World Journal of Surgical Oncology

REVIEW

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Timing effects of short-term smoking cessation on lung cancer postoperative complications: a systematic review and meta-analysis

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Abstract

Background Preoperative smoking cessation may reduce postoperative complications in patients with lung cancer. However, the optimal duration of short-term preoperative smoking cessation remains unclear.

Methods Three databases, PubMed, Embase, and the Cochrane Library, were searched for studies published up to April 5, 2024. The Newcastle–Ottawa scale was used to assess the risk of bias. The included studies compared the incidence of postoperative complications between patients with different preoperative smoking cessation times and those with persistent preoperative smoking. A meta-analysis of postoperative complications and events such as pneumonia was performed in patients with lung cancer.

Results Fourteen studies met the inclusion criteria and included a total of 50,741 patients who had undergone pulmonary resection. The meta-analysis showed that preoperative smoking cessation of > 2 weeks and < 1 month did not reduce the incidence of postoperative complications (odds ratio [OR] 1.05; 95% confidence interval [CI] 0.76–1.44; $P = 0.78$) and pneumonia (OR 0.98; 95% CI 0.60–1.61; $P = 0.95$). Moreover, preoperative smoking cessation for > 1 month was effective in reducing the incidence of postoperative complications (OR 0.72; 95% CI 0.63–0.83; $P < 0.01$) as well as pneumonia (OR 0.80; 95% CI 0.49–1.33; $P = 0.40$).

Conclusions This meta-analysis suggests that preoperative smoking cessation for > 1 month is effective in reducing complications and pneumonia after pulmonary resection in patients with lung cancer, especially as video-assisted thoracoscopic surgery (VATS) and robotic-assisted surgery become more common.

Keywords Smoking cessation, Lung cancer, Postoperative complications, Pulmonary resection, Meta-analysis

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Introduction

Lung cancer is the second most often diagnosed cancer and was the main cause of cancer-related deaths in 2020, with a projected 2.2 million new cancer cases and 1.8 million fatalities. Approximately two-thirds of all lung cancers worldwide are attributable to smoking [1]. Smoking not only contributes to the development of lung cancer but also affects the postoperative outcomes of patients with lung cancer. In addition to significantly improving the survival of lung cancer patients [2], smoking cessation reduces the risk of postoperative in-hospital death and complications [3]. However, approximately 24% of patients diagnosed with lung cancer are tobacco users, and approximately 30% of tobacco users continue to smoke until surgery [4].

Several researches recommend preoperative smoking cessation for lung cancer patients to minimize postoperative complications as well as to improve patient prognosis [3, 5]. Enhanced recovery after surgery (ERAS) is a multimodal perioperative management strategy proposed for the first time by Engelman in 1994 to shorten hospital stays, reduce postoperative pain, and promote patient recovery [6]. The ERAS Society and European Society of Thoracic Surgeons (ESTS) have included preoperative smoking cessation in their guidelines for enhanced recovery after lung surgery [7]. However, the minimum time to smoking cessation that improves patient postoperative outcomes has been controversial [3, 8, 9]. Understanding the impact of short-term smoking cessation on the incidence of lung cancer can encourage tobacco users to begin cessation at the time of diagnosis. Additionally, identifying an effective interval for preoperative smoking cessation is important for perioperative management.

Therefore, we screened 14 studies to perform a systematic review and meta-analysis to determine the effects of short-term smoking cessation on the postoperative complications of lung cancer.

Methods

This systematic review and meta-analysis was designed in accordance with the Meta-Analysis of Observational Studies in Epidemiology guidelines and statements and Preferred Reporting Items for Systematic Reviews and Meta-Analyses [10, 11]. The protocol for this systematic review and meta-analysis was registered on the PROSPERO website (https://www.crd.york.ac.uk/prospero/) with the registration number CRD42023403113.

Databases and search strategy

The literature review was conducted by searching three online databases: PubMed, the Cochrane Library, and Embase for articles published until April 5, 2024. Overall, 14 studies conducted between 2001 and 2023 were retrieved. Smoking, smoking behaviors, smoking habit, pulmonary surgical procedures, pulmonary surgical, lung surgical procedure, complication, complications were employed as the literature search keywords. The detailed search strategies and retrieval methods are presented in Supplementary Table 1. Articles were individually assessed and cross-checked by two authors (ZZ and YZ). In addition, we manually scanned the reference lists of the excluded studies to collect other feasible non-replicated studies. Controversial literature was thoroughly reviewed and discussed by two reviewers, along with JQ and a statistics expert, to carefully reassess whether it met the inclusion criteria for this study.

