Future Integrative Medicine **2024** vol. 3(1) | 1–10
DOI: 10.14218/FIM.2023.00041

Original Article

Meta-analysis of the Correlation between Traditional Chinese Medicine Syndrome of Lung Cancer and Tumor-node-metastasis Staging Indexes

Xukuo Liu[1#], Jiangping Zhan[2#], Xiaohui Zhao[1], Huanfang Fan[3], Lijun Zhao[4], Min Li[4], Wenli Yu[4] and Dehui Li[3*]

[1]*Graduate School of Hebei University of Chinese Medicine, Shijiazhuang, China;* [2]*Chengde Kangyang Hospital, Chengde, China;* [3]*Affiliated Hospital of Hebei University of Chinese Medicine, Shijiazhuang, China;* [4]*Xingtang County Hospital of Chinese Medicine, Shijiazhuang, China*

Received: July 02, 2023 | **Revised:** July 25, 2023 | **Accepted:** March 22, 2024 | **Published online:** March 25, 2024

Abstract

Background and objectives: With the highest incidence rate and death rate among malignant tumors, lung cancer is the most prevalent malignant tumor worldwide. Tumor-node-metastasis (TNM) staging provides a basis for clinical therapy and prognosis while the fundamental principle of traditional Chinese medicine (TCM) is the syndrome differentiation and treatment. This study offers an objective foundation for the distinction and classification of TCM syndromes by methodically assessing the relationship between TNM staging indicators and the various types of the syndrome in lung cancer.

Methods: To find pertinent material, we searched a number of databases, including CNKI, PubMed, VIP, and Wanfang. Literature on the relationship between TCM syndrome categories and TNM staging indexes of lung cancer published from the database's inception until May 2023 was gathered. The meta-analysis was carried out using Rev Man 5.4.

Results: In the end, seven pieces of literature totaling 264 patients were included. Lung cancer is mainly characterized by phlegm dampness syndrome, Qi Yin deficiency syndrome, Yin deficiency internal heat syndrome, and Qi stagnation and blood stasis syndrome. In stage I and II, phlegm dampness syndrome > Yin deficiency internal heat syndrome ($p < 0.5$), phlegm dampness syndrome > Qi Yin deficiency syndrome ($p < 0.5$), phlegm dampness syndrome > Qi stagnation and blood stasis syndrome ($p < 0.5$). In stages III and IV, Qi Yin deficiency syndrome > Qi stagnation and blood stasis syndrome > Yin deficiency internal heat syndrome > phlegm dampness syndrome ($p < 0.5$).

Conclusion: Phlegm dampness syndrome is the main syndrome in stages I and II of lung cancer, while Qi and Yin deficiency syndromes are the main syndromes in stages III and IV of lung cancer.

Introduction

Lung cancer accounts for 20% of cancer-related deaths worldwide. Among all malignancies, this tumor, with the highest incidence and fatality rates, is also one of the most common and deadly cancers in older people.[1] While the incidence and mortality of lung cancer are continually rising in our country and other emerging nations, in many developed countries the mortality and morbidity of lung cancer are progressively stabilizing and exhibiting a decreasing tendency.[2] In emerging nations, lung cancer incidence is rising annually as a result of the current air pollution, radiation, chemical pollution, and other environmental factors in addition to smoking, diet, psychological stress, and other variables. Furthermore, early lung cancer identification is often difficult in clinical practice, and the overall 5-year survival rate is still about 15%.[3] Most people with lung cancer experience a subtle onset making it hard to detect in the early stages; thus, by the time they are diagnosed, the window of opportunity for surgery to be most helpful has passed.[4] Although surgery has been supplanted by radiation and chemo-

Keywords: Lung cancer; Traditional Chinese medicine; TCM syndrome type; Tumor-node-metastasis; TNM staging; Meta-analysis.

Abbreviations: CI, confidence interval; CT, computed tomography; PRISMA, preferred reporting items for systematic review and meta-analyses; RR, relative risk; SE, standard error; TCM, traditional Chinese medicine; TNM, tumor-node-metastasis.

[*]**Correspondence to:** Dehui Li, Hebei Province Hospital of Chinese Medicine, The First Affiliated Hospital of Hebei University of Chinese Medicine, Shijiazhuang 050011, China. ORCID: https://orcid.org/0000-0001-7963-9410. Tel: +86-13230413308, E-mail: 258289951@qq.com

[#]Contributed equally to this work.

How to cite this article: Liu X, Zhan J, Zhao X, Fan H, Zhao L, Li M, *et al*. Meta-analysis of the Correlation between Traditional Chinese Medicine Syndrome of Lung Cancer and Tumor-node-metastasis Staging Indexes. *Future Integr Med* 2024;3(1):1–10. doi: 10.14218/FIM.2023.00041.

therapy as the main modalities of treatment, patients still find it difficult to accept these treatments due to their high costs, serious side effects, and toxicities.[5,6] Clinical research has demonstrated that by reducing the harmful effects of molecularly targeted therapies such as radiation and chemotherapy through boosting their efficacy and controlling their overall function, traditional Chinese medicine (TCM) syndrome differentiation can alleviate symptoms, improve quality of life, and lengthen patient survival times. These days, an increasing number of clinical research investigations have verified that TCM offers some benefits when treating lung cancer. The fundamental idea of TCM treatment is syndrome differentiation and treatment. According to TCM, sputum fever is the medium term for lung cancer, and fluid consumption is the key factor in the late stage, which is caused by the cancer poisoning of the lungs and results in stagnant blood clots, pulmonary arthritis, and other symptoms. In the clinical staging of lung cancer, tumor-node-metastasis (TNM) can be used to make clear judgments based on the primary focus of the cancer, its size and scope, and whether there are distant lymph nodes and other organ metastases. It can be divided into Qi Yin deficiency syndrome, Qi stagnation and blood stasis syndrome, Yin deficiency internal heat syndrome, phlegm dampness syndrome, and other syndrome types.[7]

Numerous clinical investigations have examined the relationship between TCM syndrome types and TNM staging in lung cancer,[8] Nevertheless, the sample size is small, and no comprehensive summary studies have been conducted. Thus, to provide a reference for the differentiation of TCM syndrome types for enhanced treatment of lung cancer patients, this study applied a meta-analysis to further clarify the correlation between TCM syndrome types of lung cancer and TNM staging, assisting in the diagnosis, treatment, and syndrome differentiation process.

Methods

Literature sources and search strategies

This meta-analysis was conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The literature was searched electronically, including the CNKI, PubMed, VIP, and Wanfang databases. The search deadline was May 2023. The Chinese search keywords were: lung cancer, lung malignancy, differential diagnosis, syndrome type, and TNM stage. First, search for subject words and unrestricted words using various database search retrieval techniques. To weed out the studies that satisfied the inclusion requirements, an advanced search was carried out in accordance with the features of various databases.

Data selection

According to the design, we imported the literature search results into Endnote to ensure that no duplicate literature appeared and that each study was performed independently by two reviewers. Any differences were resolved by discussing and backtracking the original research based on the following inclusion and exclusion criteria.

Inclusion criteria

1. Study design: This study was a controlled trial, and the design was based on published literature;
2. Subjects: According to the TNM staging system recommended by the Union for International Cancer Control, the American Joint Committee on Cancer, and the National Comprehensive Cancer Network guidelines, patients who have been diagnosed with lung cancer based on pathology or cytology are divided into four stages (I, II, III, and IV).[9] Stages I and II are categorized in this study as early to mid-stage lung cancer, and Stages III and IV are categorized as advanced-stage lung cancer. Patients of all ages, geographical areas, and genders were included in the study;
3. Treatment method: No relevant requirement;
4. Results evaluation: The four syndrome kinds that were examined the most frequently in the literature were primarily TCM syndrome types, namely Qi Yin deficiency syndrome, Qi stagnation and blood stasis syndrome, Yin deficiency internal heat syndrome, and phlegm dampness syndrome. The correlation between the four syndromes was compared.

