

Study on the Rule of Drug Use in the Treatment of Pulmonary Nodules Based on Data Mining

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Abstract: Objective: To study the rules of Chinese medicine in treating pulmonary nodules. Methods: The relevant literature on the diagnosis and treatment of pulmonary nodules by traditional Chinese medicine was retrieved from CNKI, Wanfang and Weipu databases, and the rules of drug use of traditional Chinese medicine in the treatment of pulmonary nodules was discussed and summarized through the traditional Chinese medicine inheritance computing platform software. Results: A total of 50 prescriptions were included, involving 69 traditional Chinese medicines. Common Chinese medicines include atracylodes macrocephala, licorice, Fritillaria thunbergii, Pinellia ternata, fried malt, dried tangerine peel, Poria cocos, perilla leaf, pseudostellaria, platycodon grandiflorum, dandelion, etc. The properties of traditional Chinese medicine are mainly warm, cold and calm; Traditional Chinese medicine mainly tastes bitter, sweet and bitter; The main meridians of drugs are lung, spleen, stomach, heart, liver and kidney; It is mainly used for phlegm resolving, cough relieving and asthma relieving, deficiency tonifying, heat clearing, and diuretic and moisture permeable drugs. Conclusion: In the treatment of pulmonary nodules, traditional Chinese medicine should focus on clearing the lung and removing phlegm, promoting blood circulation and removing blood stasis, detoxifying and dispersing nodules, and at the same time, it should pay attention to the role of supporting vital qi, strengthening the spleen and tonifying deficiency, and strengthening the physique.

Pulmonary nodules are round-like, focal, high density or hypo solid irregular shadows of the lung with a diameter ≤ 3 cm, which can be single or multiple, and the boundary can be clear or unclear. In clinical practice, patients with pulmonary nodules are often classified into solitary pulmonary nodules and multiple pulmonary nodules; According to the size, a small nodule with a diameter of less than 5 mm is classified as a small nodule, a small nodule with a diameter of 5-10 mm is classified as a small nodule, and a nodule with a diameter of 10-30 mm should be treated in time. Generally speaking, the larger the nodule, the higher the probability of malignant lung cancer, and the higher the risk [1]; According to the density, it can be divided into solid nodules, some solid nodules and ground glass nodules, of which some are the most malignant. In recent years, with the gradual enhancement of people's awareness of physical examination and the progress of modern

medical technology, the detection rate of pulmonary nodules in clinical has been rising, and its pathogenesis is still unclear. A small number of pulmonary nodules are the early manifestations of lung cancer. Therefore, screening and intervention treatment of early lung nodules have obviously become a very important topic at present. Pulmonary nodules can be divided into benign and malignant ones. Most patients have no obvious symptoms, but a small number of patients may have malignant lung cancer, which is often found by accident during physical examination. Therefore, scientific management of pulmonary nodules is very important. Generally, review and follow-up are required for benign nodules. Early detection and intervention are required for malignant pulmonary nodules to reduce the scope, number, anxiety and quality of life of patients. During follow-up, if nodules are found to have a growth trend, low, medium and high risk nodules should generally be treated with surgery, especially high risk nodules, which should be removed immediately [2]. The way of modern medicine to treat pulmonary nodules is limited. In addition to the pulmonary nodules that arrive at the surgical indication early, they are generally followed up by reexamination. The long-term nodules cause obvious psychological pressure, while the opposite emotions will also affect the condition, often forming a vicious circle, with poor results. Traditional Chinese medicine can play a unique role in the treatment of pulmonary nodules. Many clinical studies have found that traditional Chinese medicine has a good effect on pulmonary nodules. Now, the drug use rules of traditional Chinese medicine in the treatment of pulmonary nodules are summarized as follows.

1. Materials and Methods

1.1. Data source

The data of this study is derived from the effective medical cases of Chinese medicine in the diagnosis and treatment of pulmonary nodules in CNKI, Wanfang, and Weipu databases. 50 prescriptions were selected as the research objects, and classified and summarized according to the four qi, five flavor, meridian tropism, efficacy, and frequency of use of the drugs. Through the traditional Chinese medicine inheritance computing platform, the drug use rules of Chinese medicine in the treatment of pulmonary nodules were analyzed and summarized.

