INPLASY PROTOCOL

To cite: Peng et al. Comparative Efficacy of 13 CHIs Combined with TP regimen chemotherapy for patients Non-small Cell Lung Cancer: A Bayesian Network Meta-Analysis of Randomized Controlled Trials. Inplasy protocol 2022100093. doi: 10.37766/inplasy2022.10.0093

Received: 23 October 2022

Published: 23 October 2022

Corresponding author:
ciyan peng

pengciyan@csu.edu.cn

Author Affiliation:
The Second Xiangya Hospital, Central South University.

Support: **Hunan Provincial Health.**

Review Stage at time of this submission: **Data extraction.**

Conflicts of interest:
None declared.

Comparative Efficacy of 13 CHIs Combined with TP regimen chemotherapy for patients Non-small Cell Lung Cancer: A Bayesian Network Meta-Analysis of Randomized Controlled Trials

Peng, CY[1]; Chen, J[2]; Yang, L[3]; Zhang, Q[4]; Huang, L[5]; Wen, M[6]; Li, SN[7]; Cui, W[8]; Li, JH[9].

Review question / Objective: **Advanced lung cancer has become the top malignant tumor in terms of morbidity and mortality, and Chinese herbal injections combined with TP have been widely used to treat advanced non-small cell lung cancer. For this purpose, we conducted a Bayesian network analysis to systematically evaluate the efficacy of different herbal injections combined with TP in the treatment of NSCLC. Subjects: Patients diagnosed with NSCLC by pathological or cytological examination, locally advanced or those who refused surgical treatment were included, regardless of gender, age, stage, race, nationality and sample size; Interventions: Chinese herbal injections combined with TP were used in the experimental group, while the control group was treated with TP alone; Study type: to report the efficacy of Chinese herbal injections combined with TP in the treatment of non-small cell lung cancer efficacy in a randomized controlled trial (rct) Eligible. No restrictions were imposed on language, year of publication, or publication status. Ending indicators: Main ending indicators: (1) disease control rate (DCR), DCR = (complete remission + partialremission + stable)/total number of cases. Efficacy rate = (number of improvement cases + number of stable cases)/total number of cases. (2) Secondary outcome indicators: quality of life, determined according to the KPS behavioral status scale, improvement was defined as an increase of ≥10 points in KPS score after treatment; stability was defined as an increase or decrease of <10 points in KPS score; decline was defined as a decrease of ≥10 points in KPS score. (3) The incidence of adverse reactions, including gastrointestinal reactions, white blood cell (WBC) reduction, hemoglobin (HGB) reduction, platelet (PLT) reduction, etc.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 October 2022 and was last updated on 23 October 2022 (registration number INPLASY2022100093).

INTRODUCTION

Review question / Objective: **Advanced lung cancer has become the top malignant tumor in terms of morbidity and mortality, and Chinese herbal injections combined with TP have been widely used to treat advanced non-small cell lung cancer. For this purpose, we conducted a Bayesian network analysis to systematically evaluate the efficacy of different herbal injections combined with TP in the treatment of**

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Condition being studied: Advanced lung cancer has become the malignant tumor with the highest morbidity and mortality rate, and the treatment of advanced non small cell lung cancer with traditional Chinese medicine injections combined with TP has been widely used. The combination of Chinese herbal injections and TP in the treatment of advanced lung cancer effectively prolongs the survival time and improves the quality of life, which is an important reference value for the treatment of advanced lung cancer patients and the selection of clinical treatment plan. The remission rate of conventional radiotherapy for lung cancer is only 15%-20%. Targeted therapy has achieved good efficacy in lung cancer treatment, but for advanced lung cancer without driver mutations, chemotherapy is still the main treatment, which is usually difficult to be tolerated by patients or has a short overall survival (OS), which greatly Restricted application . Immunotherapy has increased the 5-year survival rate of patients with advanced non-small cell lung cancer (NSCLC) from 5% to about 23%, but it has limitations in clinical practice due to low antigenicity, side effects, and drug resistance. Chinese medicine can reduce the toxic side effects of western drugs, enhance their sensitivity, and reverse drug resistance. Combination of Chinese medicine is not simply a superimposed effect, but can play a better synergistic role, which can better inhibit tumor development, improve patients' quality of life, prolong their survival, and regulate the immune microenvironment. For this purpose, we conducted a Bayesian network analysis to systematically evaluate the efficacy of 13 herbal injections combined with TP in the treatment of NSCLC.

METHODS

Participant or population: Patients with pathologically or cytologically confirmed diagnosis of NSCLC, locally advanced or refusing surgical treatment, regardless of gender, age, stage, race, nationality and sample size were included.

Intervention: The test group used Chinese herbal injections in combination with TP regimen.

Comparator: Treatment with TP regimen alone.

Study designs to be included: A randomized controlled trial (rct) reporting the efficacy of Chinese herbal injections incombination with TP for the treatment of non-small cell lung cancer was eligible, with no restrictions imposed on language, year of publication, or publication status.

