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Therapeutic Effect of Chinese Herbal Medicine (Kanglaite Injection) plus Chemotherapy (Docetaxel plus Cisplatin) Versus Treatment with platinum-based Chemotherapy alone for Non-Small Cell Lungs Carcinoma Among Male and Women Adult Patients (25 to 75 years old)

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OBJECTIVE

Several systematic reviews for Therapeutic Effect of Chinese Herbal Medicine plus Chemotherapy Versus to treatment with platinum-based chemotherapy alone for Non-Small Cell Lungs Carcinoma among Male and Women Adult Patients (25 to 75 years old) have recently emerged. Their results are far from uniform. So therefore, Lungs Cancer related diseases have a profound economic impact on health care systems global wide, thus Kanglaite Injection combined with Docetaxel plus Cisplatin

have been shown to have beneficial effects than treatment with platinum-based chemotherapy alone.

METHODS

We electronically searched the literature of the China National Knowledge Infrastructure (Chinese language, English 2010-2019), The Cochrane Library (English), MEDLINE, and EMBASE, and manually searched Chinese-language oncology journals to identify randomized controlled trials (RCTs) of KLT injection plus chemotherapy (Cisplatin plus Docetaxel) versus chemotherapy alone, regardless of their having been published or not, blinding, duration of treatment, or duration of follow-up. The quality of the included trials was assessed using the method recommended by The Cochrane Collaboration (CC). If heterogeneity existed among subgroups, then overall results were calculated based on a random-effects model; otherwise, a fixed effects model was used.

RESULTS

Electronic database searches yielded 680 citations with NSCLC. Articles or Records Excluded by screening of the title/abstract level total 170, Records which are not Rcts 221, not related to therapeutic effect of KLT injection plus chemotherapy (Cisplatin plus Docetaxel) 220, due to duplicated publication 9. Finally, we identified full text articles retrieved for detailled evaluation 60. The sample size of each trial had calculated sample sizes Rev Man. Pooled analyses performed using both fixed- and random-effects models revealed that compared with chemotherapy alone, KLT injection plus chemotherapy improved the response rate (relative risk [RR}, 1.34; 95% CI, 1.19-1.51 and RR, 1.35; 95% CI, 1.2 0-1.51, respectively). KLT injection plus chemotherapy was associated with improvement in the symptoms of cough, dyspnea, chest pain, fatigue, and anorexia.

Key Words: Chinese Herbal Medicine (Kanglaite injection), Chemotherapy, Non-Small Cell Lungs Carcinoma, Systematic Review.

1. INTRODUCTION

Populations who are suffering from Lungs Cancer Also called Bronchogenic carcinoma with its type of Non-Small Cell Lungs Cancer & Small Cell Lungs Cancer which has a higher likelihood of serious health complications [1]. In fact, the term Cancer, as used here, is synonymous with the term tumor, whose original derivation from Latin simply means «swelling, » not otherwise specified. Tumors historically were referred to a carcinomas, or «crab-like» infiltrating tumors, or sarcomas, or «fleshy tumors, » derived from the Greek terms for «rab» and «flesh,» respectively. Therefore, Lungs Cancer may be defined as the uncontrolled growth of malignant cells in one or both lungs and tracheo-bronchial tree. A Proliferation of abnormal cells leads to hyperplasia, dysplasia or carcinoma in situ in Chinese language (原位癌) with clearly elevated health risks.

Lung cancer is the leading cause of cancer-related mortality in the United States [2], in China and Worldwide. When lung cancer patients are found unsuitable for surgery at diagnosis, chemotherapy remains a treatment option worldwide, while in China and some countries in the world are available to combine Chinese Medicine (CM) with western medicine (WM) treatment together. Non-Small Cell Lungs Cancer is one of the most prevalent chronic condition types of Lungs Cancer with various health adverse effects leading to serious morbidity and mortality [3]. Histologically, ~80% of these tumors are of the non-small cell type, including adenocarcinomas and squamous cell and large cell carcinomas. Non-small-cell lung cancer (NSCLC) is the most common type of lung cancer, accounting for about 80% of all cases. More than half of the NSCLC cases are diagnosed at an advanced stage (III and IV), and 63% of cases are 65 years of age or older.

Demographics that are shifting toward an older population those Oncologists will be seeing more Elderly Patients with NSCLC in years to come. In Patients with SCLC, only 20-25 % of the cases harbor treatable driver mutations, such as Epidermal Growth Factor Receptor (EGFR) for which tyrosine kinase inhibitor can be used. 75%-80% of NSCLC cases are EGFR wild type and cannot gain any benefit from Target therapy. In advanced-stage NSCLC, Chemotherapy prolongs survival and improves Patients quality of life, but its effectiveness is not completely satisfactory.

Kanglaite KLT (Zhejiang Kanglaite Group Co. Ltd, Hangzhou, China) is a botanically sourced, molecularly targeted agent that is prepared as a microemulsion for IV use [4]. The active substance is extracted from the herb Semen micis. It is used in

Combination with Chemotherapy to minimize toxic reactions and enhance the

Chemotherapy. In 1995, KLT Patent certificates were granted in China. In August 1997, Phase III clinical trials were completed and KLT was officially launched in China after final approval from the Ministry of Public Health. Since 1997, > Health500, 000 Health cancer Patients in >2000 large- and medium-sized hospitals in China have been treated with KLT. A Semen coicis extract was found to suppress the growth of squamous lung cancer cells.

KLT decreased the number of G21M phase cells, suppressed the proliferation of cancer cells, and induced apoptosis of cancer cells, actions that constitute an important mechanism of the antitumor action of KLT. KLT was found to be effective in reversing multiple-drug resistance of cells and increasing the sensitivity of mouse cancer cells to chemotherapeutic agents [5]. KLT injection might have a direct effect on cancer cell death and improvement of patient's immune function, symptoms, and quality of life. A Cochrane protocol focused on symptom palliation of patients with lung cancer rather than effectiveness. To date, no systematic review or meta-analysis of the effectiveness of KLT injection in patients with primary NSCLC has been done [5].

The aim of this Article is to evaluate therapeutic effect of Chinese Herbal Medicine (Kanglaite Injection) plus Cisplatin) Versus Treatment with platinum-based Chemotherapy alone among Patients with NSCLC.

EPIDEMIOLOGY AND STATISTIC

Lung cancer is also the most commonly diagnosed and leading cause of death by cancer in men in the United States according for 27% and 31% of all cancer death in Women and men, respectively. The median age of diagnosis is 70 years. Although many patients achieve disease-free survival, some experience a long-term impairment of their quality of life, and disease recurrence is common. Lung cancer is the most frequently diagnosed cancer. An estimated 1.8 million new lung cancer cases occur estimated million new lung cancer case occurred in 2012 accounting for about 13% of total cancer diagnoses [6]. It is also the most common cause of death from cancer worldwide, responsible for nearly one fifth of all cancer deaths (1.59 million deaths, 19.4% of the total).