1.2. Inclusion and Exclusion Criteria

1.2.1. Inclusion Criteria

(1) Prescriptions and drugs are used for pulmonary nodules, and the dosage and addition and subtraction of the syndrome are not counted; (2) The medicine is complete and the curative effect is definite; (3) The literature can be medical case arrangement, expert experience, experimental research, etc.

1.2.2. Exclusion Criteria

(1) Medical case prescriptions with duplicate literature; (2) Prescription for external use or animal experiment; (3) Unreliable data and poor quality prescriptions; (4) Prescriptions repeated in English and Chinese.

1.3. Data Processing

The names of prescription Chinese medicines shall be standardized according to the Pharmacopoeia of the People's Republic of China (2020).

1.4. Data Verification

Two person input and two-person verification mode is adopted to ensure the accuracy of the data verification process.

1.5. Data Analysis

Statistics and mining analysis of medical case data obtained from the retrieval were conducted through the traditional Chinese medicine inheritance computing platform (V3.0) software [3]. Data analysis includes statistics of medication frequency four drugs, five drugs, meridian tropism, efficacy category, extraction of statistical results, and export of statistical charts.

2. Results

2.1. Analysis of Medication Frequency

In this study, 50 prescriptions were included, involving 69 traditional Chinese medicines. The total frequency of drug use was 1011 times, of which 11 were used more than 40 times, including *Atractylodes macrocephala*, licorice, *Fritillaria thunbergii*, *Pinellia ternate*, fried malt, tangerine peel, *Poria cocos*, perilla leaf, *pseudostellaria*, *platycodon grandiflorum* and dandelion. There were 19 drugs with frequency ≥ 20 times. (Table 1)

Table 1: Statistics of Drug Frequency.

Serial No	Medicine	Frequency /time	Frequency%
1	<i>Atractylodes macrocephala</i>	50	4.95
2	Licorice	49	4.85
3	<i>Fritillaria thunbergii</i>	49	4.85
4	banxia	48	4.75
5	Stir fried malt	48	4.75
6	dried tangerine peel	48	4.75
7	<i>Poria cocos</i>	47	4.65
8	Perilla leaf	46	4.55
9	<i>Radix Pseudostellariae</i>	46	4.55
10	Chinese bellflower	41	4.06
11	Dandelion	40	3.96
12	Turmeric	37	3.66
13	<i>Kochia scoparia</i>	30	2.97
14	windproof	30	2.97
15	<i>Sophora japonica</i>	29	2.87
16	Cuttlebone	28	2.77
17	Honeysuckle vine	24	2.37
18	Perilla seed	22	2.18
19	Wax gourd peel	21	2.08

2.2. Analysis of Four Qi and Five Tastes

The results of drug properties showed that the total frequency of use of the four qi drugs was 956, mainly warm, cold, and mild drugs. Among them, warm drugs were used most frequently, 345 times, accounting for 36.09%; cold drugs 324 times, accounting for 33.89%; 254 times of normal drugs,

accounting for 26.57%; Cold drugs 33 times, accounting for 3.45%; There were no hot drugs, accounting for 0%. See Table 2.

The results of drug taste showed that the total use frequency of five drugs was 1435 times, mainly bitter, sweet, and bitter drugs, among which bitter drugs were used the most, with the frequency of 499 times, accounting for 34.77%; 459 times of sweet drugs, accounting for 31.99%; 387 times of pungent drugs, accounting for 26.97%; Acid medicine 49 times, accounting for 2.72%; 41 times of salty medicine, accounting for 2.86%. (Table 2)

Table 2: Statistical Table of Four Qi and Five Tastes of Drugs.

