

Lentianan combined with cisplatin for the treatment of non-small cell lung cancer

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Abstract

Background: A growing number of studies suggest that lentianan combined with cisplatin thoracic injection for the treatment of lung cancer is an effective combination of traditional Chinese and Western medicine, which has a continuous and beneficial effect on eliminating clinical symptoms and improving cachexia in lung cancer patients. However, whether this treatment is effective and safe for lung cancer patients or not, evidence supporting the effectiveness and safety of this treatment is still incomplete. Besides, there is lack of systematic review to assess the detailed situation (including risk of bias and methodology) of current related clinical studies.

Objective: This study aimed to evaluate the effectiveness and safety of lentianan combined with cisplatin thoracic injection in the treatment of lung cancer.

Methods: The major databases (Embase, PubMed, the Cochrane Library, China National Knowledge Infrastructure, Chinese Scientific Journals Database [VIP] Database, Chinese Biomedical Literature Service System [SinoMed], and Wanfang Database) were searched from inception to March 1, 2020. Randomized controlled trials (RCTs) of lentianan combined with cisplatin chest injection on patients with non-small cell lung cancer (NSCLC) were identified. Two assessors reviewed each trial independently. The methodological quality of the eligible studies was evaluated according to the Cochrane Collaboration's tool for assessing risk of bias. Both the data extraction and the literature quality screening evaluation were conducted independently by 2 researchers.

Results: Totally 17 clinical RCTs were included in this study, involving 1390 patients. Meta-analysis results showed that the clinical efficacy (risk ratio [RR]= 1.34, 95% confidence interval [CI] 1.21–1.48), effective subgroup analysis (RR= 1.51, 95% CI 1.3–1.77), and quality of life (RR= 1.48, 95% CI 1.27–1.72), the differences are statistically significant. In terms of adverse reactions, mainly related to gastrointestinal reactions and bone marrow suppression, the incidence and degree of adverse reactions of lentianan combined with cisplatin thoracic injection group were lower than those of cisplatin thoracic injection group alone.

Conclusions: The current evidence prompted that Lentianan combined with cisplatin in thoracic injection might benefit patients with NSCLC on a certain extent; this systematic review revealed some definite conclusions about the application of Lentianan combined with cisplatin in thoracic injection for NSCLC. Due to the low methodological quality, high risk of bias, and inadequate reporting on clinical data, these results still require verification by a large number of well designed, heterogeneous RCT studies. More rigorous, multicenter, sufficient-sample, and double-blind RCTs are warranted.

Abbreviations: CNKI = China National Knowledge Internet, CR = complete response, KPS =Karnofsky Performance Status, LNT = Lentianan, NCCN = National Comprehensive Cancer Network, NSCLC = non-small cell lung cancer, PD = progressive disease, PR = partial response, RCTs = randomized controlled trials, SD = stable disease, SinoMed = Chinese Biomedical Literature

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This systematic review does not require ethics approval and will be submitted to a peer-reviewed journal.

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CZ as the only first author.

The datasets generated during and/or analyzed during the current study are publicly available.

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Service System, TCM = Traditional Chinese Medicine, VIP = Chinese Scientific Journals Database, WHO = World Health Organization.

Keywords: chemotherapy, cisplatin, lentinan, meta-analysis, NSCLC, randomized controlled trials, review, TCM

1. Introduction

Lung cancer is a lung malignant tumor that originates in the trachea, bronchial mucosa, or glands, and has become the most common and frequent malignant tumor. NSCLC accounts for about 80% of all lung cancers, and about 75% of patients are in the middle and late stages when they are discovered, and the 5-year survival rate is very low. According to the latest global cancer statistics report in 2019, lung cancer is the malignant tumor with the highest incidence in the world^[1] and one of the main causes of death of cancer patients. In China, the situation of lung cancer is also not optimistic, and the overall incidence rate ranks first.^[2] At present, platinum-based combination chemotherapy is still the standard first-line treatment for lung cancer.^[3,4] However, chemotherapy is often accompanied by serious toxic and side effects,^[5] so looking for a drug that can both enhance the efficacy of chemotherapy and reduce the toxic and side effects of chemotherapy is one of the present research hotspots in the treatment of lung cancer.

In recent years, TCM has gradually shown its unique advantages in the treatment of lung cancer.^[6,7] TCM combined with radiotherapy and chemotherapy has become an effective method for the treatment of lung cancer, which can effectively prolong the survival period and improve the quality of life.^[8-10] Modern studies have shown that lentinan is a key factor in regulating the body's immune system,^[11,12] which not only enhances the killing effect of chemotherapeutic drugs on tumor cells and plays a sensitizing role,^[13] but also can effectively inhibit tumor angiogenesis and suppress growth of tumors,^[14] like *Salvia Officinalis* Extract and Bevasomab,^[15,16] thereby improving the quality of life of patients, prolonging survival, without any toxic and side effects, has become a more commonly used TCM anti-tumor drugs.^[17-19]

1.1. Why it is important to do this review

At present, the clinical trials of lentinan combined with cisplatin in the treatment of lung cancer are increasing. Although the application of lentinan is a commonly used clinical practice, there is still uncertainty about its effects. Moreover, the intensity of evidence has been poor and there has been lack of systematic analysis to assess the effectiveness and safety of lentinan combined with cisplatin thoracic injection in the treatment of NSCLC from randomized controlled trials (RCTs).