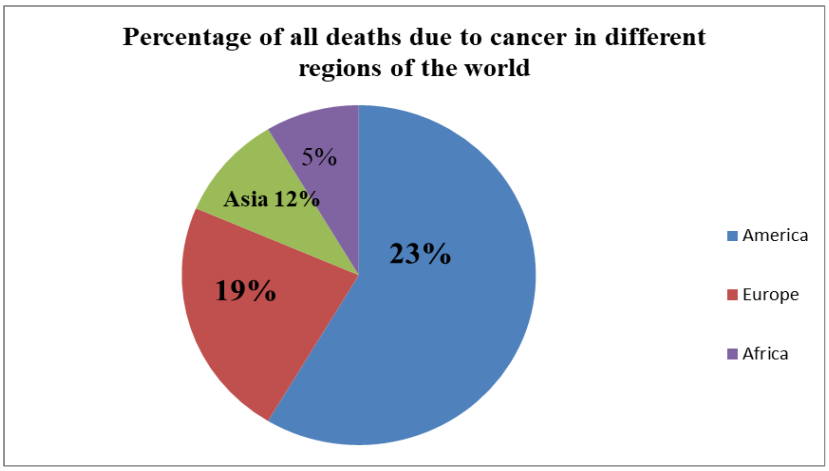
Numerous chemotherapeutic combination regimens are continuously being introduced for the treatment of advanced lung cancer to improve patient outcomes [6].

The Incidence and Mortality

The Incidence and mortality from cancer vary by tumor type and geographical region across the world. According to geographical distribution, the incidence of cancer accross the world is dependent on the local environmental factors, the diet and the genetics of the population.

Age is also a factor, as most cancers occur in those over the

age of 65, who compared 5% of the population in Africa, compared with 19.2% in Europe.



2. AETIOLOGY & FACTORS

For most patients, the case of their cancer is unknown, probably representing a multifactorial interaction between individual genetic predispositions and environmental factors.

Aetiology

Genetic factor

Rather than occurring by somatic mutation in response to mutagens, germline mutations in the genes that predispose to the development of cancer may be inherited and therefore present in all tissues. Expression of the mutation, and hence carcinogenesis, will depend on the penetrance (due to the level of expression and the presence of other genetic events) of the gene and whether the mutated allele as a dominant or recessive effect. There is a small group of autosomal dominant inherited mutations, such as RB (in Retinoblastoma) [7].

Environmental Factors

A wide range of environmental factors has been identified as being associated with the development of malignancy and may be amenable to preventative action such as smoking cessation, dietary modification and antiviral immunization. Environment factors interact with genetic predisposition. For example, subsequent generations of people moving from countries with a low incidence to those with a high incidence of breast or colon cancer many developed countries. The association of smocking with lung cancer is indisputable and causative mechanisms have been identified: cigarette tobacco is responsible for one-third of all deaths from cancer in the UK. Smocking not only causes lung cancer, but also is associated with cancer of the mouth, larynx, oesophagus and bladder [8].

Smoking factor

Prevalence

It has been known for many years that smoking causes lung cancer. An association was clearly documented in case-control in case-control studies conducted in Germany in the 1930s [9]. And in the United States and Great Britain [8,9] in the 1950s, and was strengthened by surveys of large cohorts. This led the S Surgeon General to conclude in 1964 [10] that «cigarette smoking is a cause of lung cancer in men, and a suspected cause of lung cancer in women». Further reports [8] have defined the relationship in more detail, and it has been estimated that, in the United States, 90% of male lung cancer deaths and 75%-80% of female lung cancer deaths are caused by smoking [8]. Cigarette smoking is declining in the Western World.

In 1974 in the UK 51% of men and 41% of Women smoked cigarette-nearly half the adult population. Now, about 21% of men and 19% of women aged 16 years and over smoke. The highest rates are in people aged 20-24 (28% of women and 30% of men in this age group smoke). The highest rates of cigarette consumption per capita are in Serbia, Bulgaria, Greece, China and Russia. In Global terms, the USA ranks 51st and the UK ranks 73rd, close to the rates in Sweden, Canada and the Netherlands. Smoking continues to increase in many developing countries, particularly among women [11].

High risk populations

At the population level, age-adjusted lung cancer rates, incidence rates or mortality rates, can be compared across populations to identify which populations are at highest risk.

Toxic Effects

Cigarette smoke contains polycyclic aromatic hydrocarbons and nitrosamines, which are potent carcinogens. It causes releases of enzymes from neutrophil granulocytes and macrophages that Pulmonary epithelial permeability increases, even in symptomless cigarette smokers, and correlates with the concentration of carboxyhaemoglobin in blood. This altered permeability may allow easier access for carcinogens.

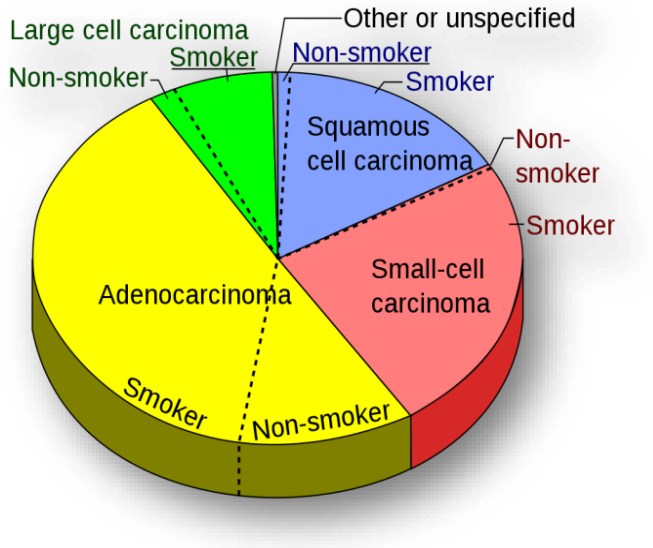
The Dangers

Cigarette smoking is addictive and harmful to health (Box1.1). People usually start smoking in adolescence for psychosocial reasons and, once they smoke regularly, the pharmacological properties of nicotine encourage persistence, by their effect on the smokers'mood. Very few cigarette smokers (<2%) can limit themselves to occasional or intermittent smoking. Significant dose-response relationships exist between cigarette consumption, airway inflammation and lung cancer mortality [12]. Sputum production and airflow limitation increase with daily cigarettes daily for 20 years increases the lifetime risk of lung cancer, by about 10 times compared to a lifelong no-smoker. Smoking and asbestos exposure are synergistic risk factors for lung cancer, with a combined risk of about 90 times that of unexposed non-smokers.

2.1. **Western Medical View Of Cancer**

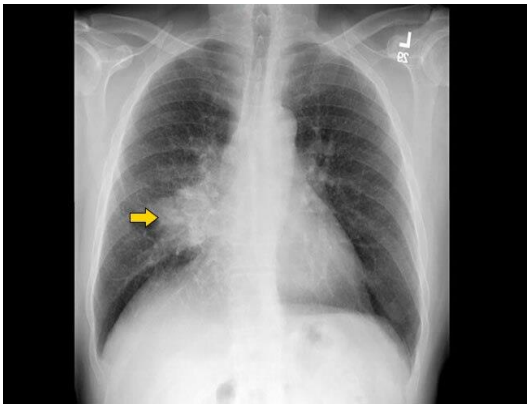
There are 100 types of cancer, including breast cancer, skin cancer or kaposi sarcomas, lung cancer, colon cancer, prostate cancer, and lymphoma. Cancer starts when a cells is somehow altered so that it multiplies out of control. A tumor is a mass composed of a cluster of such abnormal cells. Most cancers form tumors, but not all tumors are cancerous. Researchers are attempting to find screening tests that may help to dignose lung cancer early, such as Sputum cytology, CT, Imaging tests, and tissue samples (Biopsy).

