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SYSTEMATIC REVIEW

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Effects of lung protection ventilation strategies on postoperative pulmonary complications after noncardiac surgery: a network meta-analysis of randomized controlled trials

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Abstract

Background The purpose of this network meta-analysis was to assess the impact of different protective ventilatory strategies on postoperative pulmonary complications (PPCs).

Methods Several databases were searched for randomized controlled trials (RCTs) that were published before October 2023 in a network meta-analysis. We assessed the effect of different lung-protective ventilation strategies on the incidence of PPCs using Bayesian network meta-analysis.

Results We included 58 studies (11610 patients) in this meta-analysis. The network meta-analysis showed that low tidal volumes (LTVs) combined with iPEEP and recruitment manoeuvres (RM) was associated with significantly lower incidence of PPCs [HTVs: OR = 0.38, 95%CrI (0.19, 0.75), LTVs: OR = 0.33, 95%CrI (0.12, 0.82)], postoperative atelectasis[HTVs: OR = 0.2, 95%CrI (0.08, 0.48), LTVs: OR = 0.47, 95%CrI (0.11, 0.93)], and pneumonia[HTVs: OR = 0.22, 95%CrI (0.09, 0.48), LTVs: OR = 0.27, 95%CrI (0.08,0.89)] than was High tidal volumes (HTVs) or LTVs. LTVs combined with medium-to-high PEEP and RM were associated with significantly lower incidence of postoperative atelectasis, and pneumonia.

Conclusion LTVs combined with iPEEP and RM decreased the incidence of PPCs, postoperative atelectasis, and pneumonia in noncardiac surgery patients. Individual PEEP-guided ventilation was the optimal lung protection ventilation strategy. The quality of evidence is moderate.

Trial registration PROSPERO identifier CRD42023399485.

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Keywords Mechanical ventilation, Postoperative complications, Network meta-analysis

Introduction

Postoperative pulmonary complications (PPCs) are common following surgery under general anaesthesia, with an incidence ranging from 11 to 33% among the surgical population [1, 2]. Some studies have demonstrated that the use of low tidal volumes (LTVs), positive end-expiratory pressure (PEEP), and recruitment manoeuvres (RM) can reduce the incidence of PPCs. These methods are collectively referred to as lung ventilation protection strategies. Evidence suggests that lung-protective ventilation may improve the outcome in individuals with acute respiratory distress syndrome [3, 4]. The use of lung-protective ventilation in surgical patients has been studied over the past few decades, but the findings have been inconclusive. Traditional lung-protective ventilation includes moderate PEEP levels, RM, and low tidal volumes (6–8 ml/kg predicted body weight). In 2019, an international panel of experts recommended the use of conventional lung-protective ventilation for surgical patients [5]. However, traditional lung-protective ventilation has been challenging in recent years. Large randomized controlled clinical trials have shown that traditional lung-protective ventilation does not reduce the incidence of PPCs [6, 7], and another large retrospective study revealed that low PEEP (2.2 to 5 cmH_2O) increased the 30-day postoperative mortality rate [8]. A meta-analysis showed that low tidal volume combined with PEEP significantly reduced the incidence of PPCs, but different PEEP levels did not affect the occurrence of PPCs [9]. However, another network meta-analysis showed that low ventilation combined with moderate to high PEEP levels and RM reduced the incidence of postoperative pulmonary atelectasis [10]. Selecting the optimal lung-protective ventilation strategy has always been challenging in clinical practice. Over the past few years, some studies have shown that individual PEEP (iPEEP) may be an optimal lung-protective ventilation strategy [11–14]. The titration of the iPEEP includes the transpulmonary pressure and electrical impedance tomography, driving pressure and compliance of the respiratory system [12, 13, 15, 16].Previous network meta-analyses have shown that iPEEP-guided protective ventilation strategies may improve intraoperative oxygenation and reduce the incidence of postoperative pulmonary atelectasis [17–19]. However, it is still unclear which lung-protective ventilation strategy can effectively reduce the incidence of PPCs and improve patient prognosis.

This study aimed to compare the effects of different lung- protection strategies on postoperative pulmonary complications. Different lung-protective ventilation strategies exist (e.g., different tidal volumes, different PEEP levels, with or without RM). Because of this, conducting a standard paired meta-analysis is challenging. Instead, we compared several lung-protective ventilation strategies using a network meta-analysis (NMA) to identify the best lung-protective ventilation strategy.

Materials and methods

We compared the effect of different lung-protective ventilation on PPCs using NMA. The Preferred Reporting Items for Systematic Reviews and Network Meta-Analyses (PRISMA) guidelines were followed for reporting [20].

Search strategy

A search of the PubMed, Embase, and Cochrane Library databases was done for full-text English papers published before October 2023. Appendix 1 has details on the search strategy. Additionally, clinical trial registries were searched for unpublished trials. Furthermore, the references listed in the collected literature were reviewed to determine whether any trials were potentially eligible for inclusion.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) RCTs; (2) Research conducted on adult surgical patients who were 18 years or older and received mechanical ventilation under general anesthesia; (3) studies involving noncardiac surgery; (4) studies involving intervention measures for an explicit lung protection strategy. The exclusion criteria were as follows: (1) studies involving non-invasive ventilation; (2) studies in which primary data could not be extracted; (3) Nonclinical randomized controlled trials or non-English literature.

Primary outcomes

(1) incidence of PPCs; (2) incidence of postoperative atelectasis; (3) incidence of postoperative pneumonia.