Exclusion criteria

1. Repeated publication or repeated detection of literature;
2. Too few included cases (less than 10);
3. Full text unavailable;
4. Complicated with other serious diseases, such as heart failure, kidney failure, etc;
5. Those not meeting diagnostic criteria; conclusions with incomplete data or data errors.

Research quality assessment

The ROBINS-I in the Cochrane Risk of Bias tool was used to assess the quality of the included literature. Studies involved: 1 Bias due to confounding; 2 Bias due to selection of participants; 3 Bias in the classification of interventions; 4 Bias due to deviations from intended interventions; 5 Bias due to missing data; 6 Bias in the measurement of outcomes; 7 Bias in selection of the reported result. Two inspectors carried out quality checks independently and a third researcher was asked to participate in consultation and judgment when there was disagreement.

Data analysis

The Meta outcomes were analyzed using RevMan 5.4 software (Nordic Cochrane Centre, Copenhagen, Denmark). The reference data of binary variables had a relative risk (RR) and 95% confidence interval (CI), and an χ^2 test showed heterogeneity among different studies. A fixed effect model can be used if $p > 0.5$, $I^2 \leq 50\%$, indicating good homogeneity. If $p \leq 0.5$, $I^2 > 50\%$. The representative heterogeneity was large, so the random effects model could be used.

Results

Included in the study screening process

172 references were found in the initial search. After 10 duplicates were eliminated, 149 references were checked for relevance using the titles, abstracts, and keywords. Thirteen complete texts were read following the first round of screening. Finally, 7 references were included in this evaluation after 6 investigations were discarded. The sample sizes involved ranged from 11 to 120 (Fig. 1). This study mainly analyzed the TNM staging and pathological classification of four syndrome types: Qi Yin deficiency syndrome, Qi stagnation and blood stasis syndrome, Yin deficiency internal heat syndrome, and phlegm dampness syndrome.

Include the basic information of the article

The basic information included in the paper is shown in Table 1.[10–16]

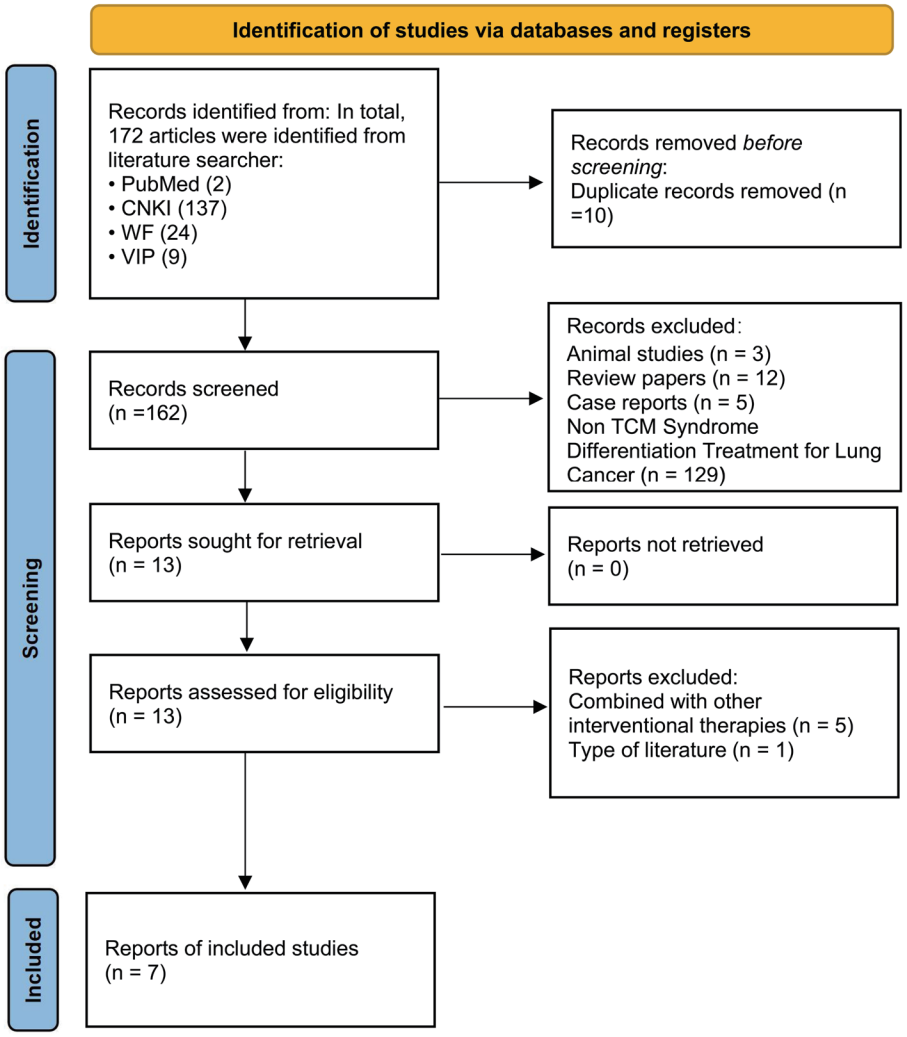

Fig. 1. PRISMA flow diagram. PRISMA, preferred reporting items for systematic reviews and meta-analyses; TCM, traditional Chinese medicine.

Table 1. Basic information about the article

Author and year	Diagnostic criteria	Phlegm dampness syndrome	Yin deficiency internal heat syndrome	Qi Yin deficiency syndrome	Qi stagnation and Blood stasis syndrome
Yu Weixia, 2017[12]	Histopathological confirmation	36	12	40	21
Zeng Liang, 2008[11]	Confirmed by CT, cytology, or pathology	20	14	11	7
Yang Qi, 2017[13]	The pathological results of lung cancer confirmed the diagnosis	27	51	85	37
He Wenfeng, 2011[16]	Guidelines for Clinical Research of New Chinese Medicines	63	29	8	12
Dong Jingbo, 2016[14]	Diagnostic criteria for primary bronchial lung cancer	16	31	51	22
Bao Jianmin, 2018[15]	Diagnostic criteria for primary bronchial lung cancer in Internal Medicine	33	22	21	26
Huang Donghua, 2013[10]	Cytological or pathological diagnosis of lung cancer,	30	40	38	32

CT, computed tomography.

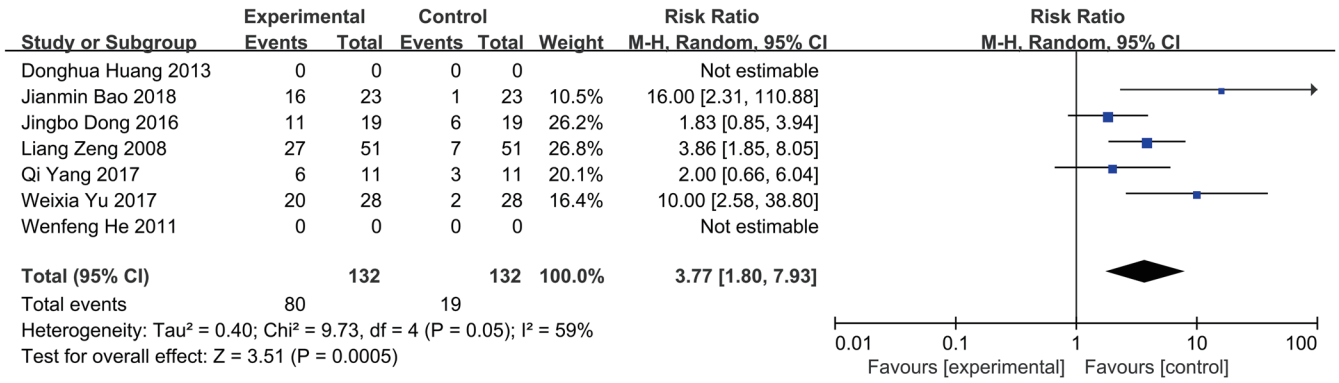

Fig. 2. Stages I and II were correlated with phlegm dampness syndrome and Yin deficiency internal heat syndrome. CI, confidence interval.