Usually, SCLC is more responsive to Chemotherapy than NSCLC. While NSCLC accounts for 80%, including three subtypes: Adenocarcinoma, which is the most common form of lung cancer in the United States among both men and women; Squamous Cell Carcinoma, which accounts for about 25 % of all lung cancers; Large Cell Carcinoma, which accounts for about 10 % of NSCLC tumors. Each subtype relates to the specific type of cell affected and are grouped together because they behave in a similar way [13].



Staging lung cancer is based on whether the cancer is local or has spread from the lungs to the lymph nodes or other organs. Because the lungs are large, tumors can grow in them for a long time before they are found. Even when symptoms - such as coughing and fatigue- do occur, people think they are due to other causes. For this reasons, early-stage lung cancer (stage I & II) is difficult to detect.

Staging in Small Cell Lung Cancer, as limited stage, in this stage, cancer is found on one side of the Chest, involving just one part of the lung and nearby lymph nodes. Extensive stage, in this stage, cancer has spread to other regions of the Chest or other parts of the body.



While, stages of Non-Small Cell Lung Cancer as known, stage I, the cancer is located only in the lungs and has not spread to any lymph nodes. Stage II, cancer is in the lung and nearby lymph nodes. Stage III, Cancer is found in the lung and in the lymph nodes in the middle of the Chest, also described as locally advanced disease. Stage III which has two subtypes, if the Cancer has spread only to lymph nodes on the same side of the Chest where the cancer started, it is called stage IIIA. If the Cancer has spread to the

lymph nodes on the opposite side of the Chest, or above the collar bone, it is called stage IIIB. While Stage IV, this is the most advanced stage of lung cancer, and therefore is also described as advanced disease. This is when the cancer has spread to both lungs, to fluid in the area around the lungs, or to another part of the body, such as the liver or other organs [14].

Evolution and Mechanism

Benign, or noncancerous, tumors do not spread to other parts of the body, and do not create new tumors. Malignant, or cancerous, tumors crow out healthy cells, interfere with body functions, and draw nutrients from body tissues. Cancers continue to grow and spread by direct extension or through a process called metastasis, whereby the malignant cells travel through the lymphatic or blood vessels-eventually forming new tumors in other parts of the body. Cancer patients undergoing aggressive therapy and those with advanced disease often experience clusters of severe symptoms, such as depression, anxiety, pain, sleep disorder, and loss of functional status [15]. Overall 50-90% of people with cancer experience fatigue [15]. NSCLC profoundly impacts on a person's physical, emotional, and mental well-being. It has a clear negative impact on the quality of life of people with cancer and their ability to maintain their usual personal, professional and social relationships. Bevacizumab, a monoclonal antibody which targets vascular endothelial growth factor, can be applied to EGFR wild-type NSCLC, but does not improve overall survival for patients over the age of 65.

To date, Chemotherapy (CT) remains the standard of care for older patients with good functional status. However, a treatment dilemma of how to choose the use of CT in the care of patients with NSCLC that is very common in the clinical setting, given CT can prolong survival but can also significantly increase the incidence of side effect [15]. Due to the fear of severe adverse reactions, many patients are being under treated through discontinuing or not receiving Chemotherapy, so therefore, in China the treatment is always combined with Chinese herbal.

2.2. Chinese Medicine View Of Cancer

Chinese Medicine has a holistic view of the body. Everything is seen to exist within the continuous circle of nature. When the elements of nature are in balance, life is in harmony, and flourishes. Humanity cannot be separated from nature; we are nature, manifested as people. Living in harmony with the world around us is the way to maintain health. If one were to live out of balance with nature, illness or disease (western terms) would develop called the body that is suffering from an imbalance, or disharmony. Every Organ in TCM has a partner organ. One is ***yin,*** the other ***yang*** they work together to keep the body in balance [16].

2.2.1. *The lungs are yin and their yang partner is the large intestine (TCM theory).*

The lungs govern ***qi In TCM. Qi*** as an energy that is needed for all the body's processes. The stronger the lungs, the more qi which are able to take in and distribute to the rest of the body, necessary for all its vital functions. The weaker the lungs, the less qi will be, and therefore, an imbalace is created while cause illness or disease. In fact, Cancer was first mentioned in Chinese medicine in The Yellow Emperor's Inner Classic of Medicine（Huangdi Neijing, 《黄帝内经》)《积聚 jiju, 癥结 zheng jie》 which means Tumor or a mass. According to TCM theory, lung cancer is the disease simply called (fei ai, 肺癌), When treating exhaustion syndromes, sudden Neijing defines the concepts of Yin, Yang, Qi, and blood and how they course through pathways in the body called meridians. In TCM, a disease is perceived as a **disharmony** (**or imbalance**) in the functions of Yin, Yang, Qi, blood. Traditional Chinese Medicine, *qi* usually refers to life energy, which manifests simultaneously on the physical and mental-spiritual levels [17].

So therefore, It's different from western medicine view which is diagnosed disease according to signs and symptoms, physical exams while Traditional Chinese medicine theory is diagnosed a disease according to syndrome differentiation, taking the pulse, looking for face color, tongue shape and color…Traditional Chinese Medicine is reported as safe alternative therapy with many roles in improving symptoms, such as reducing cancer-related fatigue, improving gastrointestinal side effects, protecting liver function, and even ameliorating bone marrow suppression[18]. TCM, as an adjunct to the conventional antitumor therapy, may improve overall survival of lung cancer patients. Our previous studies also showed that TCM plus Chemotherapy might improve overall survival compared to Chemotherapy alone. As a result of TCM's advantage in reducing side effects and its potential role in prolonging survival.

2.2.2. **Treatment**

2.2.3. **Both chemotherapy (Cisplatin plus Docetaxel) plus Kanglaite**

Systematically, the treatment is based on journal which is to identify randomized controlled trials (RCTs) of Kanglaite (KLT) injection plus chemotherapy (Cisplatin

plus Docetaxel) versus chemotherapy alone. In response to the EGFRS, numerous NSCLC treatments are commonly used on these patients. However, pharmacological drugs for the management of NSCLC, including local treatment (e.g. Surgery and radiotherapy) and systemic treatment (e.g. Chemotherapy, and biological therapy) are constantly being debated due to their side effects; the drugs could bring about many unavoidable side effects such as physiological reaction of chemotherapy which is very severe, such as hair loss, blood vessels turning blacks, vomiting, and being unable to eat anything [19].

So, furthermore Kanglaite KLT (Zhejiang Kanglaite Group Co. Ltd., Hangzhou, China) is a botanically sourced, molecularly targeted agent that is prepared as a microemulsion for IV use. The active substance is extracted from the herb Semen micis. It is used in combination with chemotherapy to minimize toxic reactions and enhance the effect of chemotherapy. In 1995, KLT patent certificates were granted in China. In August 1997, Phase III clinical trials were completed and KLT was officially launched in China after final approval from the Ministry of Public Health. Since 1997, >500,000 cancer patients in >2000 large- and medium-sized hospitals in China have been treated with KLT. A Semen coicis extract was found to suppress the growth of squamous lung cancer cells.