Study selection and criteria

The inclusion criteria were as follows: (1) studies on adult patients with lung cancer who underwent pulmonary resection; (2) studies including groups of patients who quit smoking before surgery, with data on the timing of smoking cessation; (3) studies including preoperative patients who smoked consistently or never smoked as controls; (4) studies providing a correlation between the timing of smoking cessation and postoperative complications, assessed as an odds ratio (OR) with a 95% confidence interval (CI); (5) studies reporting on at least one of the relevant outcomes of interest (see below).

The exclusion criteria were as follows: (1) ineligible article categories, including reviews, case reports, and non-comparative studies; (2) duplicate publications of data.

Data collection

Two independent reviewers (ZZ and YZ) evaluated the available studies and extracted the relevant data, and any conflicts were discussed and resolved with JQ. The data were then reviewed and assessed by a statistician for accuracy and consistency. The following data were retrieved for each study: first author, publication year, country, sample size, duration of patient cessation, and 95% CI for the OR of postoperative complications.

The definition of postoperative complications for lung cancer in this study follows internationally accepted postoperative evaluation standards [12–14]. These complications include common adverse events such as pneumonia, acute respiratory distress syndrome (ARDS), bronchopleural fistula, pulmonary embolism, prolonged mechanical ventilation exceeding 48 h, reintubation or respiratory failure, tracheostomy, myocardial infarction, and unexpected return to the operating room. Pneumonia is defined as a postoperative lung infection accompanied by imaging abnormalities, fever, or signs of infection, and typically requires antibiotic treatment.

In this study, "short-term smoking cessation" was defined based on the duration of preoperative smoking cessation. Patients were categorized into three groups:

current tobacco users (patients who continued smoking up until surgery), those who quit smoking for more than 2 weeks but less than 1 month, and those who quit smoking for more than 1 month before surgery. This categorization was used to ensure consistency across studies and accurately assess the effects of varying durations of smoking cessation on postoperative complications.

Data extraction and quality assessment

The study quality was assessed using the Newcastle–Ottawa scale (NOS) [15], which evaluates selection, comparability, and outcomes. Studies scoring above 7 were considered high quality, those scoring 5 to 7 as medium quality, and scores below 5 were classified as poor. For further meta-analysis, we included only studies with a score of 6 or higher.

Statistical analysis

We used the 95% CI of the OR to summarize the effect of the timing of smoking cessation on the postoperative complications in patients with lung cancer. The level of heterogeneity was quantified using the Cochrane q-test and I^2 statistic. An $I^2>50\%$ indicated considerable heterogeneity [16], and a random-effect model was used to calculate the size of the pooled effect to reduce possible bias. An $I^2<50\%$ was considered to indicate less heterogeneity, and a fixed-effect model was used. For outcomes with greater heterogeneity, we conducted subgroup analyses of the variables of interest in this study under the guidance of a statistician to assess the impact of different patient groups and study designs on the contribution to heterogeneity. Statistical significance was denoted by a two-sided *P*-value of <0.05. Sensitivity analysis was used to analyze the effect of each study on the overall effect value. Funnel plots, L'abbe plots, and Egger's test were applied to detect any potential publication bias [17], and an Egger's $P<0.05$ indicated significant publication bias.

The Stata software (version 14.2; StataCorp LLC, College Station, TX, USA) and Review Manager software (RevMan version 5.3; The Nordic Cochrane Center, The Cochrane Collaboration, 2014) were used for all statistical analyses.

Results

Literature selection and study characteristics

A flowchart for extracting literature is shown in Fig. 1. A total of 2,575 articles were screened by searching the PubMed, Embase, and Cochrane Library databases and reading the references of related literature. 15 studies were included in the quality evaluation by reading the title and abstract and re-reading the full text. One of the papers had an NOS score<6 after discussion, and the remaining 14 cases with an NOS score>6 were eventually included in our systematic evaluation and meta-analysis [3, 8, 9, 18–28] (Supplementary Table 2). These studies included 50,741 patients from five countries. Details of study duration, type of study, age composition of patients, sex ratio, duration of study, duration of smoking cessation, surgical methods and extent of resection are shown in Table 1.

