


Efficacy of Nonpharmacological Interventions in Acute Postoperative Pain of Patients with Lung Cancer Undergoing Video-Assisted Thoracoscopic Surgery: A Protocol for Systematic Review and Network Meta-Analysis

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Background: Acute postoperative pain is one of the most common and painful complications of lung cancer patients undergoing video-assisted thoracoscopic surgery, which seriously affects the health and quality of life of patients. Although using medication for analgesia is the standard, their risk of adverse events still cannot be ignored. Non-pharmacological interventions are increasingly studied, but their relative efficacy in a given population remains unclear. The purpose of this study protocol is to compare the efficacy of non-pharmacological interventions in acute postoperative pain of patients with lung cancer undergoing video-assisted thoracoscopic surgery.

Methods: We will search ten electronic databases, mainly including CNKI, VIP, WanFang, PubMed, Web of Science, MEDLINE, Scopus, CINAHL, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) from their inception to August 2025. We will select randomized controlled trials to evaluate the efficacy of non-pharmacological interventions on acute postoperative pain. Our primary outcome is intensity of acute postoperative pain at 24 hours. Secondary outcomes include analgesic use, patient satisfaction and adverse events. Then, standard network meta-analysis (NMA) will be conducted using Stata V.17.0.

Results: We hope that the study will identify the most effective non-pharmacological interventions to clarify relative efficacy through direct and indirect comparisons via NMA.

Conclusion: Our findings will potentially provide evidence-based guidance for acute pain management in lung cancer patients and promote optimal use of non-pharmacological interventions to improve recovery patient quality of life and reduce medication risk.

Keywords: acute postoperative pain, lung cancer, systematic review

Introduction

Cancer remains a leading cause of morbidity and mortality worldwide, with lung cancer representing the most prevalent and deadly malignancy.¹ According to the latest Global Cancer Observatory (GLOBOCAN) estimates, lung cancer accounts for approximately 2.2 million new cases and 1.8 million deaths annually, making it a critical public health challenge.² With the development of international urbanization and industrialization and the influence of air pollution and higher smoking rate, the incidence and mortality of lung cancer show a significant increasing trend.³ Lung cancer includes small cell lung cancer and non-small cell lung cancer.⁴ Non-small cell lung cancer (NSCLC) constitutes 80–85% of all lung cancer cases, and early-stage diagnosis often necessitates surgical intervention for curative intent.⁵ For early NSCLC that has been clearly diagnosed, surgical resection is the preferred treatment option if there are no obvious surgical contraindications.⁶ Although traditional thoracotomy has obvious effect in radical cure of lung cancer and reducing postoperative tumor recurrence or metastasis, it has disadvantages such as large trauma, heavy pain, slow

recovery, many complications and long hospital stay. With advancements in minimally invasive techniques, video-assisted thoracoscopic surgery (VATS) has become the standard approach for early-stage NSCLC resection, offering advantages such as reduced trauma, shorter hospital stays, and faster recovery.⁷ However, despite its minimally invasive nature, postoperative pain remains a significant clinical issue. A patient-reported outcome study of thoracoscopic surgery showed that pain is one of the five major symptoms in patients operated after thoracoscopic surgery, and that more than 50% of patients operated for lung cancer still experience postoperative pain to varying degrees.^{8,9} If the pain is not well controlled, it will affect the postoperative patient's physical health and may lead to complications such as pulmonary dysfunction, delayed mobilization, and chronic post-surgical pain (CPSP).¹⁰ Acute postoperative pain refers to pain within 7 days after surgery. During the acute period, the pain is mostly sharp pain, knife cutting pain and pulling pain. Related investigation studies show that the incidence of acute pain is 80–96%.¹¹ Acute postoperative pain is unfavorable for patients to perform the necessary early activity and lung function exercise. Some patients have increased chest pain due to breathing, which leads to the fear of pain, leading to the fear of lung function exercise. Therefore, it can be seen that pain management in thoracoscopic lung cancer is of vital importance.