益气养阴，消癥散结。适用于手术前及不宜手术的脾虚痰湿型、气阴两虚型原发性非小细胞肺癌。

In addition, KLT decreased the number of G21M phase cells, suppressed the proliferation of cancer cells, and induced apoptosis of cancer cells, actions that constitute an important mechanism of the antitumoraction of KiT. KiT was found to be effective in reversing multiple-drug resistance of cells and increasing the sensitivity of mouse cancer cells to chemotherapeutic agents.s KiT injection might have a direct effect on cancer cell death and improvement of patients' immune function, symptoms, and quality of life. A Cochrane protocol focused on symptom palliation of patients with lung cancer rather than effectiveness. To date, no systematic review or meta-analysis of the effectiveness of KLT injection in patients with primary NSCLC has been done. The aim of this meta-analysis was to evaluate the effectiveness and tolerability of KiT injection plus chemotherapy versus chemotherapy alone for patients with NSCLC [19].

3. MATERIALS AND METHODS

3.1. STUDY DESIGN

Only randomized controlled trials (RCTs) were eligible for this review; blinding, language, published or not, duration of treatment, and theduration offollow-up were not considered. Uncontrolled and observational studies were excluded. The RCT is often considered the gold standard for a clinical trial. RCTs are often used to test the efficacy or effectiveness of various types of medical intervention and may provide information about adverse effects, such as Drug reaction [20].

4. METHODS

60 cases of Non-Small Cell Lungs Cancer among Elderly Patients above 60 years of age were selected and randomly divided into two groups: treatment group and control group. Each patient will receive the treatment relevant to their group, respectively. Treatment (expermental group) groups contained 33 cases and control group 27 cases. The treatment group was given the Kanglaite KLT injecion as a Chinese herbal Medicine plus (Cisplatin plus Docetaxel) as Chemotherapy and control group was given the Chemotherapy drugs alone.

Therefore, we searched the method for identification of Studies that was identified through data base searching: Medline Pub med, Embase, CNKI, Cochrane library, web of science Wang fang, so potentially relevant articles. So furthermore, measurements will be included outcomes…While the articles were searching without restriction to language (English, Chinese) or year of publication from 2006 to 2019. In fact reviews are defined as systematic if they included an explicit and repeatable methods section describing the search strategy and explicit inclusion/exclusion criteria.

Cochrane collaboration

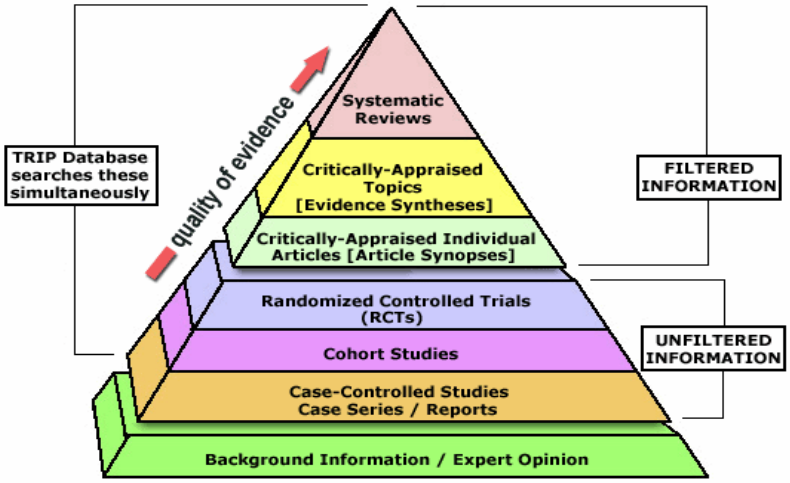
- ✧ Cochrane Reviews(>4,000) registered
- ✧ Identify, appraise and synthesize research-based evidence and present it in accessible
- ✧ Format; regularly updated
- ✧ Focus on interventions
- ✧ Outstanding general resource

Hierarchy of evidence

Systematically Review

Critically - appraised

Inclusion & Exclusion in Randomized Controlled Trials RCTs.



4.1. Significance of research

Following a systematic review, compiling an analysis of recent clinical trials, is an effort to obtain a statistically significant out- come and come to a conclusion.
Possible liver damage [19, 20]. This research is being done in hopes of future clinical trials to be conducted thereby discovering more evidence based treatment for the patient. Given that Non-Small Cell Lung Cancer. A comprehensive review of combination treatment of Chinese herbal and western medicine is needed at this time, and could have a positive and far-reaching impact on the delivery of treatment to patients worldwide.

5.2.1. Data sources

Web of Science, We also searched the databases of clinical trials such as Current Controlled Trials (http://www. controlled-trial.com).

Study selection

(Inclusion and exclusion criteria)

Types of study

This review will be confined to randomized controlled trials (RCTs) comparing Chinese herbal plus to chemotherapy alone. If the trial states the "randomization" phase, it will be deemed a randomized study, and the blinding will not b**e restricted.**

Inclusion criteria

i. Age 25-75 and older.
ii. Patients were eligible for the study if they had primary NSCLC that was confirmed cytologically, pathologically, or by computed tomography
iii. Or if they had inoperable stage II to IV cancer or stage II cancer and had refused surgery.
iv. Patients with a Karnofsky Performance Status (KPS) scores 250 and an expected survival time. Finally, patients not treated with chemotherapy or radiotherapy.
v. EGFR wild type or untested.
vi. Received CHM plus CT
vii. RCTs

Exclusion criteria

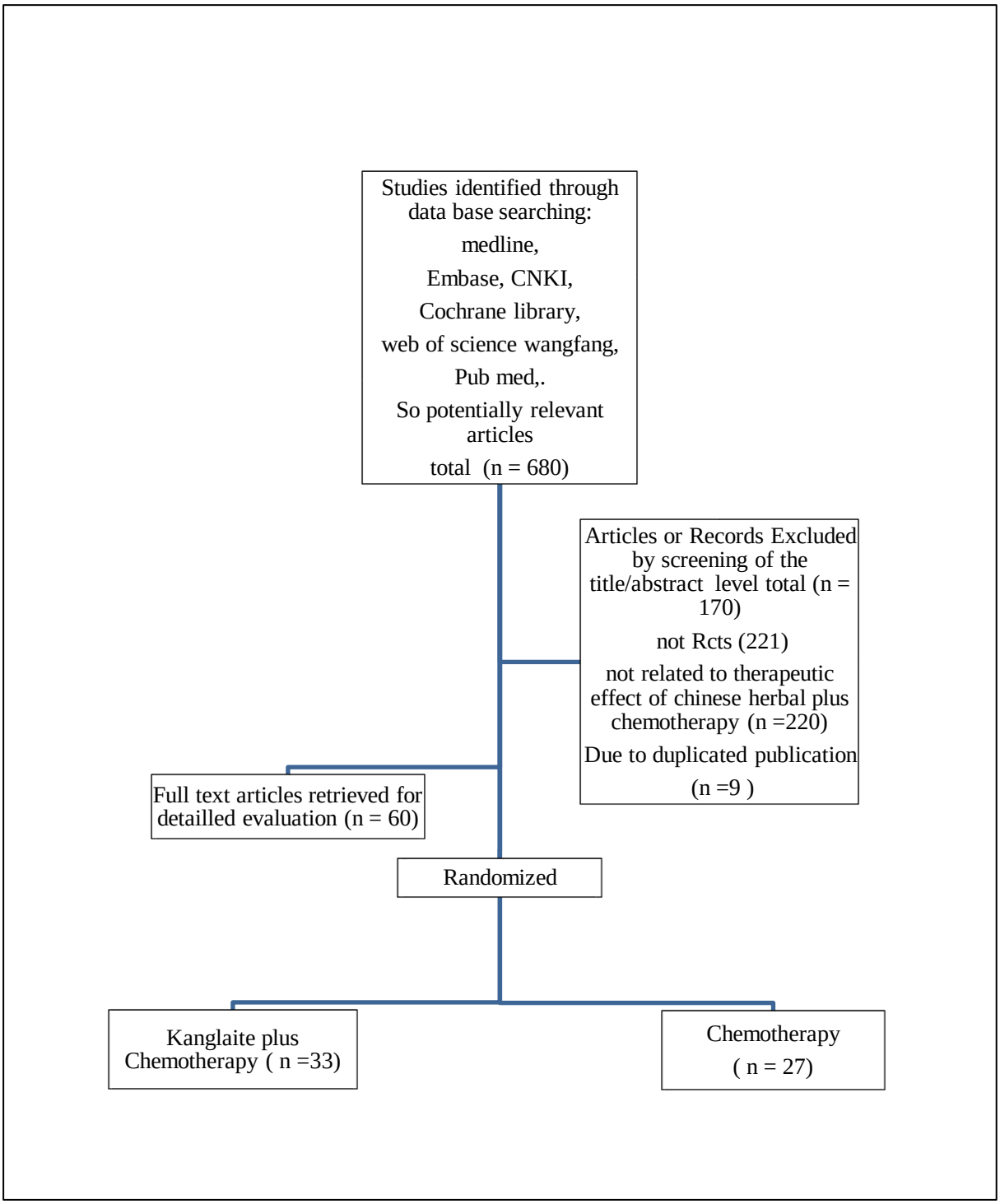
Individuals are not eligible if they are

