

BMJ Open Enhanced recovery after surgery management of perioperative period in surgical lung cancer patients: protocol for a systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Introduction Enhanced recovery after surgery (ERAS) has been widely used in the perioperative period of lung cancer surgery. However, there remains a lack of comprehensive and systematic evidence on the effectiveness and safety of ERAS. This study aims to evaluate the efficacy and safety of ERAS in patients with lung cancer.

Methods and analysis Eight databases (PubMed, Web of Science, Embase, Cochrane Library, CNKI, CBM, VIP and WANFANG) will be searched from inception to November 2021. Two reviewers will independently screen studies, extract data of interest and assess the risk of bias. The revised risk of bias tool 2 will be used to assess the risk of bias in randomised controlled trials. We will use the Grading of Recommendations, Assessment, Development and Evaluations to assess the certainty of evidence. We will carry out a random-effect meta-analysis focusing on the efficacy and safety variables. All analyses will be conducted using RevMan V.5.3.

Ethics and dissemination Since the study will be a systematic review and will not involve direct contact with patients or make alterations to patient care, ethical approval and informed consent are not required for this study. The results of this review will be published in a peer-reviewed journal.

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INTRODUCTION

Lung cancer is the most common cause of cancer-related deaths worldwide. According to the WHO, in 2020, more than 2 million new lung cancer cases were reported worldwide, and there were 1.80 million deaths.¹

Currently, surgical treatment for lung cancer is becoming more advanced. However, postoperative pulmonary complications (PPCs),² such as respiratory failure, pleural effusion, atelectasis, pneumothorax, acute respiratory distress syndrome and pneumonia, have caused widespread clinical concern. Prospective observational studies have shown that lung surgery is associated with 13%–14.5% PPCs.^{3,4} Overall, the incidence of

Strengths and limitations of this study

- We will adopt strict inclusion and exclusion criteria to evaluate the quality of the included studies. To some extent, this will ensure that our review could serve as an up-to-date and comprehensive summary of the published evidence on the topic of enhanced recovery after surgery (ERAS) in the perioperative period for patients with lung cancer.
- We will use the Grading of Recommendations Assessment, Development and Evaluation approach to evaluate the certainty of evidence.
- Heterogeneity might be caused by various features in specific settings, such as the general strategy of perioperative management at each institution, inconsistent assessment of the outcomes and the difference of ERAS elements used.

PPCs in lung surgery is approximately 7.4%–20.6%, and the number of deaths caused by PPCs accounts for about 84% of all deaths in hospitalised patients.⁵ Thus, optimising therapies for patients with major complications in modern lung cancer surgery has become increasingly important.⁶ Multiple therapeutic strategies and perioperative management plans have been introduced into the surgical field, such as infection control, nutritional support, improvement of fluid management and pursuit of ideal preoperative evaluation.⁷ Enhanced recovery after surgery (ERAS) pathways, also known as fast track surgery (FTS), have been shown to be associated with better patient outcomes.^{8,9}

FTS is an evidence-based, multimodal approach aimed at reducing surgical stress response and organ dysfunction, promoting patient postoperative recovery, and it involves the participation of surgeons, anaesthesiologists, nurses and physical therapists.¹⁰ FTS combines various techniques used in the

care of patients undergoing elective operations, such as regional anaesthesia, minimally invasive techniques, intraoperative normothermia, optimal pain control and aggressive postoperative rehabilitation.¹¹