Therefore, this study aims to evaluate objectively the effectiveness and safety of lentinan combined with cisplatin thoracic injection in the treatment of NSCLC by integrating the existing trials. This study aims to further improve and update the clinical data by collecting RCTs of lentinan combined with cisplatin thoracic injection in the treatment of lung cancer, using the method of meta-analysis, follow the evidence-based medicine model to systematically evaluate the efficacy and adverse reactions of lentinan combined with cisplatin thoracic injection in the treatment of NSCLC, provide evidence-based evidence for its clinical effectiveness and safety research, and provide reference for clinical treatment of lung cancer.

The article searches for relevant literature through a certain search strategy, extracts data and evaluates the quality of the finally included literature according to the inclusion and exclusion criteria, and finally uses Revman 5.3 software to perform statistical analysis on the collected information, and draw results and conclusions.

For the first time, this article systematically summarized the efficacy of lentinan combined with cisplatin pleural injection in the treatment of lung cancer, and subgroup analysis was carried out on cisplatin alone and cisplatin-containing regimen alone, which strongly confirmed the efficacy of lentinan in the treatment of lung cancer.

2. Methods

2.1. Registration

The study protocol has been registered on international prospective register of systematic review (PROSPERO). These records have been submitted for publication and are being assessed by the editorial team (Once the registration number is generated, the author contacts the editor). The procedure of this protocol will be conducted according to the Preferred Reporting Item for Systematic Review and Metaanalysis Protocols (PRISMA-P) guidance.^[20]

2.2. Eligibility criteria

2.2.1. Types of studies. All the RCTs reporting the application of lentinan combined with cisplatin thoracic injection for the treatment of NSCLC were included. Studies irrelevant to RCTs or trials that participants, control measures, interventions, and outcomes did not meet the criteria were excluded.

2.2.2. Participants. All the participants enrolled in this study had to meet at least one of the current or past diagnostic criteria of NSCLC. The diagnostic criteria's included "Lung cancer patients diagnosed by pathology or cytology" or "NCCN guidelines" or "relevant expert consensus."^[21]

2.2.3. Interventions. The experimental group was treated with lentinan combined with cisplatin thoracic injection, and cisplatin thoracic injection alone must be used in the control group.

2.2.4. Outcomes. The primary outcome measures will include first reference to the WHO solid tumor efficacy evaluation criteria: the efficacy indicators are divided into CR for the complete disappearance of all measurable lesions for at least 1 month; PR is the reduction in the product of the diameters of all measurable lesions $\geq 50\%$, maintained for >1 month; SD is the product of all measurable lesion diameters shrinking $<50\%$ or increasing $<25\%$; PD is the product of all measurable lesion diameters $\geq 25\%$ or new lesions appear. The effective rate is $CR + PR / \text{total number of cases} \times 100\%$. Secondly, Quality of life score (KPS score): improvement is a score increase of ≥ 10 points; decline is a score decrease of ≥ 10 points; stability is a score increase or decrease of <10 points. Thirdly, with reference to the

Table 1**Search terms.**

Search block	Search items
Participants	Pulmonary Neoplasms OR Neoplasms, Lung OR Lung Neoplasm OR Neoplasm, Lung OR Neoplasms, Pulmonary OR Neoplasm, Pulmonary OR Pulmonary Neoplasm OR Lung Cancer OR Cancer, Lung OR Cancers, Lung OR Lung Cancers OR Pulmonary Cancer OR Cancer, Pulmonary OR Cancers, Pulmonary OR Pulmonary Cancers OR Cancer of the Lung OR Cancer of Lung
Intervention	cis-Diamminedichloroplatinum (II) OR Platinum Diamminodichloride OR Diamminodichloride, Platinum OR cis-Platinum OR cis Platinum OR Dichlorodiammineplatinum, cis-Diamminedichloroplatinum OR OR cis Diamminedichloroplatinum OR Platino OR NSC-119875 OR OR Platinol OR Biocisplatinum OR Platidiam, Chinese Herbal OR Chinese Drugs, Plant OR Chinese Herbal Drugs OR Herbal Drugs, Chinese OR Plant Extracts, Chinese OR Chinese Plant Extracts OR Extracts, Chinese Plant OR Medicine, Chinese Traditional OR Traditional Chinese Medicine OR Chung I Hsueh OR Hsueh, Chung I OR Traditional Medicine, Chinese OR Zhong Yi Xue OR Chinese Traditional Medicine OR Chinese Medicine, Traditional OR Traditional Tongue Diagnosis OR Tongue Diagnoses, Traditional OR lentinan
Study design	Randomized controlled trial OR controlled clinical trial OR randomized OR drug therapy OR randomly OR trial OR groups

classification of toxic and side effects of anticancer drugs formulated by WHO, it is divided into 0-IV degrees.