- Not RCTs;
- they have a medical history of cardiovascular disease,
- Colorectal cancer,
- Endocrine cancer or abnormalities,
- Renal disease and contagious skin condition.
- Patient had liver, brain, or bone metastasis (although asymptomatic patients were eligible).
- Patients who had just undergone surgery or radiotherapy treatment were also excluded.

5.2.2. INTERVENTIONS

The trial groups received KLT injection plus chemotherapy and the control groups received chemotherapy alone, regardless of the duration of treatment or follow-up. The basic treatment in both trial and control groups was identical except for KiT injection.

(Clinical Trials; CENTRAL), MEDLINE being used the strategy of Dickersin and Larson for controlled clinical trials and EMBASE, CNKI, Pub med. (Excepta Data base) until November 2019.



Result: The result will be showed after the completion of the study. Thus, providing the total number for the **Therapeutic Effect of Chinese Herbal Medicine plus Chemotherapy Versus to treatment with platinum-based chemotherapy alone for Non-Small Cell Lungs Carcinoma among Male and Women Adult Patients (25 to 75 years old)** which would be randomly assigned to 2 groups and would be compared with the pretreatment baseline. The outcome and data is be measured and analyzed by **rev.man5.3.**

5. OUTCOME MEASURES

5.1. Mortality Rate

Mortality rate at the end of treatment or follow-up was calculated. Response Rate Response Evaluation Criteria in Solid Tumors, formulated by the World Health Organization (WHO), was used to evaluate the response rate. Based on the degree of tumor absorption, response was classified as follows: (1) complete response (CR) = chest radiograph or computed tomography and/or fiber bronchoscopy revealed complete absorption of the lesion; (2) partial response (PR) = lesion decreased by greater than 50% but ~99% [21]. Based on the comparison of chest radiograph or computed tomography before and after treatment, the response rate was defined as CR + PR [22].

6.1.2. Quality-of-Life

Improvement Quality of life before and after treatment was assessed using the KPS. Only data for patients whose KPS scores improved by less than 10 points (the minimal clinically significant difference) after treatment were extracted.

6.1.3. Symptom Improvement

The percentage of patients exhibiting improvement in the symptoms of cough, hemoptysis, chest pain, fever, fatigue, and anorexia was assessed. We also calculated the percentage of patients whose symptoms resolved completely. Improvement in symptoms was assessed according to the information provided in each included study. Specifically, for the pooled analysis of the trials in which symptom improvement was reported, symptoms were scored according to their degree of severity (ie, grades 1III). For the symptoms of cough, chest pain, and dyspnea, grade I was assigned when the symptoms did not influence daily life, and grade III was assigned when the symptoms were severe, with a marked influence on daily life; symptoms between grade I and III were assigned grade II. For hemoptysis, sputum with blood was assigned grade I,

sputum with blood clots or sputum with ~10 mUd of blood was assigned grade II, and extremely bloody sputum or sputum with>10 mUd of blood was assigned grade III.

6.1.4. Adverse Events

Adverse events (AEs) were evaluated at the completion oftreatment and included bone marrow suppression (leukopenia, anemia, and thrombocytopenia), nausea and vomiting, phlebitis, hepatic dysfunction, and renal dysfunction. According to the WHO grading criteria for acute and subacute toxicity of anticancer drugs, we only calculated AEs of grades II to IV. If patients withdrew from the study due to an AE, we also included these AEs.

6.1.5. Quality Assessment

The quality of the trials was assessed according to the Cochrane Collaboration's criteria11: (1) minimization of selection bias (ie, were the randomization procedure and the allocation concealment adequate); (2) minimization of performance bias (ie, were the patients who received treatment and people who administered the treatment blinded to the interventions); (3) minimization of attrition bias (ie, were withdrawals and dropouts completely described and was the analysis based on intent to treat [ITT}); and (4) minimization of detection bias (ie, were outcome assessors blinded to the interventions). Based on these criteria, the studies were broadly subdivided into the following 3 categories: A = all quality criteria met, low risk of bias; B = greater than 1 of the quality criteria only partially met, moderate risk of bias; and C = greater than 1 criteria not met, high risk of bias.

Each trial was assessed independently by one author (Wang) and was checked by another author (Shu). Differences were resolved by discussion.

6. Data Extraction

Data from each included trial were extracted independently by one author (Wang) and checked by another author (Shu) using a standard extraction form. The form included the following items:

- General information: published/unpublished; language; authors; article; journal title, year, volume, issue, and page numbers; and funding source;
- Trial design: predetermined sample size, generation of randomization sequence, allocation concealment method, blinding of information, statistical methods, and attrition;

- Participants: diagnostic criteria, total number of patients and number of patients in the comparison groups, baseline characteristics (eg, age, gender), inclusion criteria, exclusion criteria, and study settings;
- Intervention: type of chemotherapy regimen, duration, time, and dose; co-intervention; control; withdrawals, dropouts, and lost to follow-up; and
- Outcome: outcomes at the end of treatment. The number and type of AEs were also extracted. If the aforementioned data were not available in the trial report, further information was sought by corresponding with the original principal investigator.

6.1. Data Analysis

Data were analyzed using Meta View 4.2.8 in Review Manager 4.2 (Cochrane collaboration, Oxford, United Kingdom). Meta-analysis was conducted by pooling the different chemotherapy regimens combined with KLT injection and comparing these with chemotherapy regimens alone for an overall analysis; however, the analysis was divided according to subgroups that were formed based on chemotherapy regimens. Sensitivity analyses were conducted by excluding low quality trials. Analyses were conducted using the ITT principle when possible. Relative risk (RR) was used to analyze dichotomous data. If heterogeneity existed among subgroups, then overall results were calculated based on the random effect model; otherwise, the fixed effect model was used [22]. The random effect model was also used to check whether its use might change the direction of the results in cases where heterogeneity was not tested. Heterogeneity was tested using the Z score and X2, and $P < 0.1$ was considered statistically significant.