Relationship between time to smoking cessation and postoperative complications of lung cancer

As shown in Fig. 2, patients who quit smoking before surgery had a lower incidence of postoperative complications compared with those who continued smoking until surgery (11.12% vs. 15.41%; OR 0.76; 95% CI 0.65–0.90; $P<0.01$). Funnel plots, and L'abbe plots and Egger's test ($P=0.87$) did not reveal significant publication bias (Supplementary Fig. 1). However, there was no significant difference (Fig. 3A) in the incidence of postoperative complications between patients who quit smoking between 2 weeks and 1 month before surgery and those who continued smoking until surgery (OR 1.05; 95% CI 0.76–1.44; $P=0.78$). Funnel plots, and L'abbe plots and Egger's test ($P=0.96$) did not reveal significant publication bias (Supplementary Fig. 2). As shown in Fig. 3B, the incidence of postoperative complications was lower in patients who quit smoking>1 month before surgery than in those who continued smoking (OR 0.72; 95% CI 0.63–0.83; $P<0.01$), with low heterogeneity ($I^2=24.9\%$; $P=0.207$). Funnel plots, and L'abbe plots and Egger's test ($P=0.95$) did not reveal significant publication bias (Supplementary Fig. 3).

A total of 9 studies reported the surgical methods used. Subgroup analysis by surgical methods revealed that in studies utilizing VAST or robotic-assisted surgery, postoperative complication rates were significantly lower in patients who quit smoking more than 1 month before surgery (OR 0.61; 95% CI 0.43–0.88; $P<0.01$) (Fig. 3C). However, in studies involving only open thoracotomy, there was no significant difference in postoperative complication rates between patients who quit smoking 1 month prior and those who continued smoking until surgery (OR 0.88; 95% CI 0.68–1.14; $P=0.34$), with no observed heterogeneity ($I^2 = 0.00\%$; $P=0.67$) (Fig. 3C). Funnel plots, L'Abbé plots, and Egger's test ($P=0.28$) did not indicate significant publication bias (Supplementary Fig. 4).

Relationship between time to smoking cessation and postoperative pneumonia of lung cancer

As shown in Fig. 4A, there was no statistical difference in the incidence of postoperative pneumonia among patients with lung cancer who quit smoking between 2 weeks and 1 month before surgery compared to those who continued to smoke until surgery (OR=0.98; 95% CI=0.60–1.61; $P=0.95$). Funnel plots, and L'abbe plots