Second outcomes

(1) Postoperative oxygenation index; (2) Incidence of intraoperative hypotension; (3) length of hospital; (4) postoperative short-term mortality.

Data extraction

Two reviewers (Jun Mo, and Dan Wang) independently extracted data from each included study. We collected the following data: author; year of publication, type of lung protection strategy, sample size, and type of surgery.

A PEEP of 4–8 cmH_2O or less than 4 cmH_2O or more than 8 cmH_2O has been reported in the literature, which we defined as moderate PEEP(MPEEP) or low PEEP(LPEEP) or high PEEP(HPEEP), respectively. Individual PEEP (iPEEP) settings are based on the patient's compliance of the respiratory system, which we define as iPEEP.

If the necessary data did not include specific data, the authors were contacted to provide more details. Furthermore, if the amount required was presented as a numerical value, we utilized Engauge Digitizer software (version 4.1, Mitchell) to obtain the data from the graph. In the case where the dichotomous data had a value of 0, we have taken into account the decision to add 1 to each group [21]. When the data showed an interquartile(IQR) range, we utilized the IQR as the mean, and IQR/1.35 as the standard deviation [22]. When the data showed minimum-maximum and median, we did not statistically analyze this data.

Data synthesis and analysis

The qualifying articles were assessed independently for their quality using the Cochrane Collaboration methodology. The assessment of the certainty of confidence in the network meta-analysis was conducted using the Confidence in Network Meta-analysis (CINeMA 0.6.1 version) tool, which is based on the six fundamental components of the GRADE approach. These variables include the evaluation of bias within the study, bias in reporting, lack of directness, imprecision, and heterogeneity [23, 24].

The Del Simonian-Laird random effects model was used to do standard pairwise meta-analyses. The effect measure for each outcome was calculated by generating the weighted mean difference (WMD) combined with a 95% credible interval (CrI). The I^2 statistic was used to assess heterogeneity, which quantifies the proportion of overall variation that may be associated with differences between studies.

A random-effects Bayesian framework was utilized to conduct a meta-analysis of network-based studies [25]. A WMD for each outcome with a 95% CrI was calculated and summarised. Moreover, a calculation was made regarding the probability of each intervention being evaluated among all treatments. The treatment rankings were condensed and presented as a cumulative rank under the curve (SUCRA). The SUCRA value represents the probability of a treatment being effective, where a value of 1 indicates that the treatment is the most effective and a value of 0 signifies that the treatment is the least effective.

Examination of assumptions

To assess the overall consistency of the assumptions made across the analysis network, a design-by-treatment approach was employed. Furthermore, a loop-specific methodology and node splitting were applied to inconsistencies [26, 27]. An I^2 statistic was utilized to assess global heterogeneity, incorporating the degree of heterogeneity to ascertain the degree of uncertainty in the estimated effect size at the local level [28].

The potential for publication bias in the results of small and large trials was assessed using comparison-adjusted funnel plots. To investigate whether the results were influenced by study characteristics, a subgroup network meta-analysis was conducted according to the type of surgery. Furthermore, a meta-regression in the Bayesian framework was performed to examine the potential impact of modifying the surgery type.

We performed the network meta-analysis in STATA 17.0 using the network and R version 3.6.2(gemtc package) [29, 30]and self-programmed STATA routines available [31].The SMD and OR for each outcome with a 95% CrI were summarized.

Results

Study characteristics

A total of 6,956 citations were identified from the databases. Following the established eligibility criteria, a total of 58 studies comprising 11,610 patients were ultimately included in the NMA. The search strategy and results are presented in Appendix 1. The flow chart of literature screening is presented in a flow chart in Fig. 1.

The basic characteristics of the included studies are outlined in Appendix 2. Eleven lung protective ventilation strategies were reported, including LTVs+iPEEP+RM, LTVs+MPEEP+RM, LTVs+MPEEP, LTVs+HPEEP+RM, LTVs+LPEEP, LTVs+MPEEP+use of ultrasound for RM (URM), high tidal volumes (HTVs)+MPEEP, HTVs+HPEEP, HTVs+RM, LTVs and HTVs. The reference for the included trials and characteristics can be shown in Appendix 2.

Among the literature on iPEEP-guided lung protective ventilation strategies, eight involved dynamic compliance-guided PEEP, four involved driving pressure-mediated PEEP, and four involved the guidance of electrical impedance tomography.

Quality assessment

The risk of bias is detailed in Appendix 3. Twenty-five trials were assessed as high risk, ten trials were assessed as moderate risk, and twenty-three trials were assessed as low risk. The most common risk was incomplete blinding of the participants and personnel, as well as allocation concealment.