Results of meta-analysis

Correlation analysis of syndrome types in stages I and II

Seven studies reported a correlation between stages I and II and phlegm dampness syndrome and Yin deficiency internal heat syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 9.73$, $p = 0.05$, $I^2 = 59\%$, and there was no significant difference among all studies, allowing for the use of a fixed effects model. The difference between phlegm dampness syndrome and Yin deficiency internal heat syndrome was statistically significant (n = 264, RR = 3.77; 95%CI: 1.80–7.39, $p = 0.0005$; Fig. 2). The results show that in early lung cancer, phlegm dampness syndrome is more common than Yin deficiency internal heat syndrome.

Seven studies reported a correlation between stages I and II and phlegm dampness syndrome and deficiency of Qi Yin deficiency syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 2.07$, $p = 0.72$, $I^2 = 0\%$, and there was no significant difference among all studies, allowing for the use of a fixed effects model. The difference between phlegm dampness syndrome and Qi Yin deficiency syndrome was statistically significant (n = 264, RR = 6.67; 95%CI: 3.83–11.6, $p < 0.00001$; Fig. 3). The results show that in early lung cancer, phlegm dampness syndrome is more common than Qi Yin deficiency syndrome.

Seven studies reported a correlation between stages I and II and phlegm dampness syndrome and Qi stagnation and blood stasis syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 10.86$, $p = 0.03$, $I^2 = 63\%$, and there was no significant difference between the studies; thus, a fixed effects model could be used. The difference between phlegm dampness syndrome and Qi stagnation and blood stasis syndrome was statistically significant (n = 264, RR = 3.81; 95%CI: 2.50–5.79, $p < 0.00001$; Fig. 4). The results show that in early lung cancer, phlegm dampness syndrome is more common than Qi stagnation and blood stasis syndrome.

Seven studies reported a correlation between stages I and II and Yin deficiency internal heat syndrome and Qi Yin deficiency syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 6.32$, $p = 0.18$, $I^2 = 37\%$, and there was no significant difference among all studies; thus, a fixed effects model could be used. The difference was not statistically significant (n = 264, RR = 1.58; 95%CI: 0.8–3.15, $p < 0.18$; Fig. 5).

Seven studies reported a correlation between stages I and II and Yin deficiency internal heat syndrome and Qi stagnation and blood stasis syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 8.49$, $p = 0.08$, $I^2 = 53\%$, there was no significant difference among all studies, allowing for the use of a fixed effects model. The difference was not statistically significant (n = 264, RR = 0.90; 95%CI: 0.51–1.61, $p = 0.73$; Fig. 6).

Seven studies reported a correlation between stages I and II and Qi Yin deficiency syndrome and Qi stagnation and blood stasis syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 7.16$, $p = 0.13$, $I^2 = 44\%$, and there was no significant difference among all studies, allowing for the use of a fixed effects model. The difference between Qi Yin deficiency syndrome and Qi stagnation and blood stasis syndrome was statistically significant (n = 264, RR = 0.57; 95%CI: 0.29–1.12, $p = 0.1$; Fig. 7).

To sum up, in the middle of stages I and II, phlegm damp-

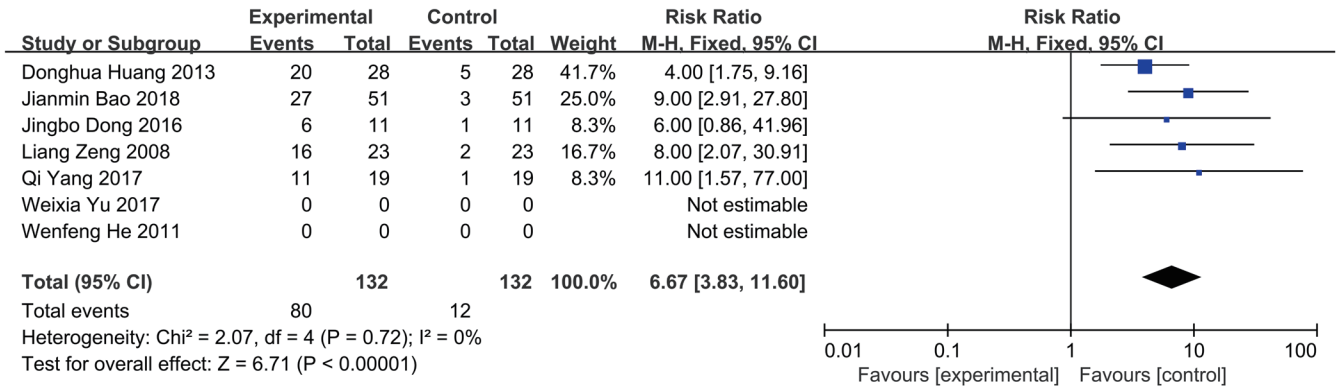

Fig. 3. Stage I and stage II were correlated with phlegm dampness syndrome and deficiency of Qi Yin deficiency syndrome. CI, confidence interval.

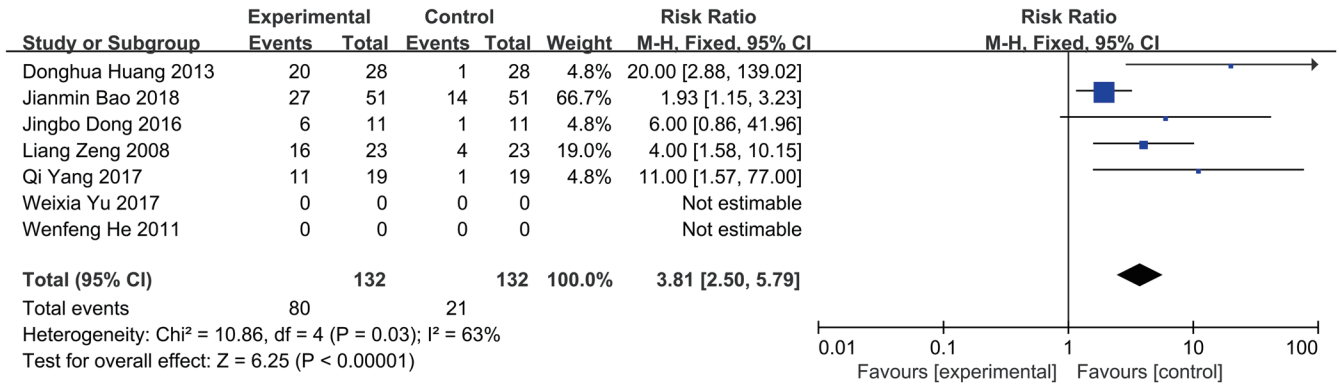

Fig. 4. Stages I and II were correlated with phlegm dampness syndrome and Qi stagnation and blood stasis syndrome. CI, confidence interval.