7. Results 2.1

7.1. Comparison on clinical efficacy between the two groups

Comparison on total effective rate between the two groups showed that data from treatment group was apparently better than those from control group with **significant statistical differences (P<0.05), the I^2= 99% in Mean difference IV Fixed CI 95% see Tab. 1.**

TABLE I

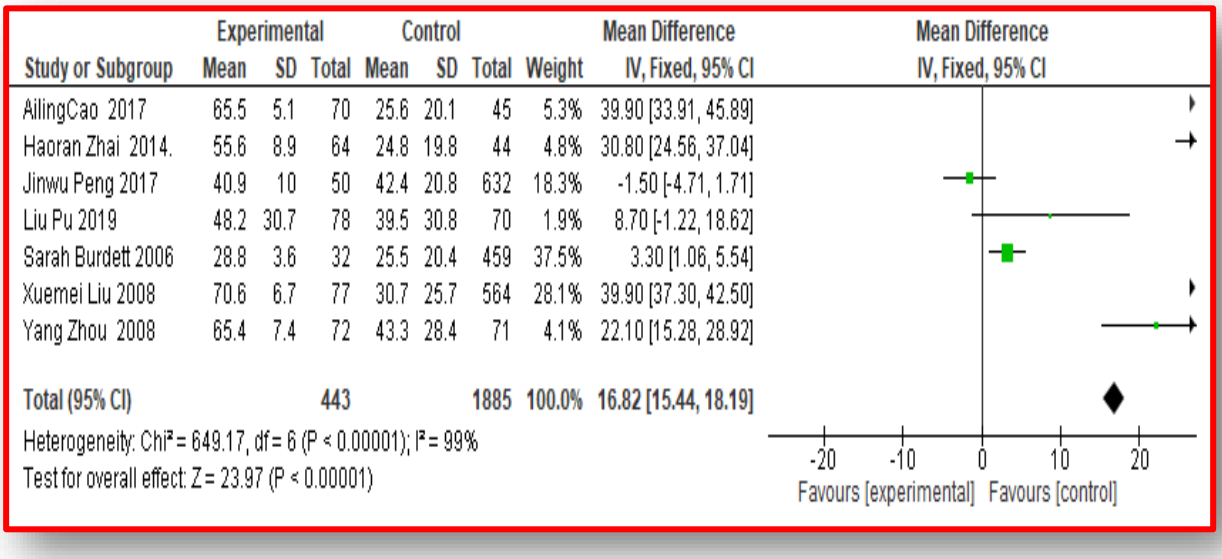
Comparison On Karnofsky Score between Two Groups

Authors Names	Year	Group I Experimental Group			Group I Control Group			
		Mean	SD	Total	Mean	SD	Total	%
Ailing Cao	2017	65.5	5.1	70	25.6	20.1	45	5.3%
Haoram Zhai	2014	55.6	8.9	64	24.8	19.8	79.8	4.8%
Sarah Burdett	2006	28.8	3.6	32	25.5	20.4	45.9	37.5%
Total %	-	149.9	17.2	300	75.9	60.3	170.7	47.6%

Electronic database searches yielded 680 citations, 60 cases of Non-Small Cell Lungs Cancer among Elderly Patients above 70 years of age were selected and randomly divided into two groups: treatment group and control group. Each patient received the treatment relevant to their group, respectively. Treatment as compared (expermental group) groups contained 33 cases and control group 27 cases. So therefore, **Kanglaite (TCM) plus Cisplatin & Docetaxel (CM) was effective than Chemotherapy drugs alone (P<0.05), the I^2= 99% in Mean difference IV Fixed CI 95% See Figures 1, 2…**

Figure 1 (Analysis 1.1)

Outcome: 1.1 KarnofskyPerformanceStatus (KPS).



Forest plot of comparison: 1 TCM (Kanglaite Injection) plus Chemotherapy (Docetaxel plus Cisplatin) Versus Platinum-based Chemotherapy alone.

Outcome: 1.1 KarnofskyPerformanceStatus (KPS).

Figure 2 (Analysis 1.1)

Funnel plot of comparison: 1

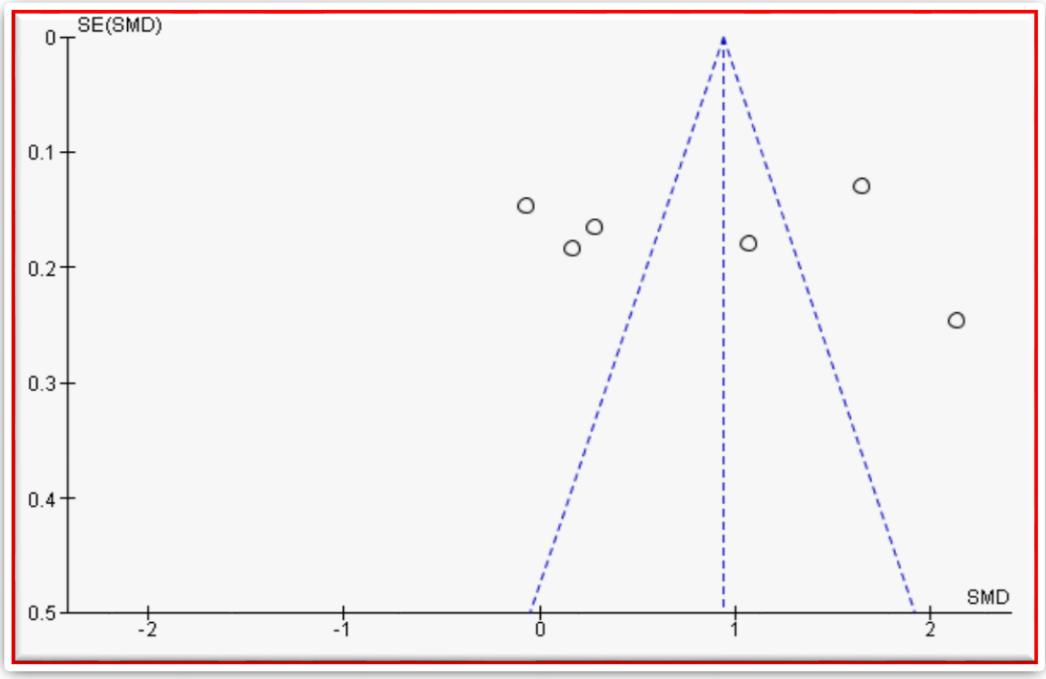


Figure 2 (Analysis 1.1)

Funnel plot of comparison: 1

TCM (Kanglaite Injection) plus Chemotherapy (Docetaxel plus Cisplatin) versus platinum-based Chemotherapy alone, outcome: 1.1 KarnofskyPerformanceStatus (KPS).