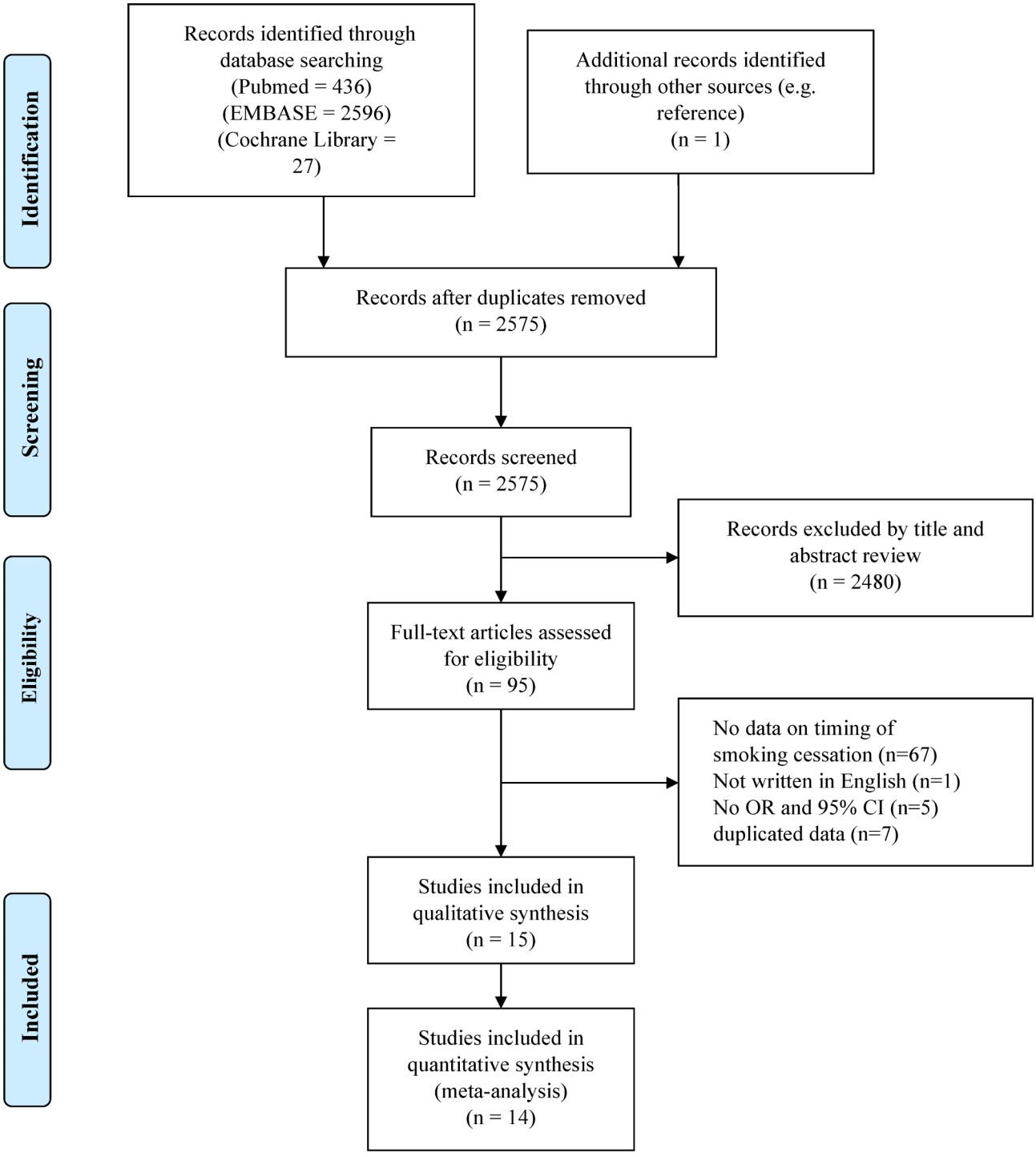

Fig. 1 Flow diagram of study selection process

and Egger's test (P=0.57) did not reveal significant publication bias (Supplementary Fig. 5). The incidence of postoperative pneumonia in patients who had quit smoking for >1 month was not significantly different from that in patients who continued to smoke until surgery (OR 0.80; 95% CI 0.49–1.33; P=0.40) with high heterogeneity (I^2=78.7.0%; P<0.01). Funnel plots, and L'abbe plots and Egger's test (P=0.51) did not reveal significant publication bias (Supplementary Fig. 6). Among the four studies that reported patients' surgical methods, we performed a subgroup analysis based on whether VATS or robot-assisted surgery were utilized. We found that in studies where VATS and robot-assisted surgery were applied, the incidence of postoperative pneumonia

Table 1 Study characteristics and patient characteristics

Study (year)	Country	Study Period	Study type	Sample size	Age(years)	Gender (male ratio)	Surgery method	Extent of surgical resection	Preoperative smoking cessation time
Nakagawa et al. [20]	Japan	1997–1998	RCS	308	60.2 ± 12.3	177 (57.5)	Open	Pneumonectomy, Lobectomy, Wedge resection	Never, >2 weeks, >1 month, current
Vaporciyan et al. [24]	USA	1990–1999	RCS	257	60 ± 10	179 (69.6)	Open	Pneumonectomy	Never, >2 weeks, >1 month, current
Barrera et al. [25]	USA	1999–2001	PCS	300	64 ± 12	144 (48.0)	Open	Pneumonectomy, Lobectomy, Wedge resection	Never, >1 month, current
Mason et al. [3]	USA	1999–2007	RCS	7990	64.2 ± 15.2	3862 (48.3)	Open	Pneumonectomy, Lobectomy	Never, >2 weeks, >1 month, current
seok et al. [26]	Korea	2005–2009	RCS	232	62.7 ± 11	217 (93.5)	Open VATS	Pneumonectomy, Lobectomy, Subsegmentectomy, Wedge resection, Sleeve lobectomy	Never, >2 weeks, >1 month, current
Lugg et al. [27]	UK	2010–2014	PCS	462	68.9 ± 3.9	277 (60.0)	Open VATS	Pneumonectomy, Lobectomy, Subsegmentectomy, Wedge resection, Sleeve lobectomy	Never, >1 month, current
Fukui et al. [19]	Japan	2012–2016	RCS	666	65.9 ± 12.5	376 (56.5)	NA	Pneumonectomy, Lobectomy, Subsegmentectomy, Wedge resection	Never, >2 weeks, >1 month, current
Tezel et al. [28]	NA	2017–2019	PCS	138	NA	NA	VATS	Lobectomy	Never, >1 month, current
Clark et al. [29]	USA	2014–2016	RCS	24,912	67.3 ± 9.5	11,103(44.6)	NA	Lobectomy	Never, >1 month, current
Heiden et al. [8]	USA	2006–2016	RCS	9509	68.4 ± 9.8	9170 (96.4)	Open VATS Robotic	Lobectomy	Never, >2 weeks, current
Napolitano et al. [9]	USA	2012–2018	RCS	1716	66.0 ± 7.4	1649 (96.1)	Open VATS	Pneumonectomy, Lobectomy, Subsegmentectomy, Wedge resection	Never, >2 weeks, current
Jeganathan et al. [30]	AUS	1995–2018	RCS	787	62.5 ± 16.9	489 (62.1)	NA	Pneumonectomy, Lobectomy	Never, current
Corsini et al. [31]	USA	2012–2017	RCS	1038	67.2 ± 6.8	554 (53.4)	Open VATS	Pneumonectomy, Lobectomy, Subsegmentectomy, Wedge resection	Never, >2 weeks, >1 month, current
Amber et al. [32]	UK	2012–2021	PCS	2426	68.0 ± 9.0	1203 (49.6)	Open VATS	Subsegmentectomy	Never, >1 month, current