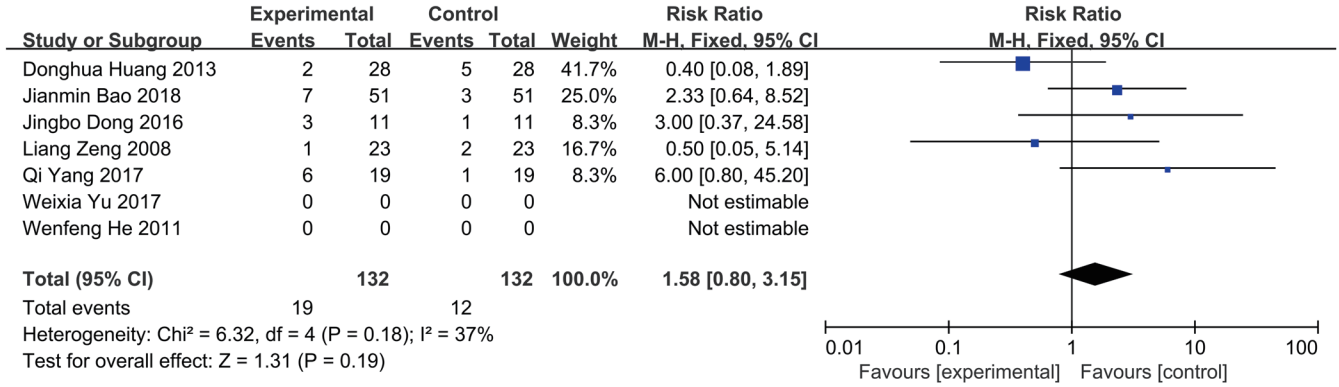

Fig. 5. Stages I and Stage II were correlated with Yin deficiency internal heat syndrome and Qi Yin deficiency syndrome. CI, confidence interval.

ness syndrome > Yin deficiency internal heat syndrome ($p < 0.5$), phlegm dampness syndrome > Qi Yin deficiency syndrome ($p < 0.5$), and phlegm dampness syndrome > Qi stagnation and blood stasis syndrome ($p < 0.5$).

Correlation analysis of stage III and IV syndrome types

Seven studies reported correlations between stages III and IV and phlegm dampness syndrome and Yin deficiency internal heat syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 81.29$, $p < 0.00001$, $I^2 = 93\%$, and there was no significant difference among all studies; thus, a fixed effects model could be used. Yin deficiency internal heat syndrome was higher than phlegm dampness syndrome, and the difference was statistically significant (n = 264, RR = 0.61; 95%CI: 0.26–1.42, $p = 0.25$; Fig. 8).

Seven studies reported a correlation between stages III and IV and phlegm dampness syndrome and Qi Yin deficiency syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 97.64$, $p < 0.00001$, $I^2 = 94\%$, and there was no significant difference among all studies, allowing for the use of a fixed effects model. The difference between phlegm dampness syndrome and Yin deficiency internal heat syndrome was statistically significant

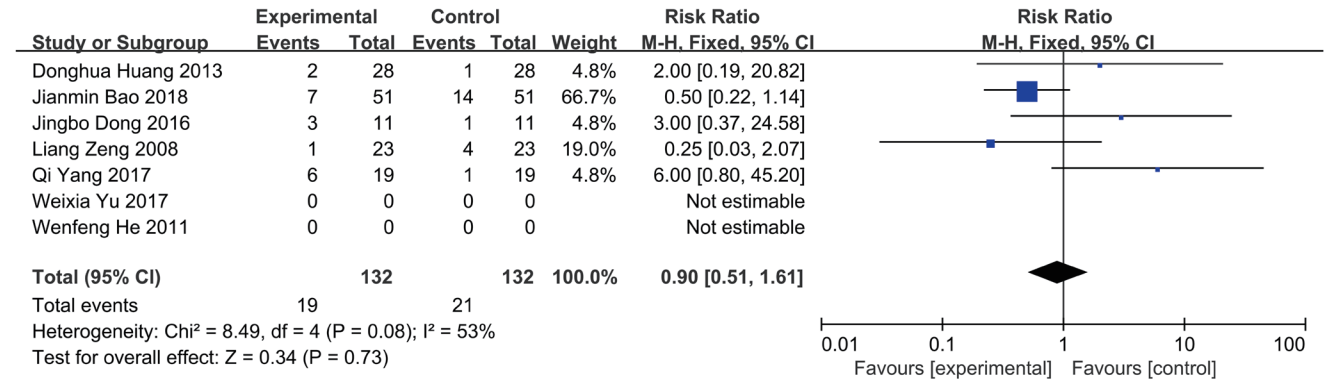

Fig. 6. Stage I and stage II are correlated with Yin deficiency internal heat syndrome and Qi stagnation and blood stasis syndrome. CI, confidence interval.

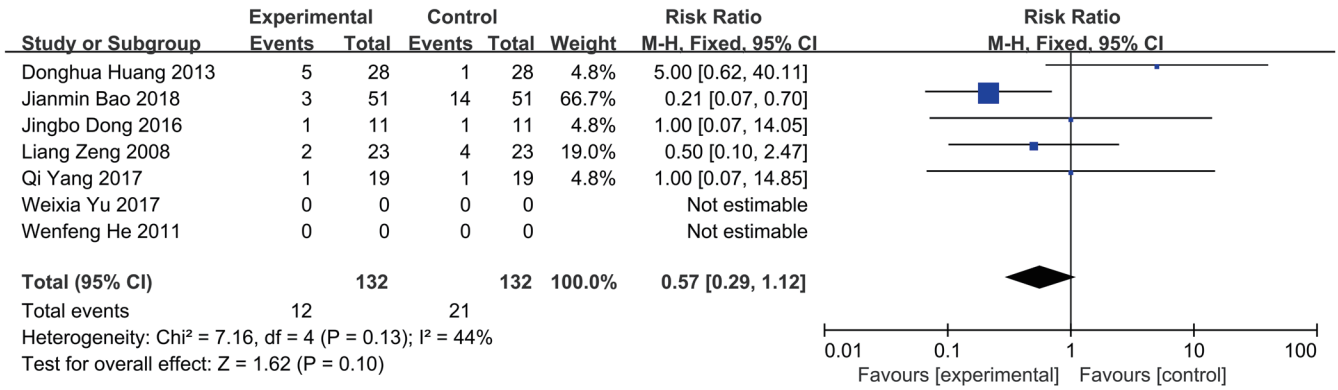

Fig. 7. Stage I and stage II were correlated with Qi Yin deficiency syndrome and Qi stagnation and blood stasis syndrome. CI, confidence interval.

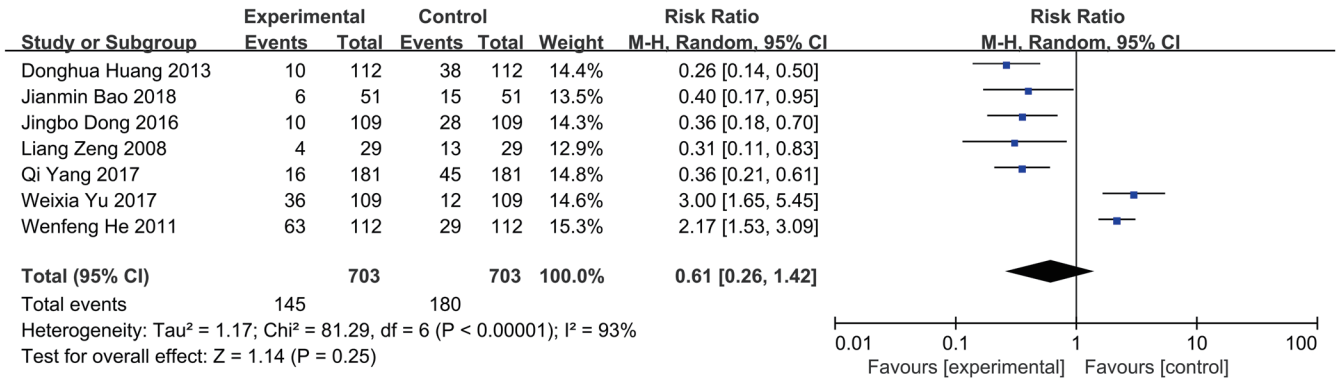

Fig. 8. Stages III and IV were correlated with phlegm dampness syndrome and Yin deficiency internal heat syndrome. CI, confidence interval.