As they evolved from the FTS approach, ERAS pathways emphasise that the key surgical endpoint is the quality, rather than the speed of recovery,¹² which includes epidural or local anaesthesia, laparoscopic techniques, optimal pain control and enhanced postoperative rehabilitation. ERAS focuses on engaging patients and their families in their care, which includes minimising surgical stress, optimising patients for surgery and restoring normal physiology as expeditiously as possible after surgery. The objective of ERAS is to incorporate evidence-based strategies into the preoperative, intraoperative and postoperative care plan that reduce patients' surgical stress response and accelerate their functional recovery, and to improve quality of care, decrease complications and shorten hospital stays.¹² As a multidisciplinary collaborative process, ERAS can be implemented with the cooperation of specialist doctors, ward nurses, anaesthesiologists, operating room nurses and the patients themselves. Standardised perioperative care helps ensure that patients receive optimal treatment, and lately, some recommendations for guidelines have been developed for ERAS.¹³ ERAS has been used in the surgical treatment of malignant tumours by mainly laparoscopic surgery, and it has recently been applied to lung cancer surgery.^{14–16} However, the efficacy and safety of ERAS during the perioperative period in lung cancer patients are still unclear. The purpose of this systematic review is to conduct a meta-analysis of randomised controlled trials (RCTs) to evaluate the efficacy and safety of ERAS during the perioperative period in patients with lung cancer.

METHODS

This study will be conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.¹⁷

Inclusion and exclusion criteria

Type of participants

The study will only include RCTs having participants over 18 years old with a pathological diagnosis of primary lung cancer and without mental disorders regardless of sex, age, nationality or educational background. Studies will also be included if data from studies that patients with lung and non-lung cancers in ERAS programmes could be identified separately. Reviews, non-RCTs, cohorts and case reports will be excluded.

Type of intervention

Studies disclosing findings on the comparison between ERAS (intervention group) vs standardised nursing care (control group) perioperative management before, during or after surgery will be enrolled. ERAS pathways are composed of elements applied in the entirety of the

patient's pathway phases—preoperative, intraoperative and postoperative phases—and included studies should have reported at least one of the outcomes of interest. Standardised nursing care includes performing preoperative preparations, patient education before the surgery, improving patient compliance, cooperating with doctors and nurses during the operation, monitoring vital signs and providing rehabilitation guidance after surgery. Based on guidelines¹² and common clinical measures, ERAS mainly involves preadmission education and counselling, nutrition management, smoking cessation, alcohol dependency management, preoperative fasting, carbohydrate treatment in the preoperative phase, prevention of hypothermia, improvement of surgical techniques (eg, minimally invasive surgery or thoracotomy), continuous monitoring of vital signs during the operation, analgesia management, early mobilisation and adjuncts to physiotherapy, urinary drainage and chest drain management in the postoperative phase. We will exclude RCTs reporting outcomes for an ERAS pathway that did not cover any of the patient's pathway phases (preoperative, postoperative or intraoperative).

Type of outcomes

The primary outcomes are the length of hospital stay, and mortality rates. The secondary outcomes include morbidity of complications, pain score, adverse events, quality of life and patient satisfaction. The complications reported in RCTs are included in the Clavien-Dindo classification¹⁸—a standardised system including seven grades for the registration of surgical complications, such as noninfectious diarrhoea, brain haemorrhage, multi-organ dysfunction and death.

Data sources and search strategy

A systematic electronic search will be carried out in PubMed, Web of Science, Embase, Cochrane Library, CNKI, CBM, VIP and WANFANG databases from inception to November 2021. In addition, grey literature, such as bibliographic references, will be included. The search strategy for PubMed is shown in [table 1](#). See online supplemental material for the search strategies of the other databases.

Study selection

Search records will be imported into the reference management software Rayyan.¹⁹ Two reviewers will independently screen the titles and abstracts of each record, and further review the full texts of any potentially eligible studies for eligibility. Any disagreements will be resolved by discussion between the two reviewers or consultation with a third reviewer.