2.3. Search strategy

We searched electronic literature databases including PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure, Chinese Scientific Journals Database (VIP) Database, Chinese Biomedical Literature Service System (SinoMed), and Wanfang Database. The retrieval time was from the inception date of the databases to March 1, 2020. There was no limitation on the language of publication. Only clinical trials as a limitation were included and searched. Moreover, the search strategy for selecting the fields of title, abstract, or keyword was different referring to the characteristics of databases. Search terms were grouped into 3 blocks (Table 1).

2.4. Study selection and data extraction

Literature retrieved citations were managed by Note-Express software. Both the data extraction and the literature quality screening evaluation were conducted independently by 2 researchers (CZ and FL). Studies which were duplicated or not accordant with eligibility criteria including types of studies, participants, interventions, and outcomes in this study were excluded. Disagreements were resolved by discussion or arbitrated by a third author (YJ) if needed. The following data items were extracted: first author, publication year, sample size, sex, age, diagnosis standard, intervention and control measures, course of treatment, adverse effects report, and outcome assessment.

2.5. Risk of bias assessment

The methodological quality of the eligible studies was evaluated according to the Cochrane Collaboration's tool for assessing risk of bias.^[22] The assessment details included: sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other sources of bias. Each assessment was graded into 3 levels: "low risk" or "high risk" or "unclear risk." A funnel plot was applied to evaluating publication bias of the included studies. For example, if the correct random method is applied, it should be evaluated as low risk, and if the random method is not used, it should be evaluated as high risk. For those that only mention the random method but do not record the random method in detail, it should be evaluated as unclear risk.

2.6. Data synthesis and statistical analysis

Statistical analyses were performed by RevMan 5.3 software provided by Cochrane Collaboration. Data were presented by risk ratio (RR) with its 95% confidence interval (CI) for dichotomous outcomes (total effective rate of NSCLC and total effective rate of KPS improvement and total incidence of adverse reactions). The I^2 test was calculated to determine the amount of heterogeneity. According to the results of the heterogeneity test, a fixed effect model ($P > .05$, $I^2 < 50\%$) or a random effect model ($P < .05$, $I^2 > 50\%$) was selected.

2.7. Sensitivity analysis and subgroup analysis

Sensitivity analysis or subgroup analysis was performed to analyse the heterogeneity or inconsistency among the studies and to explore potential sources of heterogeneity. We created a qualitative analysis when data extraction was insufficient.

2.8. Quality of evidence

The quality of evidence for each outcome was assessed according to the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) Handbook^[23] by 2 reviewers (CZ and TW) independently. Any disagreements about assessments were resolved by a third reviewer. The scores of GRADE were downgraded based on 5 factors:

1. Risk of bias (if there were poor trials with a high risk of bias and sensitivity analysis results had poor robustness through excluding the poor trials, evidence rated down by 1 level. If the most domains had unclear methodological bias risk, evidence rated down by 1 level).
2. Inconsistency (Inconsistency was assessed according to the outcomes of the χ^2 test and I^2 statistic reported in the systematic reviews. If I^2 was $>50\%$, $P < .05$, and the heterogeneity could not be explained by conducting subgroup analysis, the quality of evidence was downgraded).
3. Indirectness (if the participants, intervention, outcomes, or comparison had an indirect comparison in the study, evidence rated down by 1 level).
4. Imprecision (for dichotomous outcomes, if the number of events for each outcome was <300 , evidence was downgraded. For continuous outcomes, if the number of events for each outcome was <400 , evidence was downgraded).
5. Publication bias (publication bias was assessed by presenting funnel plot and conducting Egger test. A 2-tailed P value of $<.05$ was considered to indicate publication bias).