(n = 264, RR = 0.53; 95%CI: 0.21–1.35, p = 0.18; Fig. 9). The results show that in advanced lung cancer, phlegm dampness syndrome is more common than Qi Yin deficiency syndrome.

Seven studies reported correlations between stages III and IV and phlegm dampness syndrome and Qi stagnation and blood stasis syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 65.19$, $p < 0.0001$, $I^2 = 91\%$, there was no significant difference between various studies; thus, a fixed effects model could be used. The difference between phlegm dampness syndrome and Qi Yin deficiency syndrome was statistically significant (n = 264, RR = 0.88; 95%CI: 0.38–2.02, $p = 0.77$; Fig. 10). The results show that in advanced lung cancer, phlegm dampness syndrome is more common than Qi stagnation and blood stasis syndrome.

Seven studies reported a correlation between stages III and IV and Yin deficiency internal heat syndrome and Qi Yin deficiency syndrome.[10–16] A heterogeneity test of the meta-analysis showed that $\chi^2 = 42.48$, $p < 0.00001$, $I^2 = 86\%$, and there was no significant difference among all studies; thus, a fixed effect model could be used. The difference between Yin deficiency internal heat syndrome and Qi deficiency syndrome was statistically significant (n = 264, RR = 0.86; 95%CI: 0.53–1.38, $p = 0.52$; Fig. 11). The results show that in advanced lung cancer, Qi Yin deficiency syndrome is

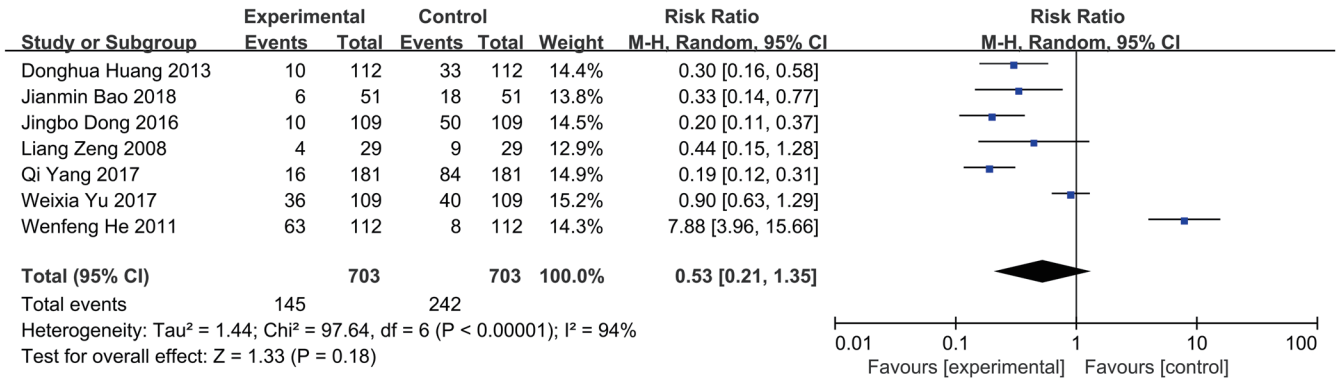

Fig. 9. Stages III and IV were correlated with phlegm dampness syndrome and Qi Yin deficiency syndrome. CI, confidence interval.

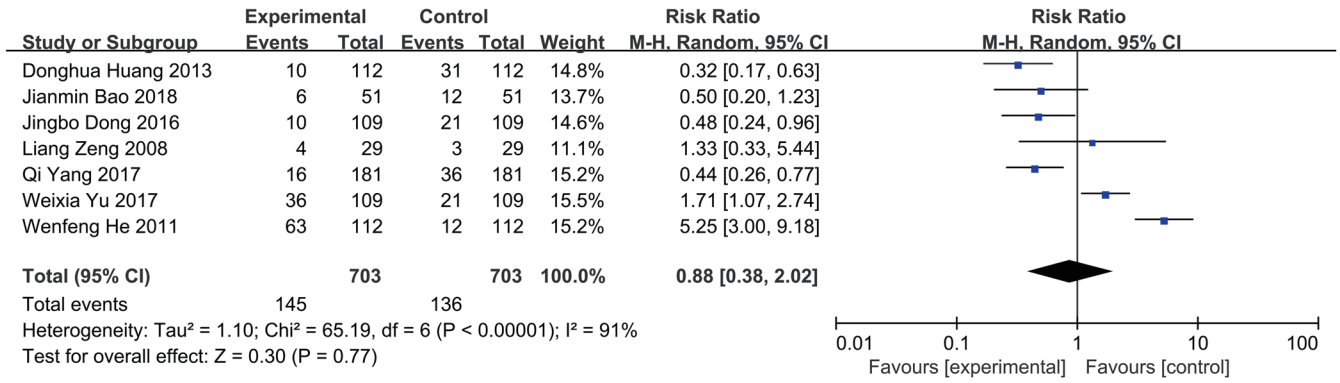

Fig. 10. Stages III and IV are correlated with phlegm dampness syndrome and Qi stagnation and blood stasis syndrome. CI, confidence interval.

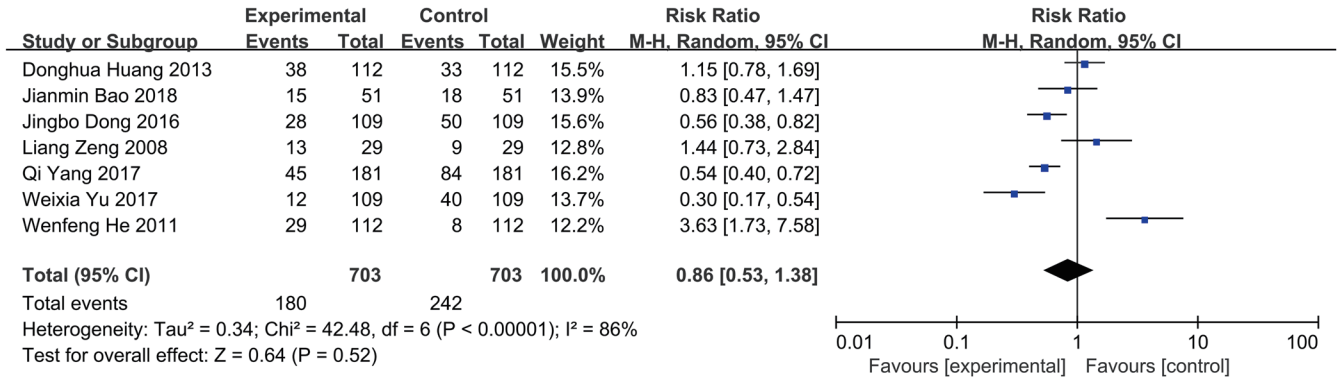

Fig. 11. Stages III and IV were correlated with Yin deficiency internal heat syndrome and Qi Yin deficiency syndrome. CI, confidence interval.

more common than Yin deficiency internal heat syndrome.