Data extraction and management

Outcome indicators for eligible studies will be independently extracted and filled in the data extraction form by the two reviewers. The data to be extracted are as follows: title, author, publication year, study design, sample size, age, sex, stage of disease, ERAS pathway

Table 1 PubMed database search strategy

Order	Strategy
#1	Enhanced recovery after surgery [MeSH Terms] OR fast track surgery [MeSH Terms]
#2	“enhanced recovery”[Title/Abstract]OR “ERAS”[Title/Abstract]OR “enhanced recovery after surgery”[Title/Abstract] OR “fast track surgery”[Title/Abstract]OR “FTS”[Title/Abstract]OR “fast track rehabilitation”[Title/Abstract]OR “fast track recovery”[Title/Abstract]OR “rapid rehabilitation”[Title/Abstract]OR “accelerated rehabilitation”[Title/Abstract] OR “accelerated care”[Title/Abstract]
#3	#1 OR #2
#4	lung cancer [MeSH Terms]
#5	“lung neoplasm”[Title/Abstract]OR “lung cancer”[Title/Abstract]OR “lung neoplasia”[Title/Abstract]OR “lung tumour”[Title/Abstract]OR “lung carcinoma”[Title/Abstract]OR “lung adenocarcinoma”[Title/Abstract]
#6	#4 OR #5
#7	Randomised Controlled Trials [MeSH Terms]
#8	“randomised controlled trial”[Publication Type] OR “controlled clinical trial” [Publication Type] OR randomised[Title/Abstract]OR placebo[Title/Abstract]OR randomly[Title/Abstract]OR trial[Title/Abstract]
#9	#7 OR #8
#10	#3 AND #6 AND #9

details (including preoperative, intraoperative and post-operative phases), control measures, follow-up, outcome measures, adverse reactions and funding source. Reviewers will resolve conflicts by discussion, and a third reviewer will make an adjudication if necessary.

Risk of bias assessment

The quality of RCTs will be assessed using the Cochrane risk of bias 2 tool.²⁰ Bias is assessed in five distinct domains, which are randomisation process, deviations from intended interventions, missing outcome data, measurement of the outcome and selection of the reported result. Within each domain, we will answer one or more signalling questions, which lead to judgements of ‘low risk of bias’, ‘some concerns’ or ‘high risk of bias’. Two reviewers will independently assess the risk of bias for each study, and any disagreements will be resolved by a third reviewer.

Assessing certainty of the evidence

We will assess the certainty of evidence using the Grading of Recommendations Assessment, Development and Evaluation system.²¹ The results will be categorised as high, moderate, low and very low certainty of evidence. The certainty can be downgraded for five reasons: risk of bias, imprecision, inconsistency, indirectness and publication bias.

Data analysis

We will conduct meta-analyses using Review Manager software (RevMan, V.5.3, Copenhagen; The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). For dichotomous data, we will calculate the relative risk with corresponding 95% CIs, whereas continuous data will be expressed as mean difference (MD) with 95% CI. Missing data will be processed according to the Cochrane Handbook for Systematic Reviews of Interventions.²² We will calculate all results using the random-effects model. Statistical heterogeneity will be assessed with I^2 statistics,

and values of <25%, 25%–50% and >50% will be considered low, moderate and high levels of heterogeneity, respectively.²³ Funnel plots will be used to detect the potential publication bias if the number of included trials is larger than ten for an outcome. Subgroup analysis will be conducted based on the different causes of heterogeneity. If a meta-analysis cannot be performed, we will perform a general descriptive analysis.

Patient and public involvement

Patients and/or the public will not be involved in the design, implementation, reporting or dissemination plans of this research.

DISCUSSION

As a form of surgical treatment, ERAS has been widely used in patients with cancer. Studies have found that ERAS is also beneficial for lung cancer during the perioperative period.^{24 25} Currently, there are no systematic reviews on the effects of ERAS in patients with lung cancer. Therefore, this study will be a comprehensive systematic review and meta-analysis of the effectiveness of ERAS in the treatment of lung cancer, aiming to provide the latest evidence for the use of ERAS and guide clinical decision making.

ETHICS AND DISSEMINATION

Since the study will be a systematic review and will not involve direct contact with patients or make alterations to patient care, ethical approval and informed consent are not required for this study. The results of this review will be published in a peer-reviewed journal.

Contributors XF made substantial contributions to conception and design of the protocol. TC and HW performed the preliminary search. TC, WY and YS drafted the manuscript and XF revised it critically for intellectual content.

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Competing interests None declared.

Patient consent for publication Not applicable.

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