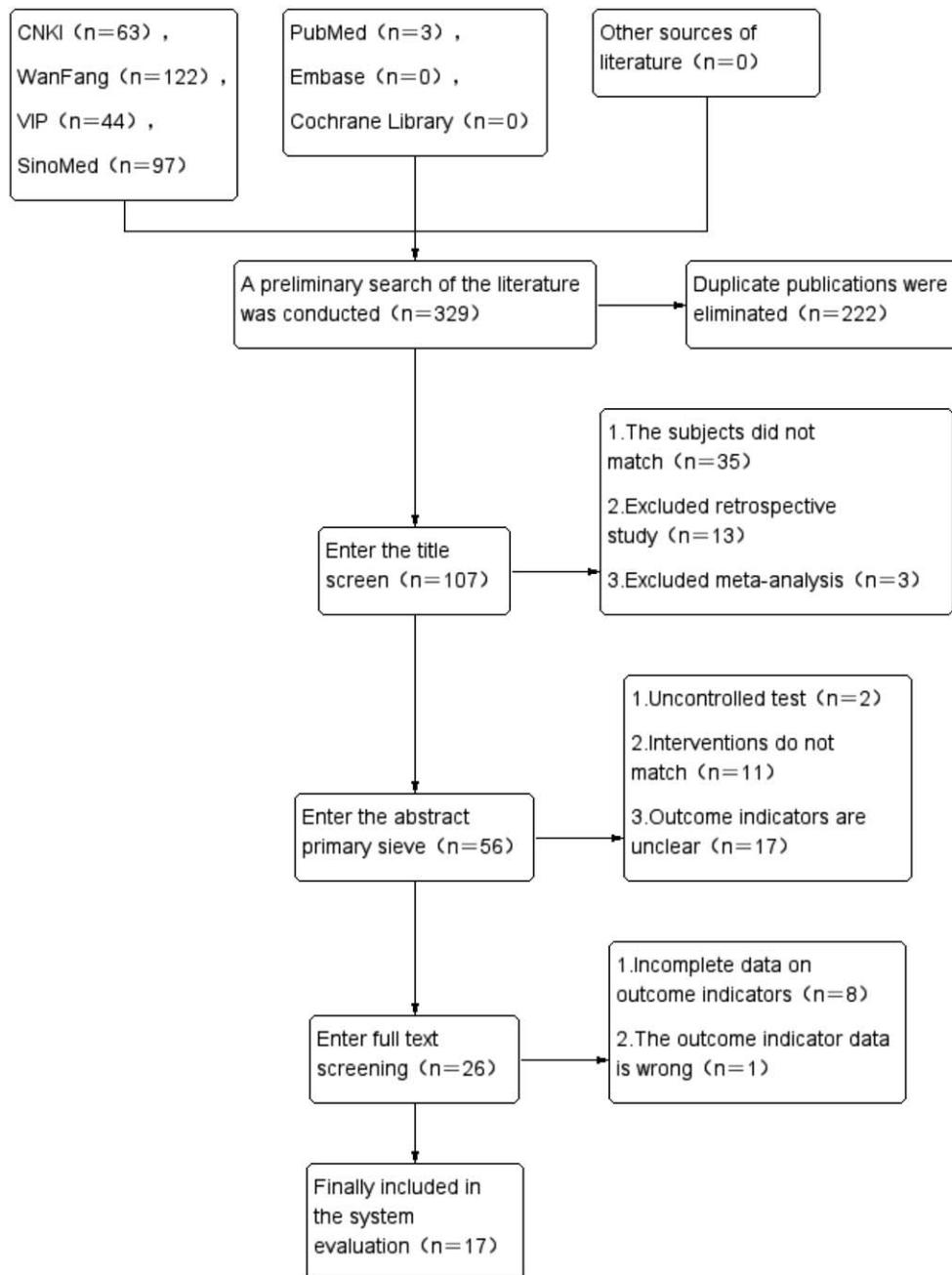


Figure 1. Flow diagram of studies identified, included, and excluded.

2.9. Communicate with the authors of the primary studies

Two reviewers (CZ and YJ) contacted the authors of the included primary studies for detailed information if the information in the original article did not provide.

3. Results

3.1. Study identification

The process of study selection and identification is shown in PRISMA Flow Diagram. A total of 326 Chinese literatures and 3 English literatures potentially relevant articles were initially

screened in the electronic databases based on our literature searching strategy. After removing 222 duplicates, 107 articles were identified for further analysis. Through screening the titles and abstracts, 56 articles were excluded. A total of 26 full-text articles were retrieved for further assessment. Finally, 17 full-text articles were then assessed for eligibility (Fig. 1).

3.2. Study characteristics

The included studies were all in Chinese. They were first published in 2006 and latest in 2017. A total of 1390 patients with NSCLC were included in 17 studies. Among them, the

Table 2
The basic characteristics of the included studies.