Network meta-analysis

Incidence of PPCs

Forty trials (10330 patients) reported the incidence of PPCs for different lung protective ventilation strategies. Twenty-nine RCTs defined PPCs as: hypoxemia,

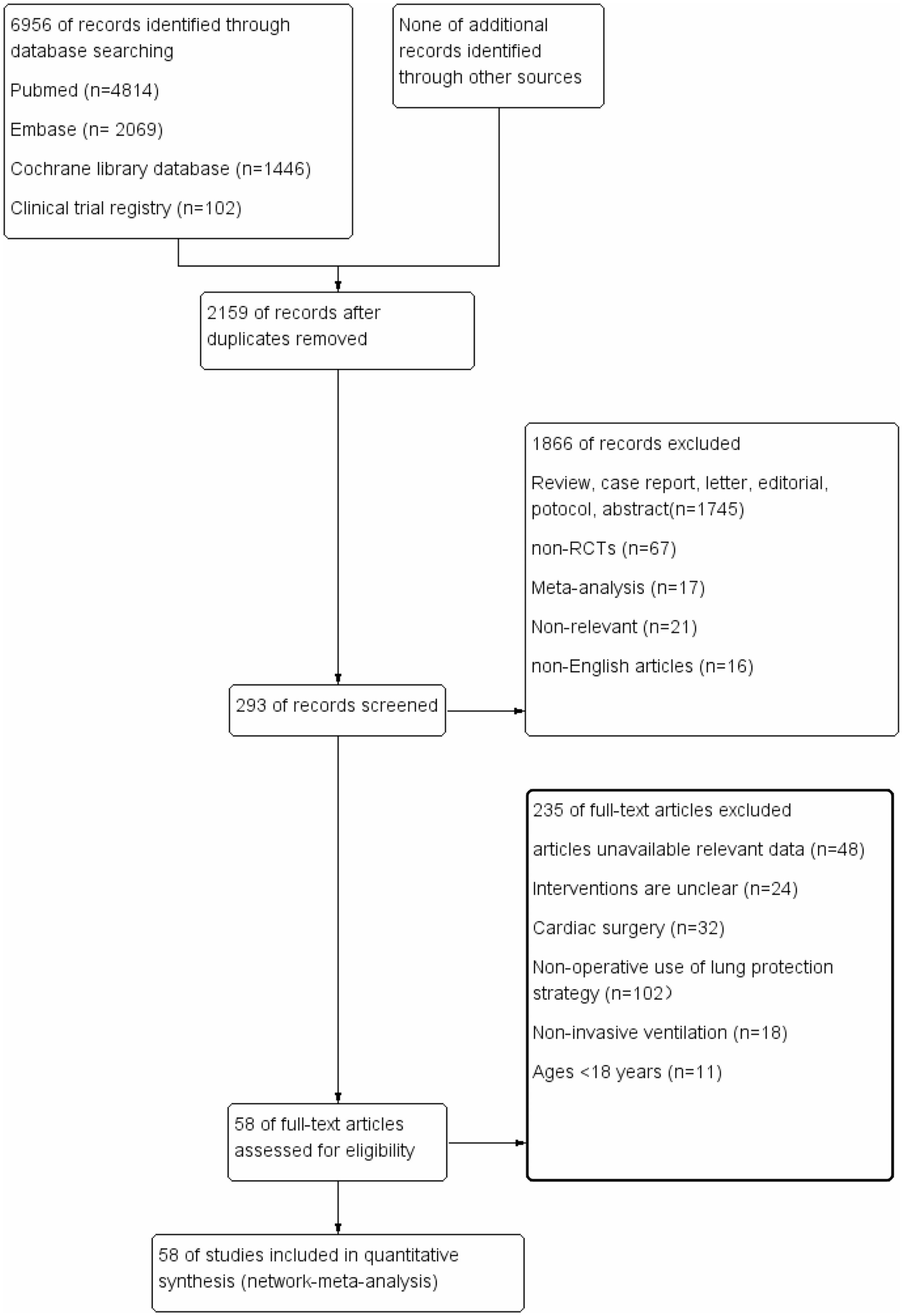

Fig. 1 Flow chart of literature screening

oxygen, re-intubation and mechanical ventilation, tracheostomy, pneumonia, pulmonary empyema, atelectasis, ARDS, or acute lung injury. Four RCTs defined PPCs as: hypoxemia, pneumonia, atelectasis, or pulmonary embolism. Six RCTs defined PPCs as: pneumonia, atelectasis, or hypoxemia. One RCTs defined PPCs as dyspnea, pneumonia, pneumothorax, respiratory distress or chronic respiratory failure. The definition of PPCs included in the literature is shown in Appendix 16. The results of the NMA showed that LTVs combined with iPEEP and RM were associated with a significantly lower incidence of PPCs than LTVs combined with MPEEP [OR=0.47, 95%CrI (0.22, 0.97)], LTVs [OR=0.33, 95% CrI (0.12, 0.82)] and HTVs [OR=0.38 95%CrI (0.19, 0.75)], respectively. The combination of LTVs with iPEEP and RM (90.7%) was found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Incidence of postoperative atelectasis

Twenty-seven trials (6584 patients) reported the incidence of postoperative atelectasis for different lung protective ventilation strategies. Seventeen RCTs diagnosis of atelectasis was based on chest radiographs by radiologists. Three RCTs diagnosis of atelectasis was based on computed tomography chest by radiologists. Two RCTs diagnosis of atelectasis was based on chest radiographs by radiologists X ray or computed tomography chest. Three RCTs diagnosis of atelectasis was based on using ultrasound. One RCT did not have details on diagnosis of atelectasis. The diagnosis of postoperative atelectasis included in the literature is shown in Appendix 17. The results of the network meta-analysis showed that LTVs combined with iPEEP and RM were associated with a significantly lower incidence of postoperative atelectasis than LTVs [OR=0. 47, 95%CrI (0. 11, 0. 93)], HTVs

