Improvement Of Surgical Complications Using Single-Lumen Endotracheal Tube Intubation And Artificial Carbon Dioxide Pneumothorax In Esophagectomy: A Meta-analysis

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Research article

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Abstract

Background: Esophageal cancer has a poor prognosis. Surgery is the main treatment but involves a high risk of complications. Some surgical strategies have tried to eliminate complications. Our meta-analysis tried to find the benefits of single-lumen endotracheal tube intubation with carbon dioxide (CO₂) inflation.

Methods: A systematic search of studies on esophagectomy and CO₂ inflation was conducted using PubMed, Medline, and Scopus. The odds ratio of post-operative pulmonary complications and anastomosis leakage were the primary outcomes. The standardized mean difference (SMD) in post-operative hospitalization duration was the secondary outcome.

Results: The meta-analysis included four case-control studies with a total of 1503 patients. The analysis showed a lower odds ratio of pulmonary complications in the single-lumen endotracheal tube intubation in the CO₂ inflation group (odds ratio: 0.756 [95% confidence interval, CI: 0.518 to 1.103]) compared to that in the double-lumen endotracheal tube intubation group, but anastomosis leakage did not improve (odds ratio: 1.056 [95% CI: 0.769 to 1.45]). The SMD in hospitalization duration did not show significant improvement. (SMD: -0.141[95% CI: -0.248 to -0.034]).

Conclusions: Single-lumen endotracheal tube intubation with CO₂ inflation improved pulmonary complications and shortened the hospitalization duration. However, no benefit in anastomosis leakage was observed.

Background

Esophageal cancer has poor overall survival because of delayed diagnosis. Surgery (esophagectomy) followed by chemoradiotherapy is the main treatment strategy. However, the surgical procedure will carry a high risk of morbidity such as pulmonary complications, anastomosis leakage, and long hospitalization duration.

Surgeons are interested in decreasing post-operative complications and have developed methods to improve outcomes. Some studies focused on the anesthesia method with single-lumen endotracheal tube intubation with artificial pneumothorax induced by carbon dioxide (CO₂) inflation. Our meta-analysis tried to compare single-lumen endotracheal tube intubation anesthesia with or without CO₂ inflation with double-lumen endotracheal tube intubation.

We present the following article in accordance with the PRISMA reporting checklist.

Methods

Search strategy and inclusion criteria

PubMed, Medline, and Scopus were searched for studies with keywords including “artificial pneumothorax or CO₂” and “esophagectomy or VATS.” A total 136 results were found. We excluded literature which were not written in English and were not human studies. We also excluded robotic surgery, case reports, and literature reviews. Studies on minimally invasive esophagectomy using single-lumen intubation with CO₂ inflation were included.

All included studies were case control studies. All retrieved studies were required to include two treatment arms. One was CO₂ inflation for induction of artificial pneumothorax and intubated with single-lumen endotracheal tube. The other was traditional one-lung ventilation by double-lumen endotracheal tube intubation. The target population included patients diagnosed with esophageal cancer.

Data extraction and quality assessment

Three reviewers critically read all the studies that were included in our analysis and extracted the data. We recorded the year, first author, number of treatment arms, and results concerning three different parameters, including pulmonary complications, anastomosis leakage, and hospitalization duration. The quality of enrolled studies was evaluated by the two reviewers using the Newcastle-Ottawa Scale. The scale includes three parts for the case control study, namely, “SELECTION” (4 items), “COMPARABILITY” (1 item), and “EXPOSURE” (3 items). Disagreements between reviewers were discussed by other authors and the corresponding author.

Data synthesis and analysis

The odds ratios (ORs) of post-operative pulmonary complications and anastomosis leakage in the single-lumen endotracheal tube intubation in the CO₂ artificial pneumothorax group (SLET group) compared with those in the double-lumen endotracheal tube intubation group (DLET group) were the primary outcomes. The standardized mean difference (SMD) in post-operative hospitalization duration in SLET group compared with that in the control group comprised the secondary outcome. A random effects model was employed to pool individual SMDs and ORs. The heterogeneity was determined by I₂ tests, in which values >50% were regarded as obvious heterogeneity. Potential publication bias was examined by Egger's test and Funnel plots. Statistical significance was defined as p-value <0.05. All statistical analyses were performed using Comprehensive MetaAnalysis software, version 3 (Biostat, Englewood, NJ, USA).

Ethical statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

This article used published accessible literature without containing deeply personal, sensitive, or confidential information from participants. Therefore, institutional review board approval is not necessary.