Eligibility criteria: Inclusion and exclusion criteria of the literature Inclusion criteria: (1) meet the requirements of the previous

inclusion population requirements; (2) the type of study is a randomized controlled trial; (3) the outcome indicators are: a: disease control rate (DCR), DCR = (complete remission + partial remission + stable)/total number of cases. Effective rate = (number of improved cases + number of stable cases)/total number of cases. b: Secondary outcome indicators: quality of life, as determined by the KPS behavioral status scale, improvement as an increase of ≥10 points in KPS score after treatment; stability as an increase or decrease of <10 points in KPS score; decline as a decrease of ≥10 points in KPS score. c: incidence of adverse effects, including gastrointestinal reactions, white blood cell (WBC) decrease, and WBC decrease. The incidence of adverse reactions included two of them, such as gastrointestinal reactions, white blood cell (WBC) reduction, hemoglobin (HGB) reduction, platelet (PLT) reduction, etc. The exclusion criteria were as follows: 1) Other western medical treatment options (Radiotherapy, Surgical and Local interventional therapy) ; 2) Other traditional Chinese Medicine treatment options (Decoction for oral and external use, emotional therapy, static breathing control, acupuncture); 3) repeat publications; and 4) Studies with incomplete or incorrect data.

Information sources: Computer search of China Knowledge Network, Wanfang database, China Biological The database of medical literature, Vipul.com, and foreign language databases Pubmed, EMBase, and Cochrane Library were searched. EMBase, Cochrane Library, etc. The RCTs of Chinese medicine injections in combination with TP were searched compared with western drugs alone for NSCLC, and the search period was from the date of creation to October, 2022. In addition, the literature can be supplemented by retrospective references and other resources such as conferences and books.

Main outcome(s): Endpoint indicators: Main outcome indicators: (1) Disease control rate (DCR), DCR = (complete remission + partial remission + stable) / total number of cases. Efficacy rate = (number of improvement cases + number of stable cases)/total number of cases. (2) Secondary outcome indicators: quality of life, determined according to the KPS behavioral status scale, improvement was defined as an increase of ≥10 points in KPS score after treatment; stability was defined as an increase or decrease of <10 points in KPS score; decline was defined as a decrease of ≥10 points in KPS score. (3) The incidence of adverse reactions, including gastrointestinal reactions, white blood cell (WBC) reduction, hemoglobin(HGB) reduction, platelet (PLT) reduction, etc.

Quality assessment / Risk of bias analysis: Information from the eligible RCTs was extracted by two researchersv independently based on a custom-made form. The data consisted of the following v items: (I) basic information of the eligibility: the first author, nationality, publication year, and study design; (II) basic characteristics of patients: sample size, sex composition, average age, course of disease, and cardiac function classification; (III) details of intervention; and (IV) the results of outcomes and information about quality assessment of RCTs. For dichotomous outcomes, the number of responders and the total number of participants for each study arm were extracted. For continuous outcomes, the mean and standard deviation for the mean in each group of the trial were extracted along with the total number. The quality assessment was independently performed by two reviewers with the Cochrane Collaboration's tools (version 5.1.0, http://handbook-5-1.cochrane.org/). The quality assessment items of Cochrane tools included the following: (I) selection bias: random sequence generation and allocation concealment; (II) performance bias: blinding of the participants and personnel; (III) detection bias: blinding of the outcome assessment; (IV) attrition bias: incomplete outcome data; (V) reporting bias: selective reporting; and (VI) other bias. Each aspect was categorized into three levels: high risk, unclear risk, and low risk. Any disagreements were resolved by a third researcher.

Strategy of data synthesis: All meta-analyses were performed within a Bayesian framework using R4.11 software for statistical analysis of data and research, and a Markov chain Monte Carlo method for Bayesian inference. The parameters set in R4.11 software were as follows: number of chains, 4; tuning iterations, 50,000; simulation iterations, 100,000; thinning interval, 1; settings of tuning iterations and simulation iterations were adjusted according to the actual situation. Potential scale reduction factors were used to evaluate the convergence of Markov chains. Models were compared using the deviance information criterion, which is equal to the sum of the posterior mean of the residual deviations and the number of valid parameters. Results for comparisons of dichotomous variables were calculated as odds ratios (OR). Differences between groups were considered statistically significant when the 95% confidence interval (CI) of OR values did not contain 1. Network diagrams showing indirect comparative relationships among different interventions were generated, where the nodal areas for each intervention represent the number of patients, and the thickness of lines between different interventions represented the number of RCTs. R4.11 and Stata17 software were used to plot cumulative probability ranking, and to generate mesh and funnel plots for each intervention. A surface under the cumulative ranking area (SUCRA) curve is used to estimate the probability of ranking each intervention; the larger the area under the curve, the higher the ranking and the higher the probability that the CHIs are the best interventions (Salanti et al., 2011). Clustering analysis was used to synthesize and compare interventions with two different outcome indicators, to obtain the best choice of injection for both outcome indicators: the farther away from the origin in the clustering plot, the better the outcome indicator. Acomparison-adjusted funnel plot was used to assess potential publication bias. If points on both sides of the midline in the funnel diagram were symmetric, which meant the correction guideline was at right angles to the midline, it was considered indicative of no significant publication bias.

Subgroup analysis: No.

Sensitivity analysis: Sensitivity analysis based on heterogeneity.

Language restriction: No language restrictions.

Country(ies) involved: China.

Keywords: network meta-analysis, Bayesian model, Chinese herbal injections, non-small cell lung cancer, Combined therapy, Chinese medicine.

Contributions of each author:

Author 1 - ciyan Peng.
Email: pengciyan@csu.edu.cn
Author 2 - jing Chen.
Email: 332589636@qq.com
Author 3 - lei Yang.
Email: leiyang@163.com
Author 4 - qin Zhang.
Email: zhangqin@163.com
Author 5 - li Huang.
Email: huangli@163.com
Author 6 - min Wen.
Email: wenmin@163.com
Author 7 - Sini Li.
Email: lisini@163.com
Author 8 - Wei Cui.
Email: 42010299@qq.com
Author 9 - Jianhe Li.
Email: lijianhe@163.com