Postoperative analgesia has always been a major medical challenge.¹² Standardized analgesic treatment can relieve the pain degree of patients, thus reducing the difficulty of lung function exercise. Clinical commonly used analgesia methods include paravertebral block, epidural analgesia, patient-controlled intravenous analgesia, and multimodal analgesia, but there is no unified analgesia and drugs after thoracoscopy.^{13,14} Paravertebral block can reduce blood pressure, postoperative urinary retention, nausea and vomiting, but the area of paravertebral block is limited and the cost is expensive.¹⁵ Epidural analgesia can significantly promote the postoperative rehabilitation of patients, but it is risky and time-consuming, often accompanied by nerve root injury, hypotension and dural respiratory depression.^{16,17} Therefore, this analgesia pattern needs further study. Patient-controlled intravenous analgesia is simple and easy to operate, with few contraindications, but sometimes can not achieve fully effective analgesic effect, and may be accompanied by systemic adverse reactions such as constipation, nausea and vomiting.¹⁸ Multimodal analgesia can achieve sufficient analgesic effect and reduce the related side effects, but it also has the disadvantage of time-consuming and high cost.¹⁹

Given these limitations, non-pharmacological interventions have emerged as promising adjuncts or alternatives for postoperative pain management. These methods include exercise interventions, massage therapy, patient-controlled cognitive behavioral intervention and psychotherapeutic intervention. Exercise interventions can stimulate the release of endorphins in the pituitary gland, which can help relieve pain, improve tolerance and reduce the amount of drugs used.^{20,21} Proper massage can help patients relax and improve the quality of life by stimulating acupoints, promoting blood circulation, relieving muscle tension, reducing pain and discomfort.^{22–24} A patient-controlled cognitive-behavioral intervention that primarily involves strategies for relaxation and imagination exercises.²⁵ This strategy can be used to help patients shift attention away from symptom feelings and alter maladaptive thoughts and beliefs about symptoms.^{26,27} The American Pain Association recommends the use of this strategy to promote pain relief.²⁸ Psychotherapeutic intervention (music therapy and narrative therapy) can help to relieve the degree of pain and improve the quality of life by adjusting the patient's psychological disorders.^{29,30} Psychotherapeutic intervention is considered an effective complementary treatment for psychosomatic disorders.²⁹ Although these studies have confirmed the efficacy of non-pharmacological treatments, the advantages and disadvantages between different non-pharmacological interventions have rarely been found. Therefore, this study aims to evaluate the efficacy of different non-pharmacological interventions and to identify the most effective way to improve acute postoperative pain of patients with lung cancer undergoing video-assisted thoracoscopic surgery by a systematic review and NMA.

Methods and Design

This study will be conducted as a systematic review and NMA to evaluate the efficacy of nonpharmacological interventions in managing acute postoperative pain in patients with lung cancer undergoing video-assisted thoracoscopic surgery. Our review design follows the methodological recommendations for the systematic review of interventions in the Cochrane Handbook³¹ and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.³² The study design allows for direct and indirect comparisons of multiple interventions to determine their relative efficacy. If any modifications are encountered throughout the study, we will also make ongoing

updates in the final systematic review and NMA report. The protocol for this review has been registered on the PROSPERO International Prospective Register of Systematic Reviews (CRD420251130949).

Eligibility Criteria

Study Design

All randomized controlled trials (RCTs) of nonpharmacological interventions for acute postoperative pain in VATS patients will be included. We will choose the English or Chinese publications. If the following conditions exist, we will exclude the corresponding paper.

- (1) Non-English and Chinese language publications.
- (2) Non-RCTs studies, such as letters, systematic reviews, case reports, animals or investigative studies.
- (3) For repeated published studies, we selected only one of them.
- (4) We will also exclude studies lacking extractable outcome data.