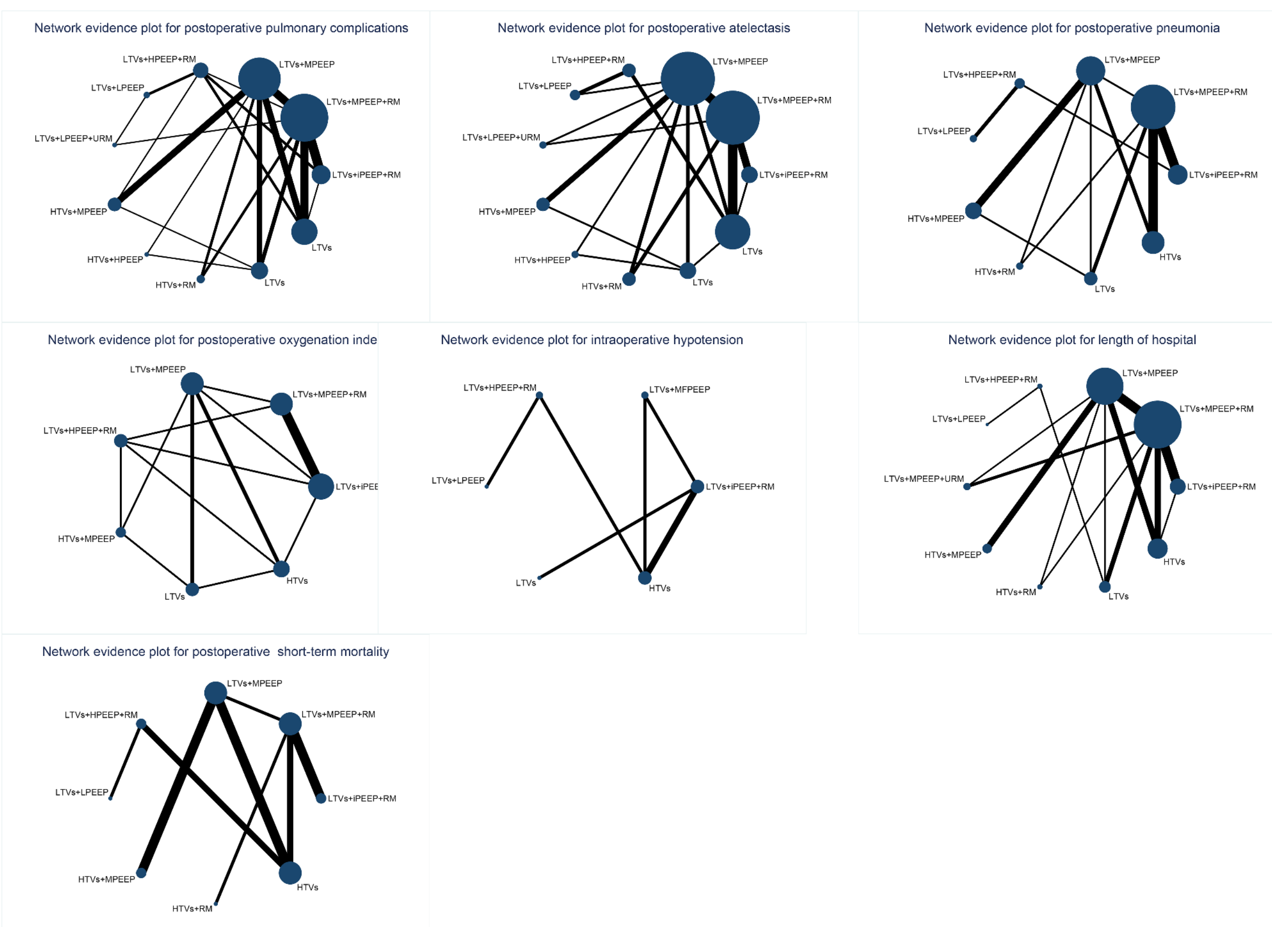

Fig. 2 Network geometry plot (LTVs: low tidal volumes, HTVs: high tidal volumes, iPEEP: individual positive end-expiratory pressure, HPEEP: high positive end-Expiratory pressure, MPEEP: moderate positive end-expiratory pressure, LPEEP: low positive end-expiratory pressure, RM: recruitment manoeuvres, URM: ultrasound-guided recruitment manoeuvres. The width of the lines represents the cumulative number of RCTs for each pairwise comparison and the size of every node is proportional to the number of randomized participants.)