Included study	Sample size (n)		Age, y	Instalment	Intervention		Course of treatment (cycles)	Outcome assessment
	Experimental group	Control group			Experimental group	Control group		
Ding et al, 2012 ^[24]	44/42		NR	IIIA-IV	LNT + NP	NP	2	(1) (2) (3)
Dai, 2014 ^[25]	34/34		25–78	IIIA-IV	LNT + GP	GP	2	(1) (2) (3)
Liu et al, 2017 ^[26]	36/36		NR	NR	LNT + cisplatin	Cisplatin	3	(1) (3)
Lu et al, 2012 ^[27]	24/28		32–70	NR	LNT + cisplatin	Cisplatin	4	(1) (2) (3)
Wu, 2015 ^[28]	126/105		NR	IIIB-IV	LNT + GP	GP	2	(1) (2) (3)
Tang and Liu, 2010 ^[29]	32/32		32–75	IIIB-IV	LNT + Cisplatin	Cisplatin	2	(1) (2) (3)
Chang et al, 2013 ^[30]	40/40		NR	NR	LNT + Cisplatin	Cisplatin	4	(1) (2)
Zhang, 2016 ^[31]	70/70		60–85	III-IV	LNT + GP/TP	GP/TP	6	(1) (2) (3)
Xu et al, 2017 ^[32]	29/29		20–80	NR	LNT + cisplatin	Cisplatin	4	(1) (2) (3)
Dai, 2010 ^[33]	26/26		43–75	NR	LNT + TP	TP	2	(1) (2) (3)
Li et al, 2013 ^[34]	30/22		43–81	IIIB-IV	LNT + GP	GP	2	(1) (2) (3)
Li et al, 2009 ^[35]	31/31		38–69	NR	LNT + GP	GP	2	(1) (2)
Wang, 2011 ^[36]	40/42		>18	NR	LNT + GP	GP	2	(1) (2) (3)
Wang and Jiang, 2014 ^[37]	40/40		NR	IV	LNT + GP/TP/DP	GP/TP/DP	4	(1) (2) (3)
Wang et al, 2006 ^[38]	42/39		>18	III-IV	LNT + cisplatin	Cisplatin	2	(1) (2) (3)
Tong et al, 2011 ^[39]	27/23		38–75	NR	LNT + cisplatin	Cisplatin	2	(1) (2) (3)
Xiao et al, 2015 ^[40]	40/40		18–70	II-IV	LNT + DP	DP	2	(1) (2)

(1)=clinical efficacy, (2)=quality of life, (3)=adverse reactions, DP=Docetaxel + cisplatin, GP=gemcitabine + cisplatin, LNT=lentinan, NP=vinorelbine + cisplatin, NR = not report, TP=paclitaxel + cisplatin.

experimental group of 7 studies^[24–30] was the treatment of pleural injection of lentinan combined with cisplatin, the control group was the treatment of pleural injection of cisplatin alone; the experimental group of 10 studies^[30–36] was the treatment of pleural injection of lentinan combined with cisplatin. The control group was treated with cisplatin-containing regimen by intrapleural injection, and the course of treatment was 2-6 cycles. The basic characteristics of the included studies are shown in Table 2.

3.3. Risk of bias within studies

Of the 17 studies included, 4 studies used the correct random method,^[26,27,32,34] which is low risk, and 8 studies only mentioned random and did not describe specific random methods,^[24,25,28,29,31,37–39] 5 studies did not mention whether it is random,^[30,33,35–37,40] which is an unclear risk. All 17 studies did not mention the allocation of hidden and blind methods,

which is an unclear risk. No experimental design was available for 17 studies, so they were rated as unclear risk in selective reporting. No data were found to be incomplete in any of the 17 studies, which was rated as low risk (Fig. 2).

3.4. Meta-analysis

3.4.1. Clinical effect. Seventeen studies^[24–40] reported the clinical efficacy of lentinan combined with cisplatin in the thoracic cavity for the treatment of NSCLC patients. Heterogeneity analysis showed that the included studies had better homogeneity ($I^2=0\%$, $P=0.7$), a fixed-effects model was selected, and the results showed that (RR = 1.34, 95% confidence interval [CI] 1.21–1.48, $Z=5.79$, $P<.00001$), indicating that the clinical efficacy of lentinan combined with cisplatin in thoracic injection was superior to that of cisplatin alone. Platinum injection into the chest, the difference was statistically significant (Fig. 3).

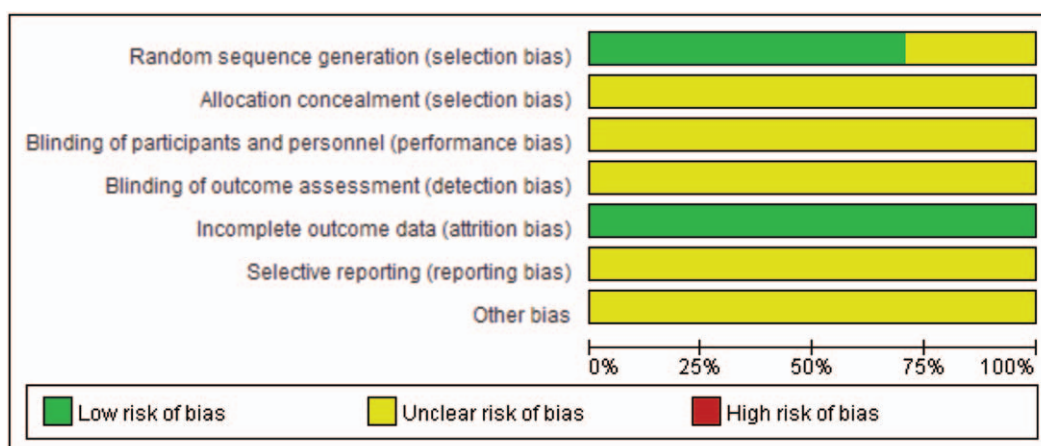


Figure 2. Risk bias analysis.