Seven studies reported a correlation between stages III and IV and Yin deficiency internal heat syndrome and Qi stagnation and blood stasis syndrome.[10–16] A heterogeneity test of meta-analysis showed that $\chi^2 = 14.27$, $p = 0.03$, $I^2 = 58\%$, and there was no significant difference among all studies, allowing for the use of a fixed effects model. The difference between Yin deficiency heat syndrome and Qi stagnation and blood stasis syndrome was statistically significant (n = 264, RR = 1.35; 95%CI: 0.97–1.87, $p = 0.08$; Fig. 12). The results show that Yin deficiency internal heat syndrome is more common in advanced lung cancer than Qi stagnation and blood stasis syndrome.

Seven studies reported a correlation between stages III and IV and Qi Yin deficiency syndrome and Qi stagnation and blood stasis syndrome.[10–16] A heterogeneity test of meta-analysis showed that $\chi^2 = 16.36$, $p = 0.01$, $I^2 = 63\%$, and there was no significant difference among all studies; thus, a fixed effect model could be used. The difference between Qi and Yin deficiency syndrome and Qi stagnation and blood stasis syndrome was statistically significant (n = 264, RR = 1.68; 95%CI: 1.21–2.33, $p < 0.00001$; Fig. 13). The results show that in advanced lung cancer, Qi Yin deficiency syndrome is more common than Qi stagnation and blood stasis

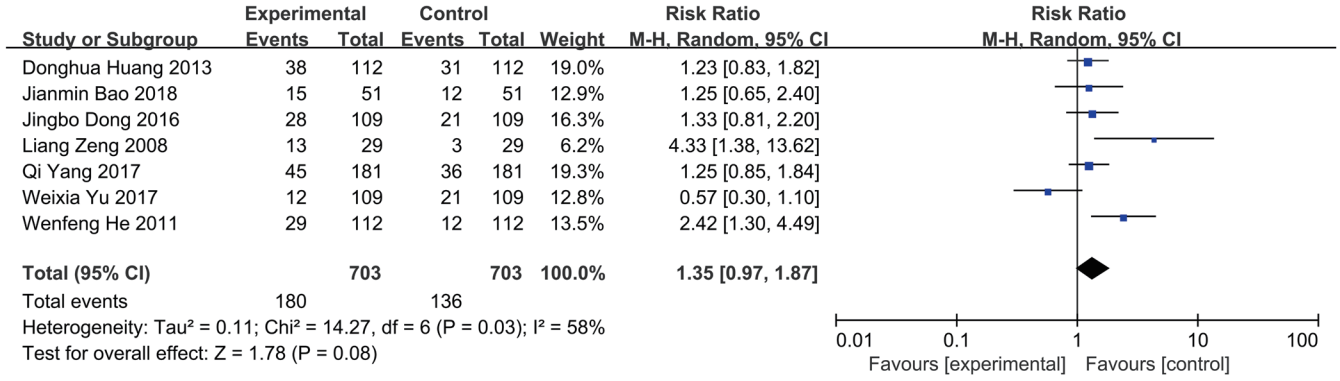

Fig. 12. Stages III and IV are correlated with Yin deficiency internal heat syndrome and Qi stagnation and blood stasis syndrome. CI, confidence interval.

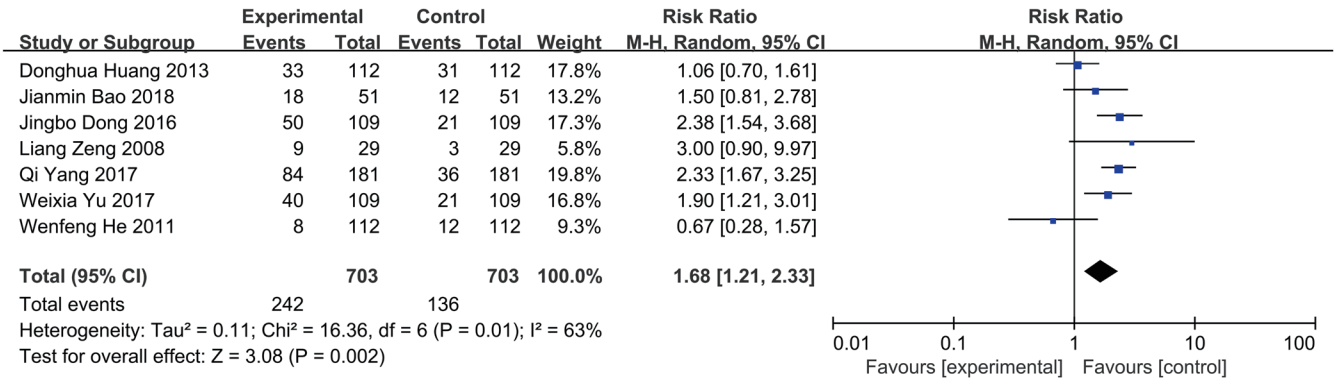

Fig. 13. Stages III and IV are correlated with Qi Yin deficiency syndrome and Qi stagnation and blood stasis syndrome. CI, confidence interval.

syndrome.

To sum up, in stages III and IV, Qi Yin deficiency syndrome > Qi stagnation and blood stasis syndrome > Yin deficiency internal heat syndrome > phlegm dampness syndrome ($p < 0.5$).

Bias risk

Figure 14 presents the Cochrane risk assessment of bias for the included articles. The results showed that 2 trials had a moderate risk of bias and 5 trials had a low risk of bias.

Publication bias analysis

Seven pieces of literature that were part of the study were analyzed using the RevMan 5.4 program. The published pieces of literature were distributed in a concentrated manner, according to a funnel plot analysis, and both the symmetrical distribution and the funnel plot's sides were invalid, indicating a potential publication bias that may be connected to the low caliber of the included research (Fig. 15).

Discussion

Chinese medicine categorizes lung cancer as "lung accumulation" and "cough" based on the clinical signs and symptoms.[17] The loss of good Qi in the body, the combination of external pathogenic factors, the stagnation of evil Qi, the stagnation of lung Qi, the obstruction of Qi and blood flow, the obstruction of body fluid transport, the stagnation of water and fluid in the lungs, prolonged phlegm, the stagnation of Qi, the stasis of the veins, and the formation of lung accumulation over time are some of the theories put forth by scholars regarding the etiology and pathogenesis of lung cancer. The phrases "where evil is gathered, its Qi will be empty" and " where healthy Qi is stored, evil cannot gather" in "Huangdi Neijing" show that the strength of good and evil Qi in the body determines the beginning, course, and prognosis of the disease.[18]

Early-stage solid lung cancer, characterized by both blood depletion and long-term deficiency, manifests as a body-wide insufficiency with local solid tumor manifestations.[19] Common indicators of lung cancer include Qi Yin deficiency syndrome, Qi stagnation and blood stasis syndrome, Yin deficiency internal heat syndrome, and phlegm dampness syndrome. The book "Za Bing Yuan Liu Xi Zhu", considers that lung cancer occurs when "evil accumulates in the chest and obstructs the airway; Qi cannot pass, becoming phlegm and blood; all the evil is fighting and winning, it is not controlled, and then forms a shape and a block." Jiaozang's lung is harmed by the external wind, cold, heat, dampness, dry fire, or internal injuries, as well as by food and exhaustion, leading to lung "Xuanfa Sujiang" function disorder and tumor formation.