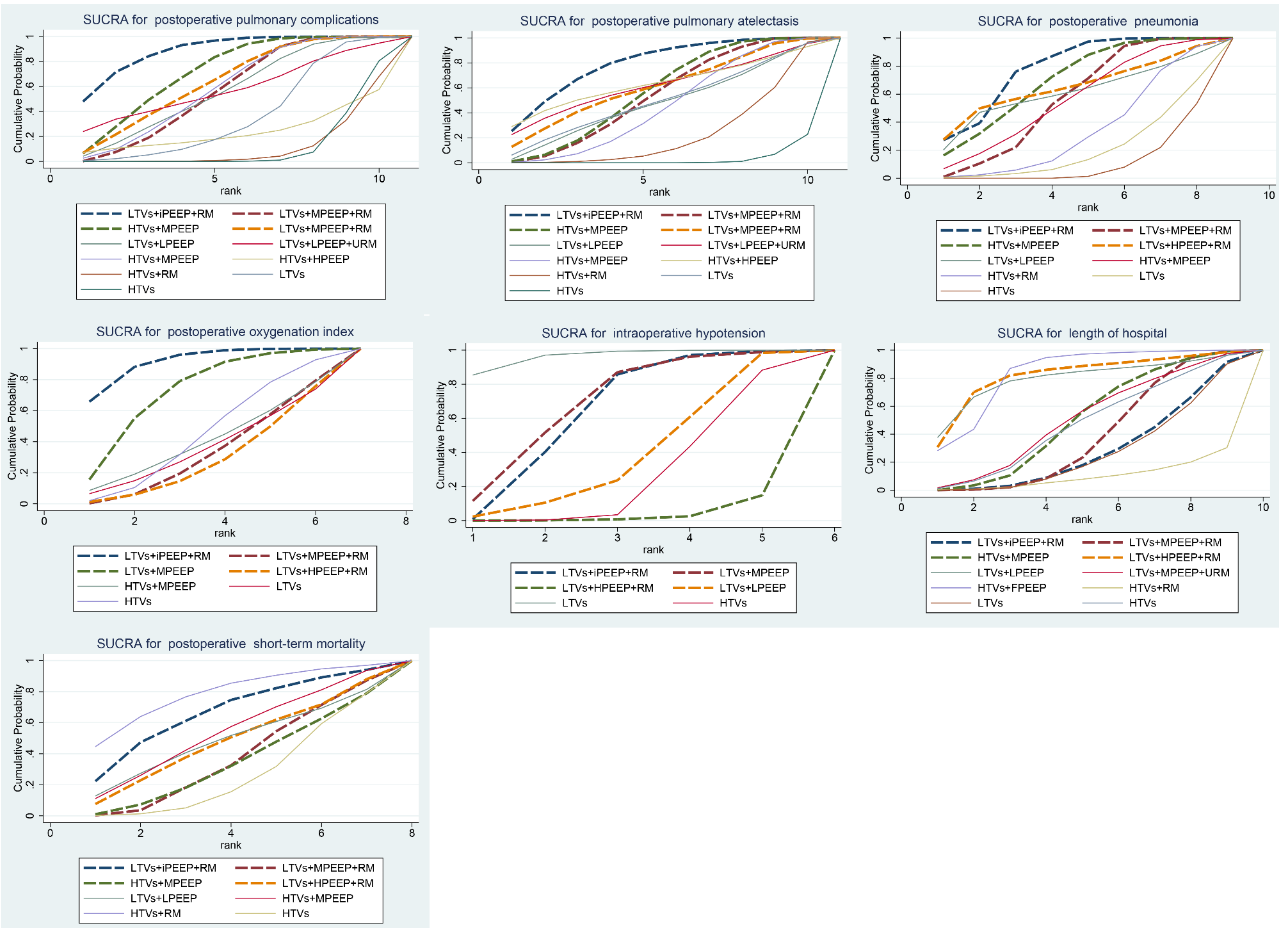

Fig. 3 The plot of cumulative ranking curve (LTVs: low tidal volumes, HTVs: high tidal volumes, iPEEP: individual positive end-expiratory pressure, HPEEP: high positive end-Expiratory pressure, MPEEP: moderate positive end-expiratory pressure, LPEEP: low positive end-expiratory pressure, RM: recruitment manoeuvres, URM: ultrasound-guided recruitment manoeuvres. The area under the curve is proportional to SUCRA.)

combined with RM [OR=0.38, 95%CrI (0.13, 0.98)], and HTVs [OR=0.2, 95%CrI (0.08, 0.48)], respectively. LTVs combined with MPEEP and RM [OR=0.32, 95%CrI (0.18, 0.56)], LTVs combined with MPEEP [OR=0.31, 95%CrI (0.15, 0.62)] and LTVs combined with HPEEP and RM [OR=0.29, 95%CrI (0.11, 0.58)] were associated with a significantly lower incidence of postoperative atelectasis than was HTVs, respectively. The combination of LTVs with iPEEP and RM (79.5%) was found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Incidence of postoperative pneumonia

Twenty-two trials (8088 patients) reported the incidence of postoperative pneumonia for different lung protective ventilation strategies. The results of the network meta-analysis showed that LTVs combined with iPEEP and RM were associated with a significantly lower incidence of postoperative pneumonia than LTVs [OR=0.27, 95% CrI (0.08, 0.89)] and HTVs [OR=0.22, 95%CrI (0.09, 0.48)], respectively. LTVs compared with MPEEP and RM [OR=0.34, 95%CrI (0.18, 0.62)], LTVs combined with MPEEP [OR=0.28, 95%CrI (0.11, 0.67)] and LTVs combined with HPEEP and RM [OR=0.58 95%CrI (0.23, 0.78)] were associated with a significantly lower incidence of postoperative pneumonia than was HTVs, respectively. The combination of LTVs with MPEEP and RM (78.3%) was found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Postoperative oxygenation index

Fifteen trials (1916 patients) reported the incidence of postoperative oxygenation index for different lung protective ventilation strategies. The results of the network meta-analysis showed that LTVs combined with iPEEP and RM were associated with a significantly higher incidence of postoperative oxygenation index than LTVs combined with MPEEP and RM [SMD=66.85, 95%CrI (4.65, 134.6)]. The combination of LTVs with MPEEP and RM (81%) was found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Incidence of intraoperative hypotension

Five trials (1366 patients) reported the incidence of intraoperative hypotension for different lung protective ventilation strategies. The results of the NMA showed that different lung protective ventilation strategies were not significantly different in terms of the incidence of intraoperative hypotension. The LTVs (96.3%) were found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Length of hospital

Twenty-eight trials (7238 patients) reported the length of hospital associated with different lung protective ventilation strategies. The results of the network meta-analysis showed that different lung protective ventilation strategies were not significantly different in terms of length of hospital stay. The combination of LTVs with MPEEP and RM (83.2%) was found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Postoperative short-term mortality

Fourteen trials (5062 patients) reported the length of hospital stay associated with different lung protective ventilation strategies. The results of the network meta-analysis showed that different lung protective ventilation strategies were not significantly different in terms of postoperative mortality rates. The combination of HTVs with RM (78.9%) was found to be the most effective, as evidenced by the SUCRA scores. Figure 2 presents the network geometry. The cumulative ranking is presented in Fig. 3 and Appendix 6. The results of the direct meta-analysis and the network meta-analysis are presented in Appendices 4 and 5, respectively.