PRS: Prospective cohort studies

RAS: Retrospective cohort study

NA: Not applicable, Information not available

Open: open thoracotomy

VAST: video-assisted thoracoscopic surgery

Robotic: Robotic-assisted surgery

was lower in patients who had quit smoking more than 1 month before surgery compared to those who continued smoking until surgery (OR 0.57; 95% CI 0.43–0.75; $P<0.01$), with no observed heterogeneity ($I^2 = 0.00\%$; $P=0.957$) (Fig. 4B). Funnel plots, L'Abbé plots, and Egger's test ($P=0.46$) did not indicate significant publication bias (Supplementary Fig. 7). In contrast, in the study where only open thoracotomy was performed, there was no statistically significant difference in the incidence of postoperative pneumonia between patients who had quit smoking more than 1 month before surgery and those who continued smoking until surgery (OR 2.64; 95% CI 0.10–72.24; $P=0.57$).

Discussion

Minimum duration of preoperative smoking cessation to reduce postoperative complications in lung cancer patients remains controversial. To date, there have been no meta-analyses evaluating the relationship between minimum preoperative smoking cessation time pairs and

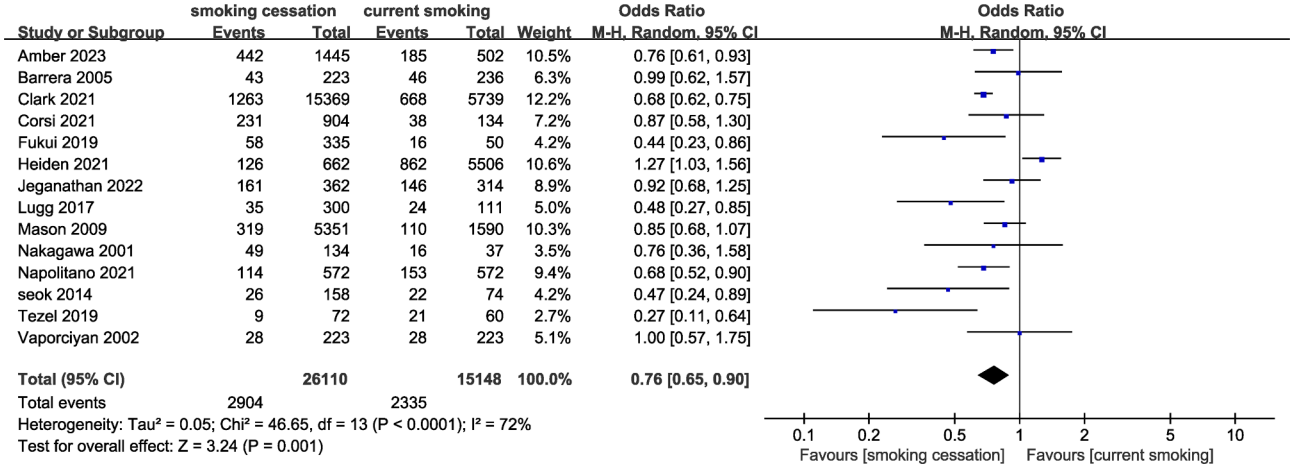

Fig. 2 Forest plot comparing postoperative complications between patients who quit smoking before surgery and those who continued smoking