Medicinal property	Frequency /time	Frequency%	Medicinal taste	Frequency /time	Frequency%
temperature	345	36.09	bitter	499	34.77
cold	324	33.89	Gan	459	31.99
flat	254	26.57	Xin	387	26.97
cool	33	3.45	acid	49	3.41
heat	0	0	salty	41	2.86

2.3. Analysis of Drug Channel Tropism

The results of drug channel tropism showed that the total frequency of use was 2217 times, mainly in the lung, spleen, stomach, heart, liver, and kidney channels. Among them, pulmonary meridian drugs were used most frequently, 605 times, accounting for 27.29%; 507 times (22.87%) of drugs were administered to the spleen meridian; Stomach meridian medicine 304 times, accounting for 13.71%; The heart meridian drugs were 229 times, accounting for 10.33%; 223 times of liver channel drugs, accounting for 10.06%; 172 times of kidney meridian drugs, accounting for 7.76%; 95 times (4.26%); 30 times of bladder medicine, accounting for 1.35%; 23 times (1.04%) were administered via small intestine; Bile channel drugs 18 times, accounting for 0.81%; Triple energizer is administered 11 times, accounting for 0.50%; Pericardial menstruation was administered 0 times (0%). (Table 3)

Table 3: Statistics of meridian tropism of drugs.

Serial No	Meridian tropism	Frequency /time	Frequency%
1	lung	605	27.29
2	spleen	507	22.87
3	stomach	304	13.71
4	heart	229	10.33
5	liver	223	10.06
6	kidney	172	7.76
7	large intestine	95	4.26
8	bladder	30	1.35
9	small intestine	23	1.04
10	gallbladder	18	0.81
11	Trifocal	11	0.50
12	pericardium	0	0

2.4. Analysis of Efficacy Categories

The results of drug efficacy showed that the total frequency of use was 956, and the main drugs

were phlegm resolving, cough relieving, asthma relieving, deficiency tonifying, heat clearing, and moisture relieving. Among them, expectorant, antitussive and antiasthmatic drugs were used most, 229 times, accounting for 23.95%; 206 times of deficiency drugs, accounting for 21.55%; 105 times of antipyretic drugs, accounting for 10.98%; 104 times of diuretic and hygroscopic drugs, accounting for 10.88%; 78 times of surface drugs, accounting for 8.16%; Qi regulating drugs 76 times, accounting for 7.95%; 57 times of astringent drugs, accounting for 5.96%; 49 times, accounting for 5.13%; Hemostatic drugs 33 times, accounting for 3.45%; 12 times of diet drugs, accounting for 1.26%; Liver calming and wind calming drugs 5 times, accounting for 0.52%; Humidifying drugs twice, accounting for 0.21%. (Table 4)

Table 4: Statistical table of drug efficacy.

Serial No	Efficacy category	Frequency /time	Frequency%
1	Resolving phlegm, relieving cough and relieving asthma	229	23.95
2	Tonic class	206	21.55
3	Antipyretic	105	10.98
4	Hydrophilic and hygroscopic	104	10.88
5	Disjunctive class	78	8.16
6	Regulating Qi	76	7.95
7	Astringent	57	5.96
8	Activating Blood Circulation and Removing Blood Stasis	49	5.13
9	Hemostatic	33	3.45
10	Digestive	12	1.26
11	Liver calming and wind calming animals	5	0.52
12	Humidifying class	2	0.21

2.5. Association Rule Analysis

Table 5: Common core drug combinations for pulmonary nodules.

Serial No	Drug combination	Frequency /time
1	Atractylodes macrocephala ,Fritillaria thunbergii	49
2	Atractylodes macrocephala, licorice	49
3	Atractylodes macrocephala, Pinellia ternate, dried tangerine peel	48
4	Licorice, Pinellia ternate	48
5	Atractylodes macrocephala, licorice, Pinellia ternate, dried tangerine peel	48
6	Fritillaria thunbergii, licorice	48
7	Licorice, orange peel	48
8	Licorice, Pinellia ternate, tangerine peel	48
9	Atractylodes macrocephala, dried tangerine peel	48
10	Pinellia ternate, dried tangerine peel	48
11	Atractylodes macrocephala, licorice, Pinellia ternate	48
12	Atractylodes macrocephala, fried malt	48
13	Atractylodes macrocephala, Fritillaria thunbergii, Licorice	48
14	Atractylodes macrocephala, licorice, dried tangerine peel	48
15	Atractylodes macrocephala, Pinellia ternate	48

According to the actual situation, the number of supports is set to 48, the confidence is set to 0.95, and a total of 15 groups of commonly used core drug combinations for the treatment of pulmonary nodules are extracted through the "Association Rules" function. (Table 5)

2.6. Cluster Analysis

According to the actual situation, set the number of clusters to 3, and extract three potentially core new prescriptions for the treatment of pulmonary nodules.(Table 6)

Table 6: New prescriptions for pulmonary nodule core.