Subgroup analysis

Incidence of PPCs

In abdominal surgery, the results of the NMA showed that LTVs combine with iPEEP and RM [OR=0. 02, 95%CrI (0, 0. 15)], LTVs [OR=0. 06, 95%CrI (0. 01, 0. 41)], LTVs combine with MPEEP and RM [OR=0. 05, 95%CrI (0. 0. 29)], LTVs combine with MPEEP [OR=0.07, 95%CrI (0. 01, 0. 37)] and LTVs combine with HPEEP and RM [OR=0.07, 95%CrI (0. 01, 0. 53)] were associated with a significantly lower incidence of PPCs than was HTVs combine with RM. HTVs had a significantly increased incidence of PPCs than LTVs combined with MPEEP and RM [OR=2.98, 95%CrI (1.64, 5.45)], LTVs combined with MEEP [OR=2.13, 95%CrI (1.05, 4.02)]and LTVs combine with HPEEP and RM [OR=2.94, 95%CrI (1.75, 5)]. Furthermore, LTVs combined with iPEEP were associated with a significantly lower incidence of PPCs than HTVs [OR=0. 16, 95%CrI (0. 07, 0. 36)], LTVs combine with MPEEP and RM [OR=0. 46, 95%CrI (0. 23, 0. 95)], and LTVs combine with MPEEP [OR=0. 33, 95%CrI (0. 12, 0. 86)]. In bariatric surgery or obese patients undergoing surgery, the results of the NMA showed that LTVs combined with iPEEP and RM [OR=0. 42, 95%CrI (0.02, 0. 97)] or LTVs combined with HPEEP and RM [OR=0. 34, 95%CrI (0. 01, 0.64)] was associated with a significantly lower incidence of PPCs than LTVs. In thoracic surgery, the results of the NMA showed that LTVs combined with iPEEP and RM [OR=0. 37, 95%CrI (0. 13, 0. 87)] and LTVs combined with MPEEP and RM [OR=0. 52, 95%CrI (0. 23, 0. 78)] was associated with a significantly lower incidence of PPCs than LTVs. In other subgroup analyses, the type of surgery did not affect the results of the comparisons. Furthermore, the type of surgery did not significantly change the SUCRA scores. The results of the subgroup analysis and SUCRA scores are presented in Appendices 13 and 14.

Postoperative atelectasis

In abdominal surgery, the results of the NMA showed that HTVs were associated with a significantly increased incidence of postoperative atelectasis than were LTVs combined with MPEEP and RM [OR=3.44, 95%CrI (1.31, 10.6)], LTVs combine with MPEEP [OR=2.29, 95%CrI (1.57, 10.17)] and LTVs combined with HPEEP and RM [OR=3.18, 95%CrI (1.74, 15.31)] than was HTVs. LTVs combined with iPEEP and RM [OR=0. 21, 95%CrI (0. 05, 0. 72)] was associated with a significantly lower incidence of postoperative atelectasis than was HTVs. In other subgroup analyses, the type of surgery did not affect the results of the comparisons. Furthermore, the type of surgery did not significantly change the SUCRA scores. The results of the subgroup analysis and SUCRA scores are presented in Appendices 13 and 14.

Others outcomes

The type of surgery did not affect the results of the comparison in postoperative pneumonia, oxygenation index, length of hospital, and postoperative 30-day mortality. Furthermore, the type of surgery did not significantly change the SUCRA scores. The results of the subgroup analysis and SUCRA scores are presented in Appendices 13 and 14.

GRADE evaluation of the quality of evidence

The quality of evidence was appraised by the GRADE criteria using CINeMA (Computer-Assisted Interviewing for Neuro-psychiatric Mapping and Automated Diagnosis) version 0.6.1. The quality of evidence was found to range from moderate to very low. The quality of evidence for PPCs, postoperative atelectasis, postoperative pneumonia, length of hospitalization, and postoperative mortality was moderate. The quality of evidence for intraoperative hypotension was low. The quality of evidence for the postoperative oxygenation index was very low. The quality of evidence was evaluated using the Cochrane Collaboration tool and confidence in network meta-analysis, as presented in Table 1 and Appendix 15.

Transitivity, inconsistency, and heterogeneity

The study was carried out using strict criteria for including and excluding participants. However, a limitation of the study is the absence of appropriate methods to accurately evaluate the assumption of transitivity. The test for overall inconsistency did not reveal any significant differences between the consistency and inconsistency modes for the outcomes. The test using the node-splitting model and inconsistency plots showed no statistically significant differences in the majority of outcomes. The funnel plot displayed a distribution that is of dots on both sides of the zero point, indicating that the risk of publication bias in the included papers was not significant. The evaluation of the global inconsistency results is presented in Appendix 7. The results of the local inconsistency evaluation using the node-splitting method are presented in Appendix 8. The evaluation of inconsistency using loop-specific heterogeneity estimates is presented in Appendix 9. The outcomes of the comparison-adjusted funnel plot are presented in Appendix 10.