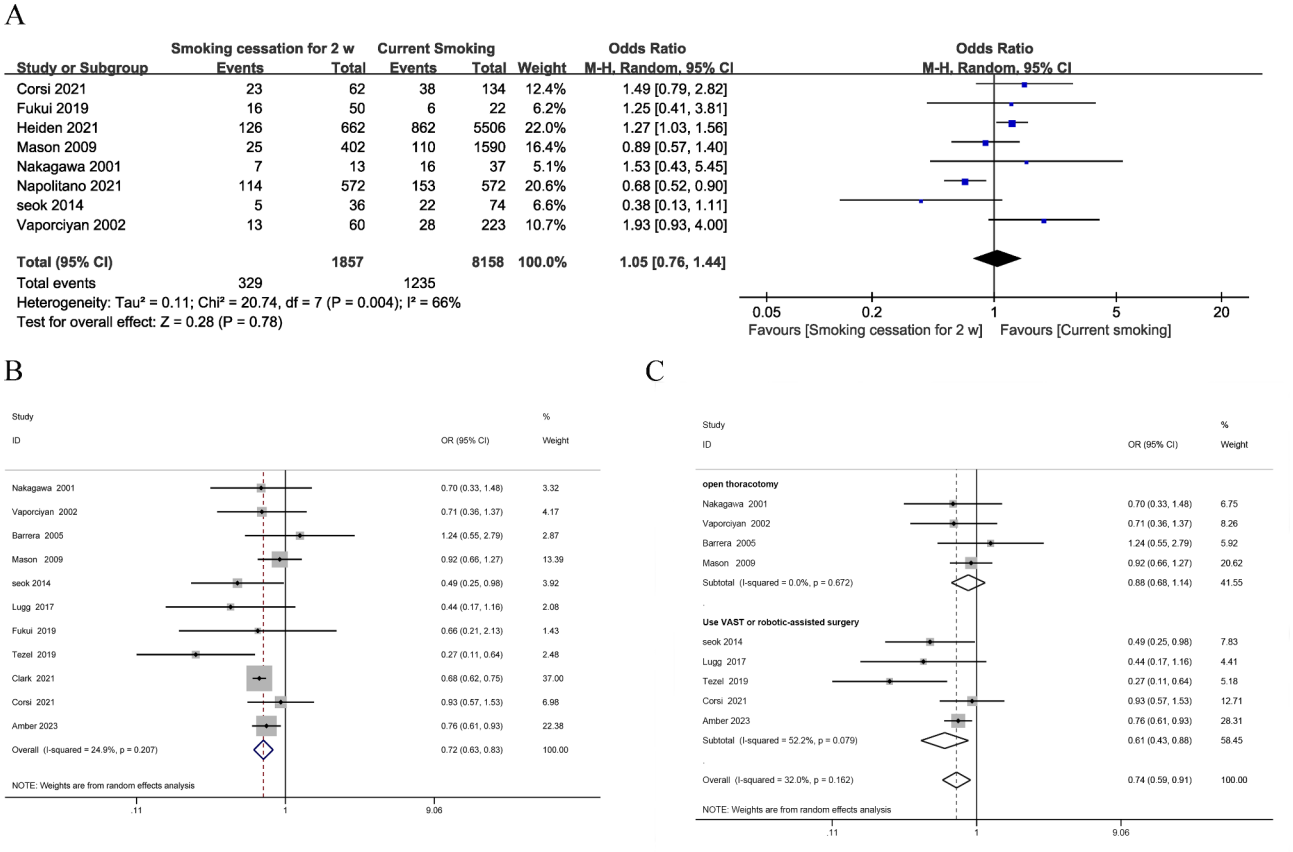

Fig. 3 Forest plots of postoperative complications based on the duration of preoperative smoking cessation. **A**) Postoperative complications for patients who quit smoking 2 weeks to 1 month before surgery vs. those who continued smoking. **B**) Postoperative complications for patients who quit smoking more than 1 month before surgery vs. those who continued smoking. **C**) Subgroup analysis of postoperative complications based on surgical methods

reduction in the occurrence of postoperative complications in patients. Therefore, we conducted a systematic review and meta-analysis of 14 studies on this topic to determine the minimum duration of smoking cessation that reduces postoperative complications in lung cancer patient. This study will help patients diagnosed with lung cancer to quit smoking because it shows that quitting for >1 month can improve surgical outcomes, especially as VATS and robotic-assisted surgery become more common.

Studies have shown that continued preoperative smoking is associated with reduced postoperative quality of

