lung cancer [J]. *Journal of Liaoning University of Traditional Chinese Medicine*, 2019, 21(06): 165-167.
- [26] Fu Yanli, Tu Hongbin, Dong Zhiyi, Dong Changsheng, XU Ling. Study on the correlation between TCM syndrome type and TNM stage and tumor antigen in primary lung cancer [J]. *World Science and Technology – Modernization of Traditional Chinese medicine*, 2015, 17(06): 1210-1214.
- [27] Shan Kuizhong, Jiang Ziyu, Huang Hui. Effects of integrated traditional Chinese and Western medicine on tumor markers and cellular immune function in patients with advanced non-small cell lung cancer [J]. *World Traditional Chinese Medicine*, 2018, 13(10): 2472-2475.

[28] Cui Yanfei, Huang Chuying. *Clinical efficacy of Qingfexiaoji Prescription combined with chemotherapy in elderly patients with advanced non-small cell lung cancer and its effect on tumor markers, inflammatory factors and immune function [J]. Chinese Journal of Traditional Chinese Medicine Information, 2018, 25(12): 19-23.*

[29] Chen Yanfeng, Zhou Deqi. *Efficacy of self-designed Yiqi Yangyin Xiaoi Decoction combined with docetaxel in the treatment of non-small cell lung cancer and its effect on serum tumor markers [J]. Journal of Modern Integrated Chinese and Western Medicine, 2018, 27(09): 942-945+1026.*