Population

The target population consists of adult patients (≥ 18 years) with lung cancer who underwent VATS and received nonpharmacological interventions for acute postoperative pain interventions. There will be no restrictions on gender, ethnicity, or stage of lung cancer of the patients. Patients with other severe diseases that may significantly affect postoperative pain will be excluded to ensure that the observed pain outcomes are mainly related to the VATS procedure and the non-pharmacological interventions being evaluated. Also, this study does not include studies involving patients with mental disorders or mental disorders.

Interventions

All types of non-pharmacological interventions designed to relieve acute postoperative pain after VATS in lung cancer patients will be considered. These interventions include psychological interventions (such as cognitive behavioral therapy and relaxation training), physical interventions (such as massage therapy, acupuncture and breathing exercises), and educational interventions (such as preoperative pain education and postoperative pain management guidance). These interventions must be implemented during the acute postoperative period because this is the most acute critical time for acute pain and requires effective management.

Comparison

Comparison group may include placebo or sham interventions, standard care, other active nonpharmacological interventions or standard pharmacological pain management alone. Placebo or sham interventions: For example, a placebo educational session with no actual pain management content, or sham acupuncture where the needles are not inserted into the correct acupoints. Standard care: Patients receive routine postoperative care without any additional nonpharmacological pain management interventions. Other active nonpharmacological interventions: This allows for the comparison of the efficacy of different nonpharmacological approaches. Standard pharmacological pain management alone: This helps to evaluate whether adding a nonpharmacological intervention to standard pharmacological treatment provides additional benefits.

Outcomes

The primary outcome is the intensity of acute postoperative pain, measured using a validated pain scale such as a Numerical Rating Scale (NRS, 0–10, where 0 indicates no pain and 10 indicates the worst possible pain). Pain intensity will be assessed at specific time points within 24 hours. Secondary outcomes include total opioid use, incidence of intervention-related side effects (eg, nausea, dizziness), reported satisfaction with pain management and postoperative hospitalization duration.

Search Strategies

We will conduct a comprehensive systematic literature search in domestic and foreign electronic databases to identify relevant studies that meet the requirements. We searched in ten electronic databases, mainly including CNKI, VIP,

WanFang, PubMed, Web of Science, MEDLINE, Scopus, CINAHL, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL) from their inception to August 2025. Our retrieval strategy was to use a combination of medical subject words and free words. Truncation included “thoroscop*neoplasm*”, free word included “VATS”, “RCT”, and subject words included “lung”, “postoperative pain” and “randomized controlled trial”. The two investigators then cross-checked the selected papers to find the corresponding eligible studies. The search strategy varies for each database, and we will make appropriate adjustments according to the specific index system of a specific database. Furthermore, to identify possible potential studies that would not be missed by electronic database searches, we also manually searched and browsed relevant systematic reviews and reference lists of included studies. We searched the three clinical trial registries (WHO, Clinical trials.gov and the International Clinical Trials Registry Platform) to identify ongoing experiments. At the same time, we searched grey literature in OpenGrey (<http://www.opengrey.eu/>) to avoid being missed.

Study Selection

After literature search, all retrieved documents in 10 databases are imported into Endnote X9 software. Duplicate studies are automatically removed, leaving only one of the duplicate studies remaining. Two reviewers will independently screen the retrieved literature against the inclusion and exclusion criteria. Secondly, based on the title and abstract of the literature, those studies that obviously do not meet the requirements will be excluded. For the remaining studies, two reviewers will be evaluated for their final inclusion by reading the full text. During the screening of the literature, any disagreement encountered between the two reviewers will be resolved through consultation and, if necessary, by consulting a third investigator to make a final decision.

Data Extraction

A standardized data extraction form will be produced and used by the two reviewers each, as intended to facilitate data extraction from the literature. The relevant data extracted will include study characteristics (author names, publication year, country, sample size, study design and duration of follow - up), patient characteristics (age, gender, stage of lung cancer and details of the VATS procedure), intervention details (type of non-pharmological intervention, duration, frequency and provider of the intervention), comparator details, (type and duration of the comparator) and outcome data (pain intensity scores, amount of analgesic drugs used, patient satisfaction scores and incidence of adverse events). If any missing data is found, we will all contact the corresponding author by email. If data are not available for a long period, we will note in the review. We will also consider taking an appropriate approach according to the extent of the missing data.