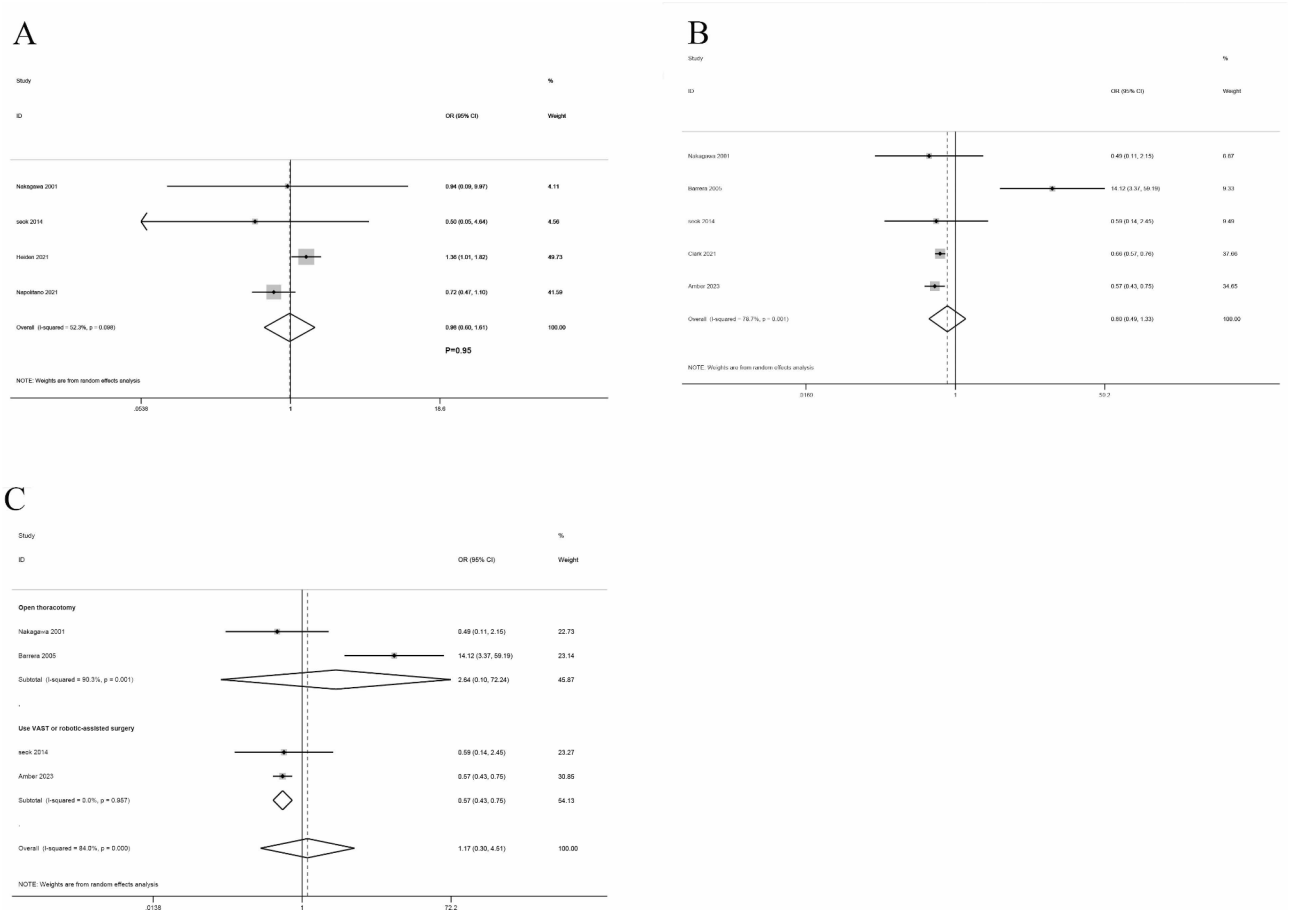

Fig. 4 Forest plots of postoperative pneumonia based on the duration of preoperative smoking cessation. **A**) Postoperative pneumonia for patients who quit smoking 2 weeks to 1 month before surgery vs. those who continued smoking. **B**) Postoperative pneumonia for patients who quit smoking more than 1 month before surgery vs. those who continued smoking. **C**) Subgroup analysis of postoperative pneumonia based on surgical methods

life and lower long-term survival [2, 18]. Several studies have reported that preoperative smoking cessation reduces the incidence of postoperative complications in lung cancer patients [19, 20]. In the guidelines for enhanced recovery after lung surgery published by the ERAS Society and ESTS, patients are recommended to reduce the incidence of postoperative complications by quitting smoking before surgery [7]. Our findings, which demonstrate that preoperative smoking cessation reduces the incidence of postoperative complications in lung cancer patients, are consistent with those of Nakagawa et al. [20]. Their study showed that patients who quit smoking more than 1 month before surgery experienced significantly fewer postoperative complications. Although smoking cessation for more than 1 month preoperatively is more beneficial, encouraging patients to quit smoking at any time remains crucial for improving long-term survival and reducing other smoking-related risks, such as cancer recurrence [2].

In this study, we discussed the minimum time required to quit smoking before surgery in patients with lung cancer. We found no significant differences in the incidence of postoperative complications between patients who quit smoking<1 month before surgery and those who continued to smoke until surgery. This might be due to the fact that smoking decreases mucociliary clearance causing excessive mucus secretion and thus increasing the incidence of postoperative respiratory complications. However, restoration of mucus cilia function requires approximately 6 weeks of smoking cessation [21]. In addition, quitting smoking for >4 weeks reduces cardiovascular complications and promotes wound healing [22].