ODDS RATIO (M-H, RANDOM, 95% CI)

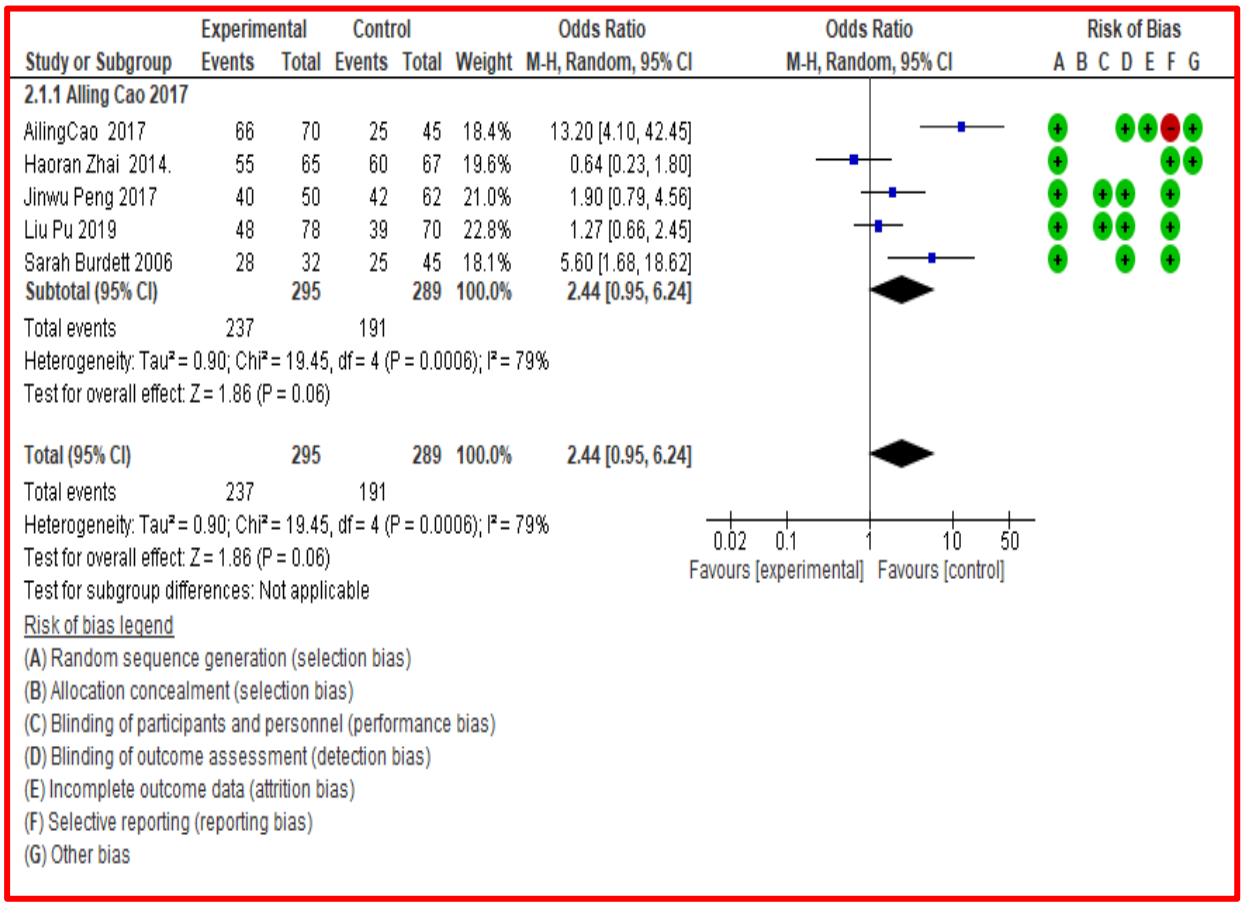
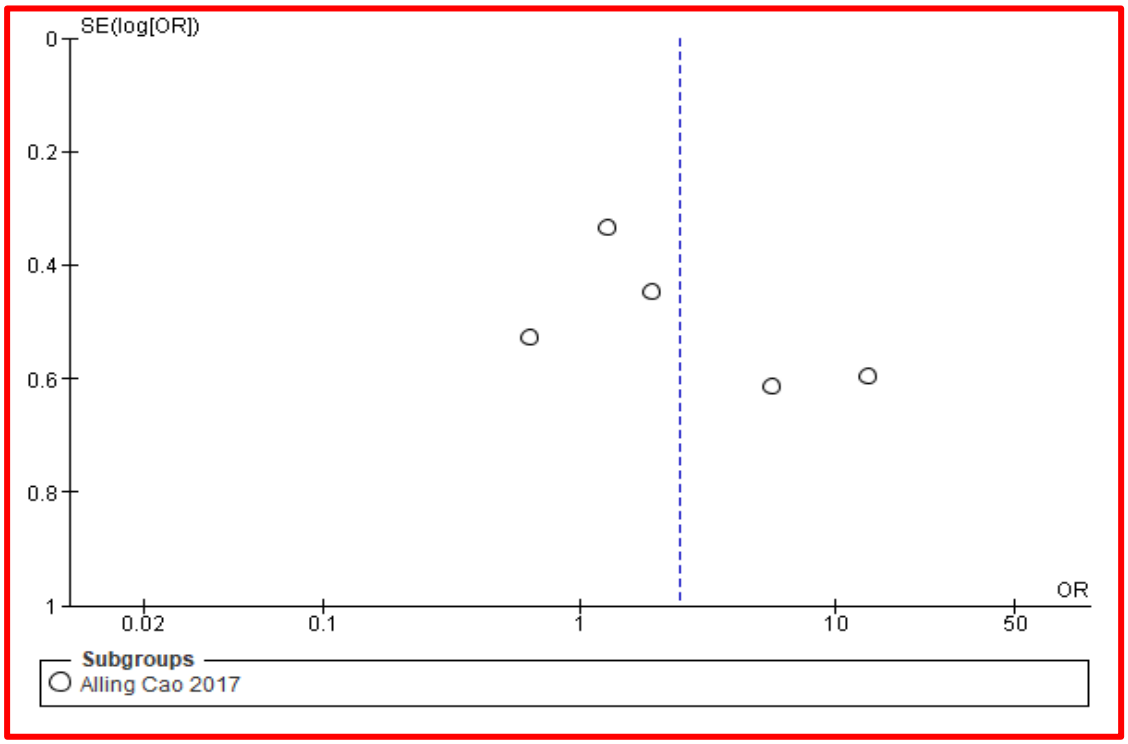