Results

Study search and characteristics of included patients

We searched the databases and retrieved 136 results. After reviewing their title, abstract, and keywords, 15 papers were selected for meticulous commentary by the reviewers. We excluded papers which did not meet our inclusion criteria (Figure 1). Four studies were excluded because they were case series that did not compare CO₂ inflation and traditional one-lung ventilation (1-4). Two studies were excluded because one introduced a surgical technique with CO₂ inflation in esophagectomy (5), and the other showed a video-assisted thoracoscopic surgical procedure (6). One study was excluded because it was a case control study that compared different surgical positions (7). One study was an editorial discussion (8). One study discussed about differences in coagulation between DLET and SLET groups (9). Two studies were literature reviews (10, 11). Finally, four case control studies were included in this meta-analysis (12-15).

The final quantitative analysis included 915 patients in the DLET group and 588 patients in the SLET group. The age ranges were from 53.91 to 76.9 years in the DLET group and 53.48 to 80 years in the SLET group. Patient characteristics, study methodology, and quality assessment of included trials are listed in Table 1. The detail of quality assessment of included trials is listed in Table 2.

Pooled odds ratio of pulmonary complication, anastomosis leakage, and SMDs in post-operative hospitalization duration

The pooled odds ratio for pulmonary complications in SLET group versus DLET group was 0.756 (95% confidence interval [CI]: 0.518 to 1.103) (Figure 2a). If we excluded the study by Zhang (12) because all groups in the study used CO₂ inflation, the pooled odds ratio was 0.775 (95% CI: 0.520 to 1.154) (Figure 2b). The pooled odds ratio for anastomosis leakage in SLET group versus DLET group was 1.056 (95% CI: 0.769 to 1.451) (Figure 3a). If we excluded the study by Zhang (12), the pooled odds ratio was 1.041 (95% CI: 0.753 to 1.439) (Figure 3b). The standardized mean difference (SMD) concerning hospitalization duration in SLET group versus DLET group was -0.141 (95% CI: -0.248 to -0.034) (Figure 4a). If we excluded the study by Zhang (12), the SMD was -0.136 (95% CI: -0.248 to -0.024) (Figure 4b).

The Egger's test revealed no significant publication bias concerning the overall odds ratio for pulmonary complications and anastomosis leakage ($p=0.348$) and overall SMDs in hospitalization duration ($p=0.023$). The funnel plots for log odds ratio for pulmonary complications and SMD in hospitalization duration are shown in Figure 5a and 5b, respectively.

Discussion

Esophagectomy is a complicated surgery which leads to high post-operative complications, morbidity, and mortality. Although minimally invasive esophagectomy can decrease hospitalization duration, it is still associated with a high post-operative risk. Double-lumen intubation with one-lung ventilation to get better surgical field exposure is a widely used anesthesia strategy, but it increases the rate of acute lung injury and increases pulmonary complications. It is difficult to perform and maintain induction and intubation with this strategy (16). Owing to the difficult manipulation regarding ventilation setting, post-operative pulmonary complications occur frequently in procedures with an extended surgical duration, such as esophagectomy (17).

Some surgeons have tried to use CO₂ inflation to induce artificial pneumothorax and prevent one-lung ventilation. Most of these studies were case control series comparing double-lumen endotracheal tube intubation with one-lung ventilation to single-lumen endotracheal tube intubation with two-lung ventilation and CO₂ inflation. All of them showed similar results in DLET and SLET groups but failed to mention whether there were differences in the rate and severity of complications.

The present meta-analysis focuses on the pulmonary complications, anastomosis leakage, and hospitalization duration in the two groups. We included four papers related to double-lumen endotracheal tube intubation and single-lumen endotracheal tube intubation. One of these studies (12) used CO₂ inflation in both groups, whereas the others used CO₂ inflation in the SLET group alone.

Compared with the DLET group, we found fewer pulmonary complications and shorter hospitalization duration in the SLET group, but the difference was not significant. In the comparison of anastomosis leak, we did not see better results in the SLET group. In these studies, the SLET group maintained ventilation in both lungs and prevented one-lung ventilation, which causes oxidative stress, capillary shear stress, and reperfusion injury. This may lead to better results in terms of pulmonary complications and hospitalization duration. As pulmonary complications improved and systemic inflammation reactions decreased (18), anastomosis leakage should also improve. However, this was not observed in the present analysis. Different surgeons bias may lead to the strange results in anastomosis leakage.