Serial No	Core new prescription
1	Fritillaria thunbergii, Pinellia ternate, Poria cocos, Atractylodes macrocephala, dried tangerine peel
2	Pinellia ternate, Poria cocos, licorice, Fritillaria thunbergii, Atractylodes macrocephala
3	Pseudostellaria, dandelion, fried malt, atractylodes macrocephala, Fritillaria thunbergii

3. Discussion

There is no specific disease name for pulmonary nodules in traditional Chinese medicine, and modern physicians have their own views. According to the characteristics of its symptoms, it can be classified into the categories of "accumulation", "breath cardia", "lung accumulation", etc.[4].The range of pulmonary nodules is limited and the course of disease is long, which is related to emotion, diet, exertion, endowment and other factors. Pulmonary sarcoidosis is located in the lung and related to liver, spleen and kidney. Its main pathogenesis is deficiency of viscera, deficiency of vital qi, invasion of evil qi, stagnation of evil toxin, disharmony of qi and blood, and mutual accumulation of phlegm and blood stasis. Traditional Chinese medicine has the advantages of multiple targets, multiple approaches and multiple links in the treatment of pulmonary nodules. Previous clinical trials have confirmed that traditional Chinese medicine methods can not only use the idea of treating the disease before it occurs to carry out early tumor prevention and intervention, but also show significant advantages in improving the quality of life of patients, reducing the toxicity of radiotherapy and chemotherapy, and preventing tumor metastasis and recurrence [5-6].It has been proposed that the treatment of pulmonary nodules should start from the internal organs, and the drug should focus on tonifying the lungs, assist in promoting blood circulation and resolving phlegm, and regulate the vital energy. The clinical effect is good [7].Some experts believe that most lung nodules are based on the deficiency of vital energy, while the phlegm and blood stasis are actually evil. In terms of treatment, we should pay attention to the importance of supporting vital energy, not just attacking the nodule itself, but often adding many tonifying drugs to help the vital energy and strengthen the physique [8].Another study pointed out that the treatment of pulmonary nodules should pay attention to the relationship between the lung and spleen. The spleen is deficient and damaged. It breeds phlegm and dampness and is stored in the lung. Therefore, the treatment of upper lung and spleen is the same [9].

In terms of medication frequency, the drugs with high frequency of use for the treatment of pulmonary nodules were Atractylodes macrocephala, licorice, Fritillaria thunbergii, Pinellia ternate, fried malt, dried tangerine peel, Poria cocos, perilla leaf, pseudostellaria, platycodon grandiflorum, dandelion. Among them, Erchen decoction (dried tangerine peel, pinellia, poria cocos, licorice) is from the book "Taiping Huimin Heji Prescription", which is the basic prescription for treating wet phlegm disease in clinical practice. It can dry dampness and remove phlegm, regulate qi and strengthen spleen. It has been found that the application of Erchen Decoction and Banxia Xiexin Decoction can narrow the range of high-risk pulmonary nodules in some patients, and the clinical effect is good. Atractylodes macrocephala is a medicine for tonifying deficiency, which can invigorate qi and spleen, and warm phlegm and dampness; Fritillaria thunbergii can clear away heat

and phlegm, soft and firm, and disperse knots; Stir fried malt can soothe the liver, regulate qi, strengthen the spleen and promote harmony; Perilla leaf can dispel cold, promote qi and stomach; *Pseudostellaria heterophylla* is beneficial to qi, spleen, fluid and lung; *Platycodon grandiflorum* relieves cough and phlegm, and ventilates lung qi; It can clear away heat and toxin, reduce swelling and disperse knots.