Risk of Bias Assessment

We will assess the risk of bias using the Cochrane Risk of Bias Tool (RoB 2.0) for RCTs included in this study. This evaluation tool includes the following six items for other biases, incomplete outcome data, random sequence generation, blinding, allocation concealment and selective reporting. Each item consists of three levels (“high risk”, “medium risk”, and “unclear risk”). The bias assessments of all studies finally summarize their risks in the table. If there is a disagreement, a third researcher will join in and discuss it together. We will present the results of the risk of bias assessment using the summary table and the risk of bias map.

Statistical Analysis

Network Meta-Analysis

In this study, all of the statistical analyses involved will be done using the Stata 17.0 software. For continuous variables, such as pain intensity, the mean difference (MD) or standardized mean difference (SMD) with 95% confidence intervals (CIs) will be calculated. The choice between MD and SMD should be based on the study design, data type and measurement methods. If all included studies use the same scale, MD is a better way to provide a clinically interpretable effect size. If different scales are used between different studies, the SMD should be preferred. At this point, SMD can eliminate differences between units and compare effect sizes. For dichotomous variables such as incidence of adverse events, the risk ratio (RR) with 95% CIs will be used. Due to differences in study populations, intervention plans and

outcome evaluation methods, both pairwise meta-analyses and network meta-analyses will use random effects models to explain heterogeneity between studies. Network consistency is assessed by using both local and global inconsistency tests. If significant disagreements occur ($P < 0.05$), we will explore the reasons for them in terms of the study population, intervention methods or outcome measures. If inconsistent cases are not resolved, we will consider using a Bayesian NMA as a sensitivity analysis to explore the impact of model assumptions.

Ranking of Interventions

The surface under the cumulative ranking curve (SUCRA) will be used to rank the efficacy of different nonpharmacological interventions. The SUCRA values range from 0 to 1, and larger values indicate the greater the intervention is the most effective. In addition, we will present the average ranking and the 95% CI to provide further explanatory strength for the ranking. For Bayesian analyses, the probability that each intervention is the best, second-best, etc., will also be presented to offer a more detailed understanding of the relative efficacy.

Heterogeneity Assessment

Heterogeneity between the included studies will be assessed using the I^2 statistic, χ^2 -test, P value and Tau^2 . The I^2 statistic will quantify heterogeneity ($I^2 < 25\%$: low; 25–50%: moderate; $>50\%$: high). The p value is <0.1 in the χ^2 -test, which will indicate the presence of significant heterogeneity. The Tau^2 will quantify the magnitude of the inter-study variance. If the P value is <0.10 and $I^2 > 50\%$, indicating substantial heterogeneity between studies, a subgroup analysis will be performed to explore possible sources of heterogeneity. Subgroup factors will include patient characteristics (age, gender and stage of lung cancer), intervention characteristics (type of nonpharmacological intervention, duration of intervention and frequency of intervention), study characteristics (study quality and year of publication). If there are enough studies (at least 10) to investigate the relationship between potential regulators and effect size, a meta-regression analysis will also be performed. We will also implement a sensitivity analysis. Sensitivity analysis is performed mainly by excluding studies with high risk of bias to assess the impact of study quality on outcomes or excluding studies with significant missing data to evaluate the influence of data completeness.

Publication Bias

If at least 10 studies are included in this study, funnel plots will be used to assess publication bias. Publication bias is indicated by visually examining whether the funnel plot has a symmetry. The Egger's test and Begg's test will also be used to perform publication bias, with the P value < 0.05 indicating significant publication bias. If publication bias is detected, trim - and - fill analysis will be used to adjust for the potential impact of missing studies.