In a subgroup analysis of surgical methods, we found no significant difference in postoperative complication rates between patients who quit smoking 1 month before surgery and those who continued smoking until surgery in studies involving open thoracotomy. However, in studies utilizing VATS or robotic-assisted surgery, preoperative smoking cessation for more than 1 month significantly reduced the incidence of postoperative complications. Consistent with our findings, Takashi et al. demonstrated that preoperative smoking cessation duration was

independently associated with the incidence of lung complications in lung cancer patients following thoracoscopic lobectomy and segmental lung resection [23]. Our study further supports that smoking cessation for more than 1 month before surgery is particularly effective in reducing postoperative complications, especially in patients undergoing VATS and robotic-assisted surgery.

Studies have shown that smoking can contribute to the risk of postoperative pneumonia by affecting the function of inflammatory cells and reducing mucociliary clearance [22]. Therefore, our study separately discussed the effect of preoperative smoking cessation on postoperative pneumonia in patients with lung cancer. We uncovered no significant difference in the incidence of postoperative pneumonia between patients who quit smoking two weeks before surgery and those who continued to smoke until surgery. This may also be due to the fact that the function of the mucous cilia had not fully recovered. We also did not find a positive effect of smoking cessation on reducing postoperative pneumonia in patients who had quit smoking for >1 month. However, due to high heterogeneity in the results ($I^2 = 78.7\%$; $P<0.01$), a subgroup analysis was performed on patients with smoking cessation durations greater than 1 month to address the heterogeneity. Among the four studies that reported surgical methods, subgroup analysis revealed that for patients undergoing open thoracotomy, smoking cessation for more than 1 month did not significantly reduce surgical complications. In contrast, for studies involving VATS and robotic-assisted surgery, quitting smoking for 1 month prior to surgery significantly reduced the incidence of postoperative pneumonia.

The present study showed that preoperative smoking cessation for >1 month effectively reduced the incidence of postoperative complications in patients with lung cancer. However, the benefit of long-term smoking cessation in reducing postoperative complications in patients with lung cancer is unclear, as patients with lung cancer are usually treated aggressively through surgery after diagnosis. Due to the lack of data, we also did not determine how long smoking cessation restores the postoperative complication rate for lung surgery to that of non- tobacco users. These questions should be addressed in future meta-analyses.

Several limitations should be considered in our study. First, the majority of the included studies were retrospective single-center cohort studies. Unavoidable biases in cohort studies, such as cohort selection bias, may reduce the reliability of the results. Second, although 14 studies were included in the analysis, not all of them reported the outcomes we were interested in, so we only analyzed the effect of short-term smoking cessation on overall complications as well as on postoperative pneumonia, and not on the effect of short-term smoking cessation on other complications, such as ARDS and so on. This is where we our next research will be. There are differences in the definition of postoperative complications among studies, which may lead to biased results. Finally, since postoperative complications in lung cancer patients are not only affected by smoking cessation, but also may be related to the use of antibiotics and the extent of surgical resection, these potential confounding factors may bias the results, and in the future, more studies can be included to stratify the discussion of these factors, so that the results of the study can be more stable.

Conclusions

Taken together, with this systematic review and meta-analysis, we have attempted to provide an up-to-date and comprehensive review of the literature on the impact of preoperative smoking cessation duration on postoperative complications of lung cancer. While encouraging smoking cessation at any time remains crucial for improving long-term survival, our study demonstrated that quitting smoking more than 1 month prior to surgery significantly reduces the incidence of postoperative pneumonia and other pulmonary complications, particularly with the widespread adoption of VATS and robotic-assisted surgery.

Abbreviations

CI	Confidence Interval
ERAS	Enhanced Recovery After Surgery
ESTS	European Society of Thoracic Surgeons
NOS	Newcastle-Ottawa Scale
OR	Odds Ratio
PCS	Prospective Cohort Study
RCS	Retrospective Cohort Study
VATS	Video-Assisted Thoracoscopic Surgery

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12957-024-03577-1.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Supplementary Material 6

Supplementary Material 7

Supplementary Material 8

Supplementary Material 9

Acknowledgements

Not applicable.

Author contributions

ZZ and YZ conceived and designed the study. ZZ and YZ conducted the literature search and data extraction. JQ and ZL performed the statistical

analysis. LL and HT provided critical revisions of the manuscript. All authors read and approved the final manuscript.

Funding
This study was supported by the Shandong Provincial Natural Science Foundation (ZR2021LSW006) and the National Key Research and Development Program of China (2021YFC2500900).

Data availability
The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This systematic review and meta-analysis did not involve any direct human participants or personal data, and thus did not require ethical approval. All data used in this study were obtained from previously published studies, and the original authors of those studies have obtained the necessary ethical approvals.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 8 August 2024 / Accepted: 26 October 2024
Published online: 07 November 2024

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