In terms of the four qi, the drugs used to treat pulmonary nodules are mainly warm, cold, and mild. At the initial stage of pulmonary nodules, most of them are cold and wet. During the use of drugs, warm drugs are used. The nodules do not heal for a long time. Phlegm and blood stasis are intertwined to form heat, forming yellow sticky phlegm. Therefore, cold drugs are needed. At the same time, the lungs are not resistant to cold and heat, so attention is paid to the use of mild drugs. In terms of five flavors, the drugs for treating pulmonary nodules are mainly bitter, sweet and acrid. The bitter drugs can clear away lung heat, clear away heat and detoxify; The sweet medicine can replenish the vital energy and ease the medicinal properties; Pungent medicine can disperse qi and promote blood circulation to remove blood stasis.

In the aspect of meridian tropism, the drugs used to treat pulmonary nodules are mainly the lung, spleen, stomach, heart, liver, and kidney meridians. Pulmonary sarcoidosis is located in the lungs. From the five elements, the spleen, stomach and lungs are the mother-child relationship, and the lungs and kidneys are also the mother child relationship; Heart and lung play an important role in the circulation of qi and blood, and they are interrelated; The relationship between liver and lung is mainly manifested in the ascending and descending of qi, which can regulate and smooth the qi. In terms of efficacy categories, the drugs used to treat pulmonary nodules mainly include those for phlegm resolving, cough relieving, asthma relieving, deficiency tonifying, heat clearing, and moisture relieving. Patients with pulmonary nodules are often accompanied by cough, expectoration, shortness of breath and asthma due to insufficient lung qi, so they often use expectorants to relieve cough and asthma; Pulmonary sarcoidosis is based on the deficiency of vital energy. In the treatment, we should pay attention to the role of supporting vital energy, so we often use deficiency tonics; Pulmonary sarcoidosis does not heal for a long time. Phlegm and blood stasis are intertwined and turn into heat. At the same time, the lungs are the organs of asthenia. Therefore, heat clearing drugs are commonly used to treat pulmonary nodules, which can achieve good results; Pulmonary nodules are often caused by deficiency of spleen and stomach, dereliction of duty in transportation, and endogenous phlegm dampness. Therefore, the treatment of pulmonary nodules often involves the use of water infiltration drugs to remove dampness and remove phlegm.

The results of association rule analysis showed that the commonly used drugs for the treatment of pulmonary nodules: *Atractylodes macrocephala*, *Fritillaria thunbergii*, *Atractylodes macrocephala*, liquorice, liquorice, *Pinellia ternata*, *Fritillaria thunbergii*, liquorice, etc; Common horn medicines: *Atractylodes macrocephala*, *Pinellia ternata*, dried tangerine peel, licorice, *Pinellia ternata*, dried tangerine peel, *Atractylodes macrocephala*, licorice, *Pinellia ternata*, etc; Commonly used drug combinations: *Atractylodes macrocephala*, licorice, *Pinellia ternata*, dried tangerine peel. Most of these drugs have the functions of resolving phlegm, strengthening spleen, regulating qi and tonifying deficiency, which is in line with the pathogenesis characteristics of pulmonary nodules from lung deficiency to liver, spleen and kidney deficiency. Cluster analysis showed that three groups of potential core new prescriptions were obtained. New Formula 1: *Fritillaria thunbergii*, *Pinellia ternata*, *Poria cocos*, *Atractylodes macrocephala*, dried tangerine peel; New Formula 2: *Pinellia ternata*, *Poria cocos*, licorice, *Fritillaria thunbergii*, *Atractylodes macrocephala*; New Formula 3: *Pseudostellaria*, dandelion, fried malt, *Atractylodes macrocephala*, *Fritillaria thunbergii*. The overall effect is in line with the main direction of clearing the lung and removing phlegm, strengthening the spleen and tonifying deficiency.

To sum up, pulmonary sarcoidosis is based on positive deficiency and marked by phlegm, blood

stasis and toxin. TCM treatment of pulmonary nodules should focus on the pathogenesis of the disease. Starting from the lungs, taking into account the related viscera, it can clear the lung and remove phlegm, promote blood circulation and remove blood stasis, detoxify and disperse the knot. At the same time, it should attach importance to the role of supporting the vital qi, strengthening the spleen and deficiency, strengthening the physique, and treating the symptoms and symptoms together.

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