Handling of Multiple Comparisons

Given the multiple outcomes and time points assessed, a Bonferroni correction will be applied to adjust the significance level for multiple comparisons. The adjusted significance level will be calculated as α/n , where α is 0.05 and n is the number of comparisons. This will help reduce the risk of type I errors.

Reporting of Results

In this study, we will present the results of the NMA in forest plots for pairwise comparisons, and we will also summarize the effect sizes between all pairs of the interventions in the league tables. The network graph will be used to clearly present the structure of the visual network. In the network graph, the nodes represent the interventions, and the edges represent the number of studies comparing the two interventions. For better interpretation of the data, the resulting ranking will be presented in tables and bar charts.

Discussion

To the best of our knowledge, this is the first systematic review and NMA to compare the efficacy of nonpharmacological interventions in acute postoperative pain of patients with lung cancer undergoing video-assisted thoracoscopic surgery. The study aims to provide valuable insights into the merits of these nonpharmacological interventions, ultimately aiming to alleviate postoperative pain levels, reduce related opioid dependence and improve patient quality of life. We seek to identify the most effective interventions by integrating data from existing nonpharmacological interventions and

providing sequencing of efficacy. This can not only provide a reference for clinical practice, but also indicate a way for the future research field.

In this study, the heterogeneity between the different studies may be a key issue that we need to consider. The sources of heterogeneity may be differences in intervention options (e.g., duration and frequency of massage therapy), patient characteristics (e.g., cancer stage and age) and time to outcome measures. For example, we speculate that subgroup analysis may show that younger patients receive faster mental health education intervention, while older patients can benefit more from physical intervention acupuncture and massage. These findings will also provide an alternative idea for future implementation of personalized pain management strategies.

If we detect inconsistent cases in the systematic review and NMA, the reasons here need to be carefully examined. This may occur because some interventions perform differently in specific circumstances. Music therapy may be more effective in reducing pain at 24 hours, but little effective at 72 hours. Furthermore, inconsistency may arise from differences between study intervention methods, such as different types of blinding or differences in randomization methods. These inconsistencies can be resolved by sensitivity analysis to improve the robustness of the conclusions.

The main strength of the study is the use of a rigorous approach, adhering to PRISMA-NMA guidelines. The most important strength of the systematic review and NMA is to allow for a comprehensive evaluation of multiple interventions that have never been directly compared with each other in a randomized trial. This study is not without its limitations. First of all, the systematic review and NMA mainly rely on randomized controlled trials, but may miss valuable data from non-randomized experiments, which limits the practicability and universality of research results in real-world clinical settings. Second, publication bias remains a matter to consider, as studies with some positive outcomes are more likely to be published, which may overestimate the efficacy of some interventions. We will use the pruning and filling analysis to adjust for this bias to help alleviate but not eliminate the problem.

In terms of the future research direction, we can start from the following aspects. First of all, high-quality, multicenter, large-scale RCTs directly comparing the most effective interventions identified in this study need to be implemented to clarify their efficacy and establish the optimal implementation protocol. Second, future studies could explore the mechanisms of nonpharmacological interventions to relieve acute pain. Studying what effects it has on neuroendocrine pathways or inflammatory responses could thus provide clues to the development of more targeted interventions. After that, investigating the cost-efficacy of these nonpharmacological interventions will help the health-care system to rationally allocate resources effectively. If nonpharmacological interventions prove to be cost-effective, policymakers may be more likely to include them in national clinical guidelines or expand insurance coverage to increase patient access. Finally, qualitative research implementing nonpharmacological interventions is needed to explore patient preferences and experiences in order to complement the results of quantitative research and ensure that future pain management strategies are effective and patient-centered.

Systematic Review Registration

PROSPERO CRD420251130949.

Data Sharing Statement

The datasets generated and analysed during the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request.

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Disclosure

The authors declare that they have no conflicts of interest in this work.

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