Figure 3 Analysis 2.1

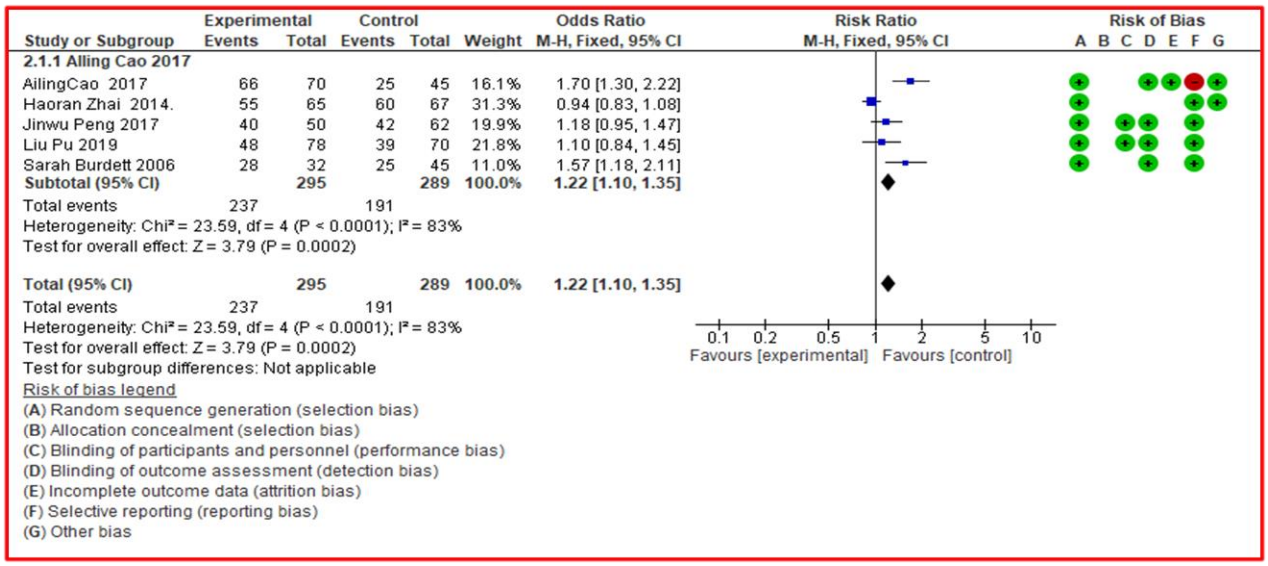
Kanglaite Injection plus Cm versus Chemotherapy Alone, Outcome: 2.1 New Outcomes.



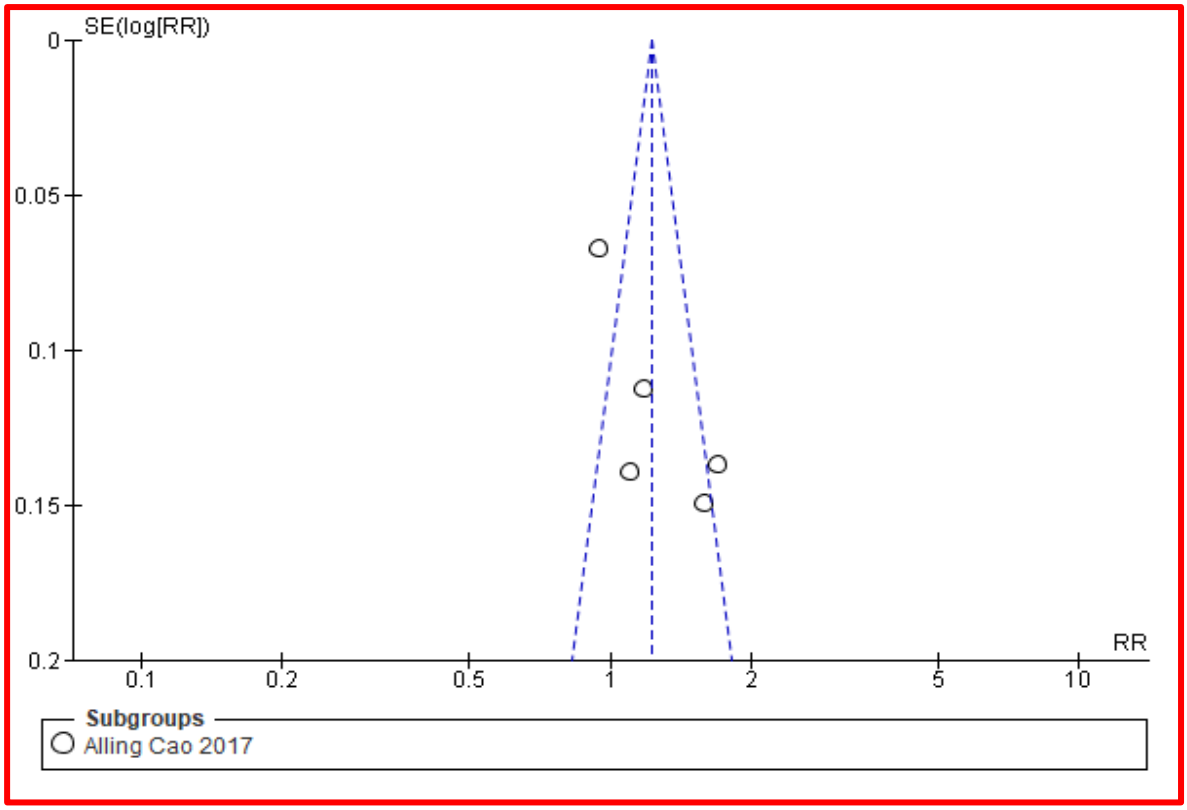
Funnel plot of comparison

Kanglaite Injection plus Cm versus Chemotherapy Alone, Outcome: 2.1 New Outcomes.

RISK RATIO (M-H, FIXED, 95%)



RISK RATIO (M-H, FIXED, 95%)



Funnel plot of comparison

Kanglaite Injection Plus Cm versus Chemotherapy Alone, Outcome: 2.1 New Outcomes.

CONCLUSISON

The onset of lung cancer is often insidious and most of the patients had developed to the advanced stage after diagnosis, and even lost the best timing/opportunity for surgery. Thus, atthistime, the chemotherapy is the first choice of treatment plan. The body immunity of patients will decline as the patients were suffering painfulness from tumor, side effects of chemotherapy, etc. Tumor immunology is divided into cellular immunity and humoral immunology, while the humoral immune function of tumor patients is not dominant in the system and it is usually no significant changes. In the cellular immunity system, T lymphocytes and natural killer cells (NK cells) are the main effector cells, which are closely related to the occurrence, development, and metastasis of tumors [5].

To reduce the side effects of chemotherapy and improve the body's immunity, our department advocates adding in the Kanglaite injection to the foundation of the

treatment of advanced non-small-cell carcinoma. Kanglaite injection is also a traditional Chinese medicine preparation for antitumor. The Kanglaite injection was extracted from Coix seed and its main component is Coix seed oil, which has good effect of invigorating spleen and stop diarrhea, clearing body heat and draining pus from body, oozing, and improve diuresis. This medicine can induce apoptosis of tumor cells and has a disturbing effect on the mitotic process of tumor cells and can reverse the multidrug tolerances of tumor cells. It can also stimulate the activation IL-2 and NK cell, effectively promote the proliferation of spleen lymphocytes, and enhance the phagocytic function of macrophages, thereby achieving the purpose of improving cellular immune function. During the chemotherapy of patients with advanced NSCLC, the injection of Kanglaite can reduce the cytotoxicity of chemotherapy drugs, and also help to alleviate pain and stabilize the condition.

The results of this study showed that the total treatment effective rate of the experimental group which using **Kanglaite (TCM) plus Cisplatin & Docetaxel (CM) was significantly higher than that of the control group (Chemotherapy drugs alone) ($P<0.05$), the $I^2= 99\%$ in Mean difference IV Fixed CI 95%**. The incidence of adverse reactions in patients of the experimental group was lower than that of the control group and the differences between groups were $P < 0.05$, with statistically significant. In addition, the study with immune indicators (CD3+, CD4+, IgG, and IgA) were better than that of the control group, the differences between the groups were $P < 0.05$, have statistically significant, and indicate that the drug can enhance the immune function of cancer chemotherapy patients.

In summary, in the chemotherapy of advanced NSCLC, the addition of Kanglaite injection can improve the effect of chemotherapy, reduce the side effects of chemotherapy, and also significantly improve the immune function of patients.

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