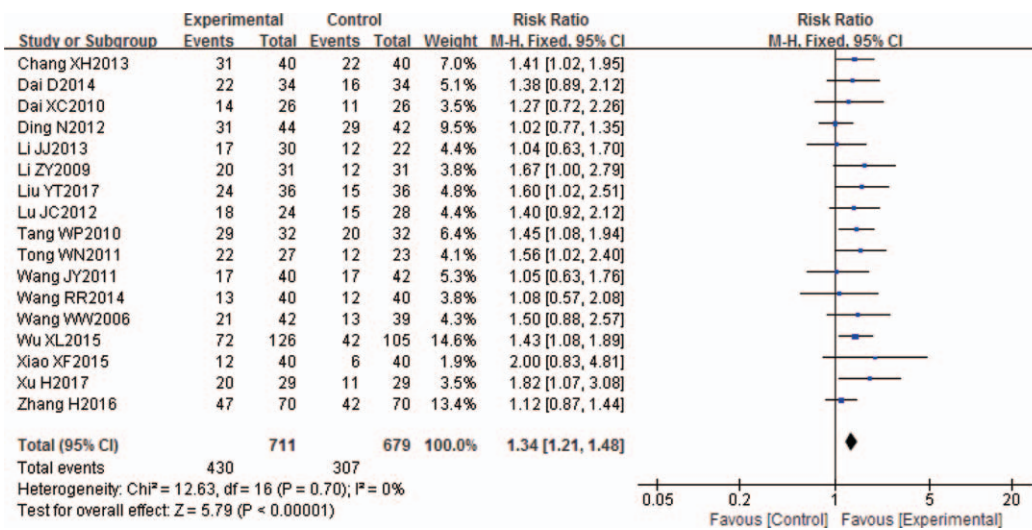


Figure 3. Meta analysis of clinical efficacy comparison of lentinan combined with cisplatin in thoracic cavity for non-small cell lung cancer patients.

3.4.2. Clinical effectiveness subgroup analysis. Seventeen studies^[24–40] reported the clinical effectiveness of lentinan combined with cisplatin in the thoracic cavity for the treatment of NSCLC patients. According to the different interventions, a subgroup analysis was performed. In the case of cisplatin alone, the difference was statistically significant (RR=1.51, 95% CI 1.3–1.77, $P < .00001$). The efficiency of pleural injection of lentinan combined with cisplatin was higher than that of single injection. The difference was statistically significant (RR=1.34, 95% CI 1.21–1.48, $P < .0007$) in the intrathoracic injection with cisplatin (Fig. 4).

3.4.3. Quality of life. Sixteen studies^[24–40] reported the quality of life of patients with NSCLC treated with lentinan combined with cisplatin in thoracic cavity, and analyzed by heterogeneity test: there was heterogeneity among the included studies ($I^2 = 63%$, $P = .0003$), using random-effects model, the results show that (RR=1.48, 95% CI 1.27–1.72, $Z = 5.07$, $P < .00001$), indicating that the quality of life of lentinan combined with cisplatin is better. There was a statistically significant difference in the intrathoracic injection of cisplatin (Fig. 5).

3.4.4. Security. Among the 17 studies, safety mainly involved digestive tract reactions, bone marrow suppression, liver and kidney damage, chest pain, fever, etc., among which 14 studies^[20–25,27–30,32–35] reported the digestive tract and bone marrow suppress adverse reactions. 14 studies^[24–26,28–35,38–40] reported adverse reactions of bone marrow suppression. The incidence and degree of adverse reactions of lentinan combined with cisplatin thoracic injection were lower than that of cisplatin thoracic injection alone, and there were fewer adverse reactions above III in both groups, which were related to the use of cisplatin. It can be relieved after treatment, and no other serious adverse events were found. From this point of view, lentinan is safe.

4. Discussion

Practice has shown that^[41–43] the TCM has a definite cure for a variety of malignant tumors, and it has gradually become a recognized method of malignant tumor treatment. The treatment

of cancer patients should be based on the overall grasp, taking into account the specimens, according to the patient’s own constitution to identify the disease and dialectical treatment, can effectively alleviate clinical symptoms, reduce the side effects of simple Western medicine treatment, prolong survival, and improve quality of life.

In this study, all published RCTs were collected and 17 clinical studies of lentinan combined with cisplatin thoracic injection in the treatment of lung cancer were obtained. Meta-analysis was used to systematically evaluate the efficacy of lentinan combined with cisplatin thoracic injection in the treatment of lung cancer. This study shows that the clinical efficacy of lentinan combined with cisplatin thoracic injection in the treatment of lung cancer patients is significantly higher than that of cisplatin thoracic injection alone, and can improve the quality of life of patients and reduce the incidence of bone marrow suppression and gastrointestinal reactions. Polysaccharide combined with chemotherapy can play a role in reducing toxicity and increasing efficacy, which can ensure the smooth progress of chemotherapy. Based on a detailed summary and analysis of the series of outcome indicators, this study also conducted a subgroup analysis of clinical effectiveness based on different interventions in the treatment group. The subgroup analysis strengthened the strength of the results.