TNM staging and TCM syndrome types have some correlation, which could serve as an additional foundation for differentiating TCM syndrome types and classifying lung cancer.[20] When assessing the many forms of syndrome for lung cancer, the TNM staging results might serve as a reference index. The differentiation and categorization of lung cancer are influenced by various aspects, including the tumor's nature, size, and development, as well as the patient's experience with it. The diagnosis of lung cancer is aided by the study of TNM staging, which is also crucial for managing treatment, raising the rate of cure, and prolonging survival.[21] The

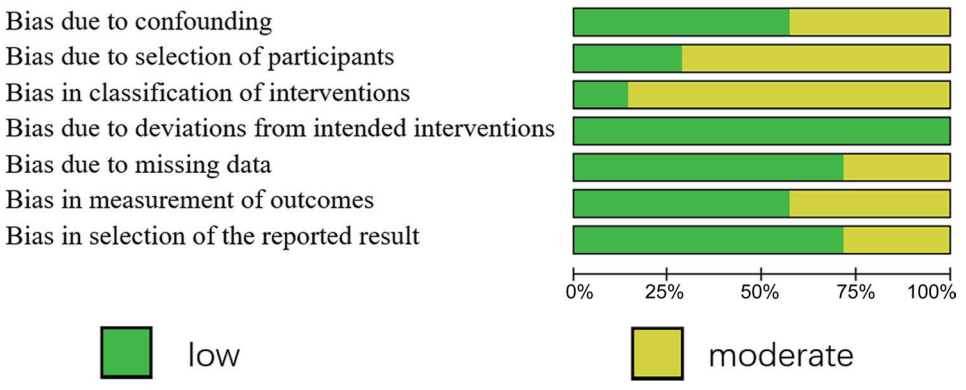

Fig. 14. Bias risk figure of included literature.

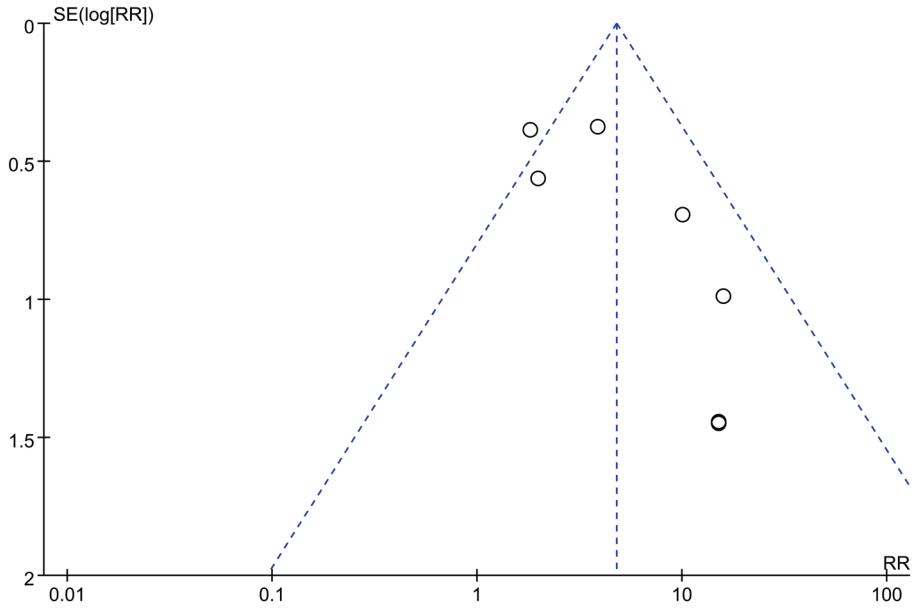

Fig. 15. Publication bias analysis. RR, risk ratio; SE, standard error.

study of Bao Jianmin confirmed that the TNM stage of NSCLC patients has a certain relationship with TCM syndrome types.[22] Using syndrome differentiation and classification of 113 cases of non-small cell lung cancer, he discovered that spleen-deficiency phlegm dampness syndrome was most common in stage I and II lung cancer; in contrast, Yin deficiency internal heat syndrome and Qi Yin deficiency syndrome dominated stage III lung cancer and stage IV lung cancer, respectively. Additionally, Dong *et al*.[23] discovered a relationship between TNM stages and various indications of intermediate and advanced lung cancer.

This study conducted a meta-analysis of 7 included literature and compared the four syndrome types of Qi Yin deficiency syndrome, Qi stagnation and blood stasis syndrome, Yin deficiency internal heat syndrome, and phlegm dampness syndrome pairwise in TNM stages I, II, III, and IV. It was found that in stages I and II, phlegm dampness syndrome > Yin deficiency internal heat syndrome ($p < 0.5$), phlegm dampness syndrome > Qi Yin deficiency syndrome ($p < 0.5$), and phlegm dampness syndrome > Qi stagnation and blood stasis syndrome ($p < 0.05$), with all having statistical significance; in stages III and IV, Qi Yin deficiency syndrome > Qi stagnation and blood stasis syndrome > Yin deficiency internal heat syndrome > phlegm dampness syndrome ($p < 0.05$), with all being statistically significant. Phlegm dampness syndrome dominated in TNM stages I and II, and Qi Yin deficiency syndrome dominated in TNM stages III and IV.

Correct syndrome distinction is the key to improving the quality of diagnosis and treatment and syndrome differentiation and treatment is an important modality of TCM diagnosis and treatment. The academic community has consistently focused on the standardization and objectification of TCM syndrome-based diagnosis.[24,25] Pathogenic buildup, phlegm dampness, Qi stagnation, blood stasis, stagnation heat, and toxicity are the key causes of cancer in its early stages. The primary causative element is phlegm dampness, which is a combination of positive deficiency and evil accumulation in the intermediate stage. Poison stasis persists during the late stage, but positive decay predominates. This is the most dangerous stage of lung cancer development if there is a coexisting Qi and Yin shortage.[26] Adopting appropriate treatment methods based on syndrome differentiation can prolong the survival period of patients with advanced lung cancer.[27,28] According to this study, the likelihood of a Qi Yin deficiency type increases the later the TMN stage, and the more likely it is that solid evil will invade the lung in its early stages or combine with a positive deficiency, mainly phlegm dampness syndrome. This observation essentially aligns with traditional Chinese medicine's understanding of the pathological development process of lung cancer. It is evident that pathogenic variables change from shallow to deep when lung cancer advances, its TMN stage progressively increases, Qi continues to be depleted, Yin is harmed, and Qi Yin deficiency syndrome emerges.

Conclusion

The small sample size of the included literature may lead to a publishing bias. Therefore, clinical experimental investigations should be used to reinforce the regulations and standards for publishing bias. Research procedures for TCM syndrome sorts and Western medicine detection indicators should also be as random as possible. In conclusion, more weight should be given to the phlegm dampness syndrome type in TNM stages I and II and the Qi Yin deficiency syndrome in TNM stages III and IV. Because of this study's shortcomings, a larger sample size and a traditional scientific research design are still needed.

Acknowledgments

None.

Funding

This research was supported by the National Natural Science Foundation of China (Grant no. 81603412); Hebei Provincial Administration of Traditional Chinese Medicine (2019008); Hebei Province "Three Three Three Talent Project" funded project (Grant no.

A202002008). General Projects for Improving Scientific Research Capacity of Hebei College of Traditional Chinese Medicine (Grant no. KTY2019009); Key Laboratory of Integrated Traditional Chinese and Western Medicine Hepatonephrosis in Hebei Province (Grant no. A201902); Hebei Graduate Innovation Funding Project (Grant nos. XCXZZSS2023017; XCXZZSS2023027).

Conflict of interest

DHL has been an editorial board member of *Future Integrative Medicine* since November 2021. The other authors report no conflict of interests in this work.

Author contributions

DHL, HFF, JPZ, and XKL designed this research and were responsible for data preparation, writing, and revision of manuscripts; XHZ, HFF, LJZ, ML, and WLY were responsible for collecting data and translating the manuscript. The final manuscript has been read and approved by all authors.

Data sharing statements

The data used to support the findings of this study are available from the corresponding author upon request.

References

[1] Wang TL, Ouyang CS, Yang LN, Chen Z, Gu J. Effect of Aidi Injection Combined with Gefitinib on Tumor Markers in Patients with Non-Small Cell Lung Cancer. China Pharmaceuticals 2018;27(12):32–35. doi:10.3969/j.issn.1006-4931.2018.12.010.