A sensitivity study of the network meta-analysis was performed by focusing on specific trials, and the findings were mainly consistent. The results of this analysis are presented in Appendix 11. The meta-regression analysis showed that the type of surgery did not have a statistically significant influence on the outcomes. These findings can be that is presented in Appendix 12. In addition, we did not find an effect of the definition of PPCs and the diagnosis of postoperative pulmonary atelectasis on the results by using meta-regression. The detailed results of the meta-regression are shown in Appendix 16 and 17.

Discussion

Traditional lung protection strategies include LTVs combined with fixed PEEP level and RM. However, fixed PEEP levels are controversial [6–9]. Evidence suggests that a fixed value of positive end-expiratory pressure is unlikely to be appropriate for all patients and that there is considerable variability in its requirements due to individual characteristics, such as size and shape of the chest wall, abdominal contents, lung weight, and pleural pressure [32–34]. Therefore, iPEEP is the optimal level of PEEP. Our NMA showed that LTVs combined with iPEEP and RM significantly reduced the risk of PPCs after noncardiac surgery. Furthermore, LTVs combined with iPEEP or medium-to-high PEEP and RM reduced the incidence of postoperative pneumonia and atelectasis, but different ventilation strategies did not affect postoperative oxygenation index, length of hospital stay, or postoperative mortality. According to the SUCRA scores, LTVs combined with iPEEP and RM may be the optimal ventilation strategy.

The HTVs reduce the incidences of hypoxemia and atelectasis but can cause alveolar and endothelial dysfunction, leading to vessel leakage and inflammation as well as acute lung injury, whereas LTVs reduce the risk of mortality in patients with ARDS, but leads to alveolar collapse and lung atelectasis if PEEP is not available [35–37]. Our NMA found that only LTVs combined with iPEEP and RM reduced the incidence of PPCs. A previous meta-analysis showed that LTVs ventilation with medium -to high PEEP reduced the incidence of PPCs [10]. However, large-sample randomized controlled trials conducted in recent years were not included in this study [6, 7], and in addition, the effect of iPEEP was not included in this study. Our NMA includes three iPEEP ventilation strategies: driving pressure-guided PEEP, electrical impedance tomography-guided PEEP, and dynamic compliance-guided PEEP. These iPEEP ventilation strategies are primarily aimed at avoiding lung collapse and hyperinflation during mechanical ventilation and reducing driving pressures. Driving pressure was the only respiratory parameter associated with adverse ventilatory events. Furthermore, PEEP, plateau pressure, and tidal volume were not associated with PPCs only if they did not affect driving pressure [38]. Our NMA showed that PEEP levels did not reduce the incidence of PPCs. Our findings align with those of a similar meta-analysis conducted by Neto and colleagues [9]. Driving pressure-mediated ventilation strategies can be based on the patient's "functional lung size" [33, 34]. Driving pressure, defined as VT/ compliant of the respiratory system (CRS), can be kept low to achieve higher respiratory compliance and a "functional

Table 1 The GRADE quality of evidence assessment for the outcomes in results of network meta-analysis

Outcome	Number of literatures included *	Number of trials	Number of interventions	Conclusions	Quality of evidence	Comments
PPCs	1–7, 10, 12, 13, 15, 17, 19, 21–25, 28–33, 34, 36, 38, 41–43, 46, 47, 49, 51–57]	40 trials (10330 patients)	11	LTVs + iPEEP + RM was associated with a significant decrease compared with the LTVs + MPEEP, LTVs and HTVs, respectively. LTVs + iPEEP + RM was ranked the highest	⊕⊕⊕ Moderate quality	Downgraded for concerns related to heterogeneity and incoherence
postoperative atelectasis	2, 4, 6, 7, 12, 13, 18, 21–28, 30, 33–37,40–43, 52	27 trials (6584 patients)	11	LTVs + iPEEP + RM was associated with a significant decrease compared with the LTVs, HTVs + RM and HTVs, respectively. LTVs + MPEEP + RM, LTVs + MPEEP and LTVs + HPEEP + RM were associated with a significant decrease compared with HTVs, respectively. LTVs + iPEEP + RM was ranked the highest.	⊕⊕⊕ Moderate quality	Downgraded for concerns related to Within-study bias and incoherence
postoperative pneumonia	1,3,4,7,13,15,24,25,28,30–33,36,38,41–43,52,54	22 trials (8088 patients)	9	LTVs + iPEEP + RM group was associated with a significant decrease compared with the LTVs and HTVs, respectively. LTVs + MPEEP + RM and LTVs + MPEEP were associated with a significant decrease compared with HTVs, respectively. LTVs + iPEEP + RM was ranked the highest.	⊕⊕⊕ Moderate quality	Downgraded for concerns related to within-study bias
Postoperative oxygenation index	1,2,11,14,16,17,20,23,36,39,40,45,53,58	15 trials (1916 patients)	7	LTVs + iPEEP + RM was associated with a significant increase compared with the LTVs + MPEEP + RM. LTVs + MPEEP was ranked the highest	⊕ Very Low quality	Downgraded for concerns related to within-study bias and incoherence
Intraoperative hypotension	13,15,18,41,43	5 trials (1366 patients)	6	No significance was detected between different lung protect ventilation.	⊕⊕ Low quality	Downgraded for concerns related to within-study bias and heterogeneity
Length of hospital	1,4,5,7–9,13,15,20,24,26,28–33,38,39,41–44,46,47,54,55,57	28 trials (7238 patients)	10	No significance was detected between different lung protect ventilation	⊕⊕⊕ Moderate quality	Downgraded for concerns related to within-study bias
Postoperative short-mortality	1,7,11–13,18–20,30–33,39,55,57	14 trials (5062 patients)	8	No significance was detected between different lung protect ventilation.	⊕⊕⊕ Moderate quality	Downgraded for concerns related to within-study bias