The results of this study are consistent with previous related literature reports, but the results are more substantial and clinically practical, which can effectively guide clinical applications. Just like Raman-enhanced spectroscopy (RESpect) probe technology or^[44] Markus Ionization Chamber Detector,^[45] new technologies have the opportunity to be transformed into clinical practice. Later, we can further study the pathophysiological mechanism of lentinan, such as how to improve the patient’s immune function, how to improve the patient’s blood indicators,^[46–49] and so on.

5. Limitations

When formulating the criteria for literature inclusion and exclusion, this study clearly stipulated the years of inclusion of

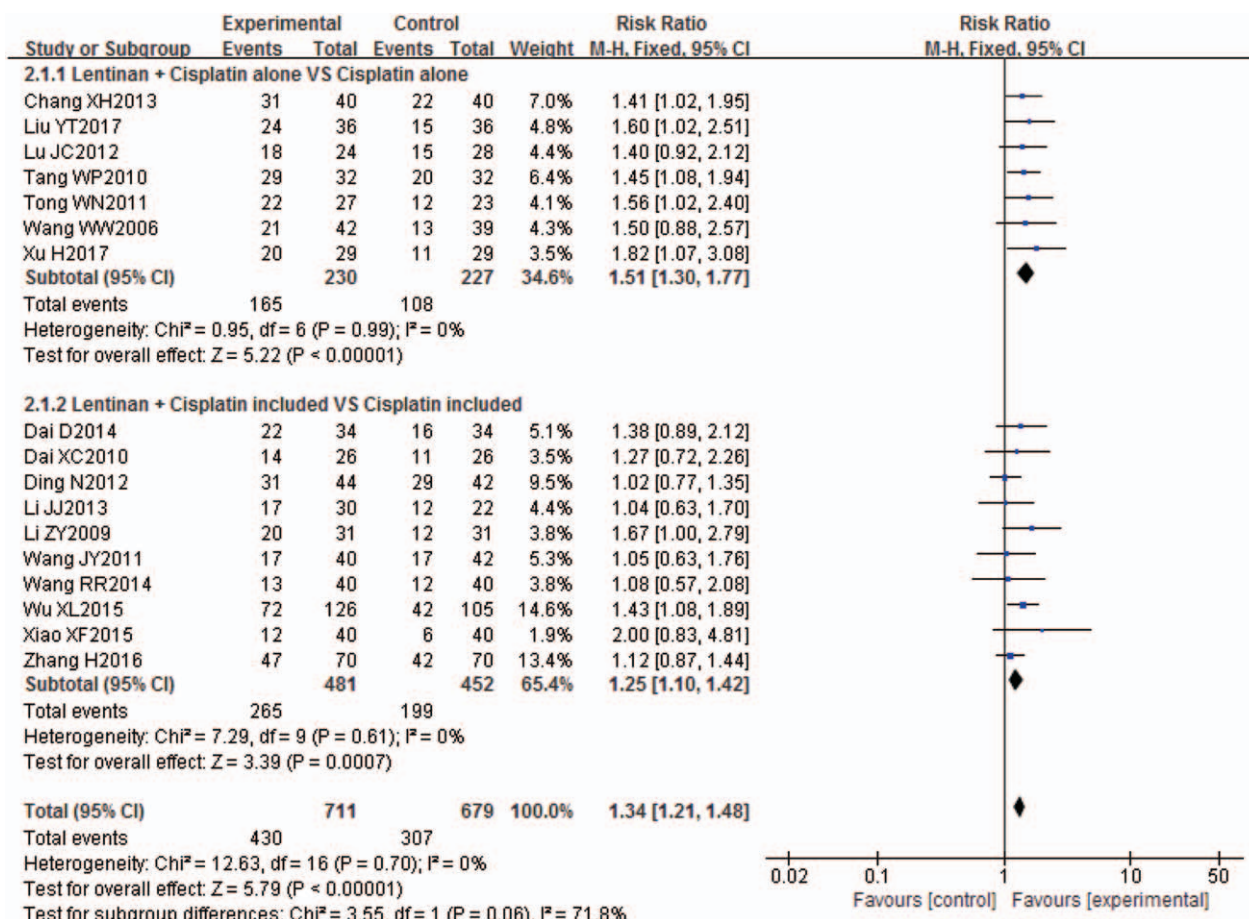


Figure 4. Meta-analysis of the subgroup analysis of clinical efficacy of lentinan combined with cisplatin in the thorax.