[2] Wei MN, Qiao YL. Progress of Lung Cancer Screening with Low Dose Helical Computed Tomography. Chinese J Lung Cancer 2019;23(10):875–882. doi:10.3779/j.issn.1009-3419.2020.101.40.

[3] Xu XY, Zhong JJ, Wang L, Xu Y, Shen HW. Study on the Correlation between Traditional Chinese Medicine syndrome type, histopathological classification and EGFR gene in non-small cell lung cancer. New Chin Med 2018;50(10):144–146. doi:10.13457/j.cnki.jncm.2018.10.041.

[4] Jia D, Wang WP. Analysis on the distribution of TCM syndromes in patients with primary lung cancer. Shanxi TCM 2019;35(11):48–50.

[5] Chen Y, Chen YB, Tao RF. Introduction of non-small cell lung cancer treatment content of "CSCO Primary Lung Cancer Diagnosis and Treatment Guidelines 2016". Chin J Practical Intern Med 2017;37(S1):35–37.

[6] Zou L, Chai KQ, Chen JB, Jiang ZK. Study on Drug use law of Professor Chai Kequn in the treatment of Lung Cancer based on data mining. The 15th National Oncology Academic Conference of Integrated Traditional Chinese and Western Medicine; 2017 Jun 16-18; Hangzhou, China 2017;32(01):123–126.

[7] Wang JY, Lu Q, Yang Y. Investigation on TCM constitution and TCM syndrome type of primary bronchial lung cancer. Hebei TCM 2019;41(10):1501–1504. doi:10.3969/j.issn.1002-2619.2019.10.012.

[8] Liu WR, Feng ZZ, Xie Y. The research status and thinking of standard diagnosis and treatment of lung cancer syndrome. Chin Med 2022;37(2):447–452. doi:10.16368/j.issn.1674-8999.2022.02.083.

[9] Xu CW, Zhang B, Lin DM. Histological classification of Lung tumors. J Diagn Pathol 2015;22(12):815–816. doi:10.3969/j.issn.1007-8096.2015.12.032.

[10] Huang DH, Zhou JQ, Lu Q, Zhou YS. Distribution of TCM syndromes in 140 patients with advanced lung cancer. New Chin Med 2013;45(6):105–106. doi:10.13457/j.cnki.jncm.2013.06.040.

[11] Zeng L, Pan T, Xi ZQ. Correlation Analysis of Traditional Chinese Medicine Syndromes, Pathological Classification, and TMN Staging in Primary Bronchial Lung Cancer. Liaoning J Tradit Chin Med 2008;35(12):1808–1809. doi:10.13192/j.ljtcm.2008.12.19.zengl.038.

[12] Yu WX, Yang BL, Zhang N. Correlation between clinicopathological features and TCM syndrome of central airway non-small cell lung cancer. China Inf J Tradit Chin Med 2017;24(001):32–36. doi:10.3969/j.issn.1005-5304.2017.01.009.

[13] Yang Q, Chen WY, Xu YF, Fang ZX, Lv XD. Analysis of the relationship between TCM constitution and TCM syndrome Differentiation and clinical TNM stage and pathological type in lung cancer patients. Chin J Tradit Chin Med 2017;35(11):2927–2929. doi:10.13193/j.issn.1673-7717.2017.11.053.

[14] Dong JB, Lu XF, Weng GA, Hu WD, Zhen JZ, Lu CC, *et al*. Study on Correlation between Constitution Types,Differentiation of Syndromes in Chinese Medicine and TNM Staging, Pathological Patterns of Lung Cancer Patients. Chin J Tradit Med Sci Technol 2016;23(5):506–509.

[15] Bao J. Study on correlation between differentiation of Chiense medecine syndromes and clinical stages, lymphatic metastasis of patients with non-small-cell lung cancer. Chin J Tradit Med Sci Technol 2018;25(4):459-460+473.

[16] He WF, Liao GA, Zhang LL, Zou ZC, Long SQ, Wu WY. TCM Syndrome in 121 Cases of IIIB/IV Non-small Cell Lung Cancer. Liaoning J Tradit Chin Med 2011;38(12):2411–2413.

[17] Zhang JH, Qiao Y, Liu DS. Liu Deshan's Experience in Treating Lung Cancer with Gualou Xiebai Banxia De-coction. World J Integr Tradit Chin Western Med 2023;18(12):2354-2357+2361. doi:10.13935/j.cnki.sjzx.231204.

[18] Sun D, Zhang H, Zheng XL, Qin HA. The Value of Yupingfeng Preparation in the Prevention and Treatment of COVID-19. Chin Med Mod Distance Educ China 2023;21(17):204–206. doi:10.3969/j.issn.1672-2779.2023.17.070.

[19] Zhuang J, Yang G. Experience of Professor Gao Pengxiang in Treating Lung Cancer with Purgative Method. Chin Med Mod Distance Educ China 2019;17(5):36–38. doi:10.3969/j.issn.1672-2779.2019.05.014.

[20] Xiao L, Wang ZW, Xuan LG, Zhen W, Zhang J, Feng Y. Analysis of TCM Syndromes and Related Factors after Anlotinib Treatment in Advanced Non-small Cell Lung Cancer. Liaoning J Tradit Chin Med 2022;49(9):74–78. doi:10.13192/j.issn.1000-1719.2022.09.021.

[21] Zhang H, Jiang H, Zhu L, Li J, Ma S. Cancer-associated fibroblasts in non-small cell lung cancer: Recent advances and future perspectives. Cancer Lett 2021;514:38–47. doi:10.1016/j.canlet.2021.05.009, PMID:34019960.

[22] Bao JM, Shen D, Yu CF, Fu HW, Chen LL, Chen D, *et al*. Correlation analysis between TCM Syndrome Types and peripheral blood dendritic cell function in patients with non-small cell lung cancer. Zhejiang J Tradit Chin Med 2017;52(11):2. doi:10.13633/j.cnki.zjtcm.2017.11.007.

[23] Dong WJ, Lu Q, Jin H, Xin ZF, Ge MN. Correlation between Morphological Indexes of Exfoliated Cells of Tongue Coating and TCM Syndromes and Pathological Stages in Advanced Lung Cancer. Hebei J Tradit Chin Med 2018;33(4):14–16. doi:10.16370/j.cnki.13-1214/r.2018.04.004.

[24] Duan F, Zhu ZZ, Hu JQ. Progress in Syndrome Diagnosis and Standardization of Coronary Heart Disease. J Tradit Chin Med 2016;31(11):1771–1776. doi:10.16368/j.issn.1674-8999.2016.11.495.

[25] Gu HR, Fu QQ, Li XH, Tan YY, Chen LM. Research progress and trend of TCM syndrome. Chin J Tradit Chin Med 2020;35(3):1340–1343.

[26] Bao Y, Zhang PT. Review on TCM syndromes of primary bronchial lung cancer. Global Tradit Chin Med 2022;15(7):1273–1279. doi:10.3969/j.issn.1674-1749.2022.07.036.

[27] Peng LZ, Tang J. Analysis of Correlation Between TCM Syndromes, Immune Function and Prognosis of Advanced Lung Cancer. Practical J Cancer 2023;38(12):1968–1971. doi:10.3969/j.issn.1001-5930.2023.12.011.

[28] Huang CM, Guan W. The Effect of Targeted Therapy Combined with Traditional Chinese Medicine Syn-drome Differentiation in the Treatment of Non-Small Cell Lung Cancer. World J Compos Med 2023;9(11):33–36. doi:10.11966/j.issn.2095-994X.2023.09.11.10.