Notes: *: For detailed inclusion of literature, see Appendix 2: references for included trials and characteristic; ⊕⊕⊕(Moderate quality): We are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. ⊕⊕(Low quality): Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect. ⊕(Very low quality): We have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect. The meaning of the symbols from the GRADE Handbook lung size". This approach avoids the need for overdistension (barotrauma) or underventilation (atelectasis) of the lungs [35].

Atelectasis is the most common complication of general anaesthesia, with an incidence of up to 90% [39]. Atelectasis can lead to infiltration of inflammatory cells [40, 41], altered alveolar deconstruction [42, 43], local hypoxia [44], and increased bacterial colonization [45]. Consequently, lung atelectasis predisposes patients to pneumonia. The results of our study demonstrated that the combination of LTVs with iPEEP or medium-to-high PEEP with RM significantly reduced the incidences of postoperative atelectasis and pneumonia. Nevertheless, no significant differences were observed between the various lung protection strategies in terms of the incidences of postoperative atelectasis and pneumonia. Consequently, LTVs combined with iPEEP and RM may be regarded as the optimal ventilation strategy, according to the cumulative ranking probability. A certain level of PEEP can maintain lung end-expiratory volume, improve lung compliance, and reduce the formation of atelectasis, thereby reducing the incidence of postoperative pneumonia. Although a low tidal volume combined with a medium-to-high PEEP reduced the incidences of postoperative atelectasis and pneumonia, it did not reduce the incidence of PPCs. PPCs represent a variety of respiratory disorders. LTVs combined with medium-to-high PEEP may only reduce the incidence of postoperative pneumonia due to atelectasis. Furthermore, differences in the definition of pulmonary complications in the included studies influenced the outcome.

Although our NMA revealed that LTVs combined with iPEEP and RM increased the postoperative oxygenation index compared with LTVs combined with MPEEP and RM, and HTVs combined with MPEEP reduced the length of hospital stay compared with HTVs combined with RM, we did not find an effect of the other lung ventilation strategies on the postoperative oxygenation index or the length of hospital stay. This may be related to the heterogeneity of the included literature. After general anaesthesia, patients are oxygenated on the ward and intraoperative lung protection strategies may have little effect on the postoperative oxygenation index. However, there was a high variability in the oxygenation index between studies, which may be related to the type of surgery and the time of the oxygenation index measurement. Our NMA revealed no effect of different ventilation strategies on the incidence of intraoperative hypotension or the incidence of postoperative mortality. Although a high PEEP may lead to obstruction of venous return and, together with the vasodilatory effect of anaesthetics, the incidence of hypotension should be higher with a high PEEP ventilation strategy, our study did not reveal an effect of different ventilation strategies on intraoperative blood pressure. Some studies have suggested that a low PEEP increases the risk of postoperative mortality [8], but our study revealed no effect of different ventilation strategies on the risk of mortality.

The type of surgery is an important factor influencing outcome. thus, we performed meta-regression and subgroup analyses according to the type of surgery. Lung compliance during mechanical ventilation varies with the type of surgery and may require different ventilation strategies. In abdominal surgery, obese patients, and thoracic surgery, LTVs combined with iPEEP, and medium or high levels of PEEP may reduce the incidence of PPCs, but according to the SUCRA scores, LTVs combined with iPEEP and RM may be the optimal ventilation strategy.

Several limitations should be considered in our analysis. Although our study reported 11 ventilation strategies, PEEP levels still varied, and we classified PEEP levels into LPEEP, MPEEP, HPEEP, and iPEEP, which may have had an impact on the results. Secondly, pulmonary complications were defined as a composite outcome of minor and major pulmonary complications, and it is important to note that considerable variation in definitions existed amongst the included studies. Thirdly, the modality of RM differed across studies. Only ultrasound-guided RM was screened, and different RM strategies may have influenced the results. Fourth, four studies included many participants, which may have affected the final NMA results.

Conclusion

In our network meta-analysis, LTVs combined with iPEEP significantly decreased the incidences of PPCs, postoperative pneumonia, and atelectasis. LTVs combined with medium-to-high PEEP levels significantly decreased the incidences of postoperative pneumonia and atelectasis. The type of surgery may influence the choice of ventilation strategy. However, according to the cumulative ranking probability, a low tidal volume combined with iPEEP combined with RM may be the optimal ventilation strategy.

Supplementary Information

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Supplementary Material 1

Supplementary Material 2

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Not applicable.

Author contributions

J.M. and D.W. participated in selecting the study and extracting data, Q. C. and JY. X. performed the statistical analysis and drafting of the manuscript. HL. L. and R. A. participated in conceptualization, formal analysis, and drafting of the manuscript. All authors read and approved the final manuscript.

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Data availability
To original contributions presented in the study are included in the article and appendix. Further inquiries can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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