There are several limitations to our meta-analysis. First, all the included papers were case control studies. Plenty of bias could be predicted in these studies. This will decrease the evidence level of the meta-analysis. Second, each study used different CO₂ inflation strategies; one even used CO₂ inflation

in both comparison groups. Third, pulmonary complications are difficult to define clearly. We found that pulmonary complications included thorax infection, pulmonary infection, and pulmonary atelectasis in the study by Zhang (12); respiratory complications in the study by Miao (14); pneumonia, atelectasis, and ARDS in the study by Ninomiya (13); and respiratory complications in the study by Shinsuke (15). Each of them defined pulmonary complications differently, which may have increased the bias of the results.

Based on these limitations, future research involving esophagectomy under SLET should focus on a randomized control study and define protocols of CO₂ inflation and criteria for pulmonary complications.

Conclusions

In this meta-analysis, single-lumen intubation anesthesia with artificial pneumothorax induced by CO₂ inflation was observed to be a better option for minimally invasive esophagectomy. The odds ratio for pulmonary complications and SMDs in hospitalization duration decreased in this surgical setting. Therefore, our meta-analysis survey suggested that single-lumen intubation with CO₂-induced artificial pneumothorax should be taken into consideration for minimally invasive esophagectomy.

List Of Abbreviations

VATS, video-assisted thoracoscopic surgery; CI, confidence interval; DLET, double-lumen endotracheal tube intubation; SLET, single-lumen endotracheal tube intubation; SMD, standardized mean difference

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

This article used published accessible literature without containing deeply personal, sensitive or confidential information from participants. Therefore, institutional review board approval is not necessary.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article (and its supplementary information files.)

Competing interests

All authors have completed the ICMJE uniform disclosure form. The authors have no conflicts of interest to declare.

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Authors' Contributions

- (I) Conception and design: CML
- (II) Administrative support: YC, LCC, HIL, YHC, SHL
- (III) Provision of study materials or patients: All authors
- (IV) Collection and assembly of data: All authors
- (V) Data analysis and interpretation: CML
- (VI) Manuscript writing: KHC, HHL
- (VII) Final approval of manuscript: All authors

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Tables

Table 1. Patient characteristics, study methodology, and quality assessment of included trials

Author, year	Patient Diagnosis	Surgery	Study Design	Enrolled sample number (Male/Female)	Average age, years	Intention-to-treat	Outcome measurement	Quality assessment
Ruixiang Zhang et.al, 2014	Esophageal cancer	MIE	Case-Control	DLET:60/21 SLET:34/8	DLET:64.3±6.5 SLET:62.5±6.5	Not mentioned	Surgical variables and postoperative complications	8
Itasu Ninomiya et.al, 2017	Esophageal cancer	MIE	Case-Control	DLET:49/9 SLET:28/9	DLET: 65.8±8.5 SLET:63.1±8.2	Not mentioned	Postoperative mortality and morbidity rates; Surgical outcomes during thoracic procedures	8
Miao Lin et.al, 2018	Esophageal cancer	MIE	Case-Control	DLET:527/178 SLET:359/102	DLET:61.8±7.89 SLET:61.4±7.92	Not mentioned	Surgical variables and postoperative complications; Parameters during surgery	8
Shinsuke Nomura et.al, 2020	Esophageal cancer	MIE	Case-Control	DLET:59/12 SLET:41/7	DLET:71.1±5.8 SLET:69.9±10.1	Not mentioned	Comparison of postoperative outcomes; Perioperative changes in SIRS criteria, PaO ₂ /FiO ₂ ratio and CRP	8

MIE: minimally invasive esophagectomy; DLET: double lumen endotracheal tube intubation; SLET: single lumen endotracheal tube intubation; SIRS: systemic inflammatory response syndrome

Table 2 Details of quality assessment of the included trials

Author, year	Selection				Comparability	Exposure			Quality assessment
	Is the case definition adequate?	Re-presentativeness of the cases	Selection of Controls	Definition of Controls		Ascertainment of exposure	Same method of ascertainment for cases and controls	Non-Response rate	
Ruixiang Zhang et.al, 2014	*	*		*	**	**	*		8
Itasu Ninomiya et.al, 2017	*	*		*	**	**	*		8
Miao Lin et.al, 2018	*	*		*	**	**	*		8
Shinsuke Nomura et.al, 2020	*	*		*	**	**	*		8

Figures

Figure 1

Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram for the searching and identification of included studies.

a

b

Figure 2

Pulmonary complications between the DLET group and SLET group, included all studies (a) and excluding Zhang's series (b).

a

b

Figure 3

Anastomosis leakage between the DLET group and SLET group, including all studies (a) and excluding Zhang's series (b).

a

b

Figure 4

Hospitalization duration between the DLET group and SLET group, including all studies (a) and excluding Zhang's series (b).

a

b

Figure 5

Funnel Plot of pulmonary complication studies (a) and hospitalization duration studies (b).