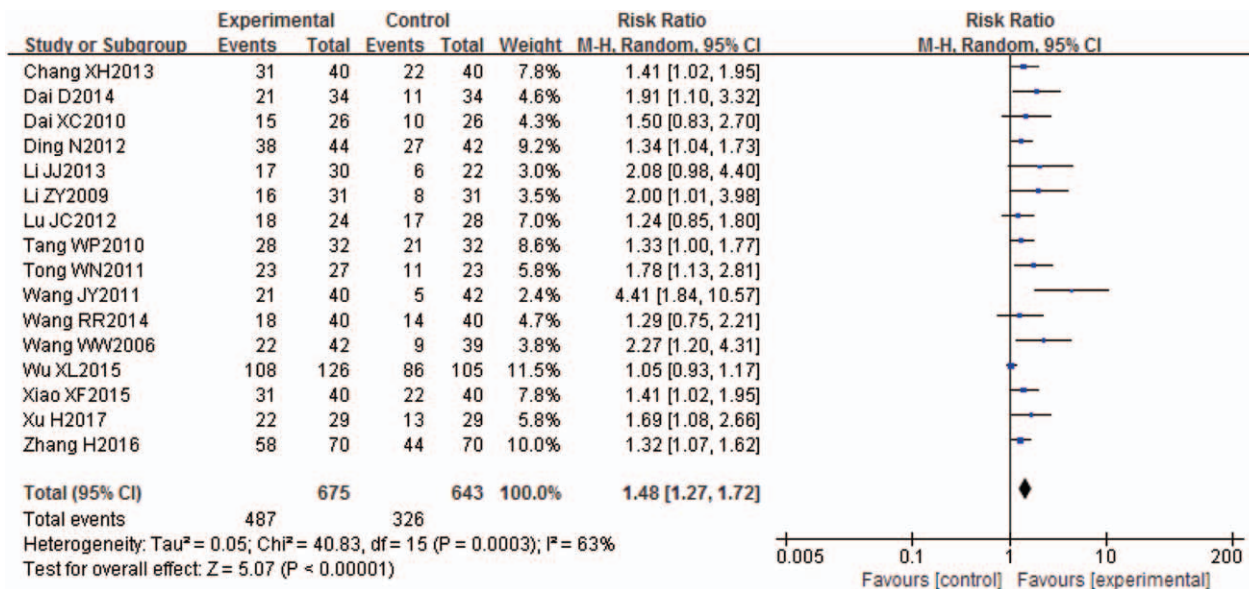


Figure 5. Meta-analysis of lentinan combined with cisplatin for intrathoracic injection in the treatment of non-small cell lung cancer patients.

the literature, the research object, and outcome indicators and other relevant conditions, which basically controlled the selection bias of this study. However, this study also has certain limitations. For example, most of the studies are based on small sample trials, and some of them have methodological problems. The conclusions obtained have limited reference value; the included studies are all positive results, and the possibility of publication bias cannot be completely ruled out. In addition, the quality of the studies included in the literature is not high, which affects the reliability of the above conclusions to varying degrees; all the included literature do not mention blinding, nor do they hide the distribution, and do not describe the loss of follow-up and withdrawal in detail. There are still some gaps in the requirements of syndrome medicine, which leads to the credibility of the research and the low quality of the literature. Based on this, in the future clinical trials, the research subjects should be randomly grouped correctly, and different interventions should be implemented in different groups to control the different effects. To the greatest extent possible to avoid the various biases that may occur in the design and implementation of clinical trials, balance confounding factors, improve the effectiveness of statistical tests, and thus improve the scientific nature of research.

6. Conclusion

Although there are some shortcomings in the literature included in this systematic review, the results show that lentinan combined with cisplatin pleural injection can effectively improve the clinical efficacy of lung cancer patients, and the safety is good. The pleural injection of lentinan combined with cisplatin has the effect of reducing toxicity and increasing efficacy, and has certain guiding significance for the clinical treatment of lung cancer. At the same time, it is recommended that researchers refer to this study with caution in contacting clinical practice and combine with the consensus of relevant guidelines to make comprehensive judgments.

In the current environment of precision medicine, precision and individualized treatment has become the mainstream direction of modern medicine development, further confirming the efficacy of Chinese medicine, laying the foundation for future clinical research, and providing references for doctors and patients to choose treatment. The clinical work and future research directions have important guiding significance. It is of great significance to enhance the efficacy of Chinese medicine, save more social resources, promote the promotion of Chinese medicine internationally, and improve the status of Chinese medicine in the field of lung cancer treatment. It is of great significance to narrow the gap with international modern medical research, and to further increase Chinese medicine in Africa. The share in the treatment of small cell lung cancer provides the basis and foundation.

6.1. Ethics and dissemination

This review does not require the ethical approval because there are no concerns about the patients' privacy. The results of the meta-analysis will be reported according to the PRISMA extension statement and disseminated in a peer-reviewed journal.

Author contributions

Conceptualization: Chenchen Zhao, Haifeng Yan, Feng Liang, Yingjie Jia.

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Writing – original draft: Chenchen Zhao, Tong Wu.

Writing – review & editing: Chenchen Zhao, Haifeng Yan, Feng Liang, Yingjie Jia.

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