Original Article

McKeown or Ivor Lewis minimally invasive esophagectomy: a systematic review and meta-analysis

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Background: Minimally invasive esophagectomy (MIE) is increasingly accepted in many countries. McKeown esophagectomy and Ivor Lewis esophagectomy are two protocols commonly used for MIE, but which one provides more benefit to the patients remains matter of controversy.

Methods: All records in PubMed, Embase, Medline, The Cochrane Library, Wanfang Database, China National Knowledge Infrastructure (CNKI) and Chinese VIP Information till May 2019 were systematically retrieved to compare the cohort studies of McKeown esophagectomy and Ivor Lewis esophagectomy. A meta-analysis of the extracted data was performed using the Review Manager 5.3 and Stata 15 software.

Results: The meta-analysis included 23 cohort studies in which a total of 4,933 patients were enrolled. The results revealed that minimally invasive McKeown esophagectomy (MIME) was superior to minimally invasive Ivor Lewis esophagectomy (MILE) in hospital cost, but inferior to it in operating time, length of hospital stay, in-hospital mortality, 30-day mortality, 90-day mortality, anastomotic leakage, anastomotic leakage requiring surgery, anastomotic stenosis, recurrent laryngeal nerve (RLN) injury, chylothorax, pulmonary complications and total complications. There were no statistical differences between MIME and MILE in blood loss, detected number of lymph nodes, blood transfusion rate, R0 resection rate, re-operation rate, drainage duration, length of the stay in intensive care unit (ICU), 1-year mortality, lung infection, cardiac arrhythmia and delayed gastric emptying.

Conclusions: Except for the cost, MILE is superior to MIME in several aspects, and may represent a better choice for MIE. The results of the present study should be interpreted with caution since the meta-analysis is based on nonrandom cohort studies which may have a selection bias.

Keywords: Minimally invasive esophagectomy (MIE); Ivor Lewis esophagectomy; McKeown esophagectomy; cervical anastomosis; intrathoracic anastomosis

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Introduction

Esophageal cancer is one of the most common cancers worldwide, with the highest incidence in the middle- and low-income countries (1). Esophageal cancer related mortality continues to increase (2), and in 2016 there were approximately 455,800 cases of this tumor and 400,200 deaths (1). Although considerable progress has been made in the diagnosis and treatment of esophageal cancer, globally, the overall 5-year survival rate is only 15–20% (3). Currently, esophageal resection and systematic lymph node dissection regarded as the best treatment methods for this type of cancer (4).

With the development of minimally invasive techniques and related devices, a growing body of evidence indicates that minimally invasive esophagectomy (MIE) has clear advantages over open esophagectomy. It is being increasingly accepted in many countries and has become the standard method for esophageal resection (5). Transhiatal esophagectomy, McKeown esophagectomy and Ivor Lewis esophagectomy are the top three procedures for MIE (6). Minimally invasive McKeown esophagectomy (MIME) and minimally invasive Ivor Lewis esophagectomy (MILE) are becoming more frequently utilized by surgeons since they allow a more thorough dissection of the thoracic lymph node (7). However, whether MIME of MILE has more clinical advantages and should become the recommended procedure remains a matter of controversy (8).

To identify the differences in short-term outcomes between the two procedures, meta-analyses have been conducted using intraoperative data, primary postoperative complications, and short-term mortality. Despite the high value of this research and the inclusion of several Chinese studies, data available from Chinese databases were not utilized. This is an important omission since according to World Health Organization, there were 572,034 new cases of esophageal cancer worldwide in 2018 and 307,359 of them were in China, accounting for 53.73% of global incidence. Therefore, it is critical to include the Chinese database in the meta-analysis. Additionally, the secondary endpoints considered in the previous studies have their limitations and the differences between two surgical procedures were not analyzed in a comprehensive way.

This report presents a systematic review and meta-analyses of the outcomes of MIME and MILE, utilizing both Chinese and English-language databases. The inclusion of the Chinese database allowed collecting a greater abundance of research data, resulting in a more comprehensive evaluation of the differences between the two surgical procedures.

Methods

This meta-analysis adheres to the requirements of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. The systematic review and meta-analysis have been registered in the PROSPERO database (registration number: CRD42019128884). An IRB approval and informed consent of the patients were not required for this systematic review.

Literature search strategy

All results pertinent to the use of MIME and MILE available from PubMed, Embase, Medline, The Cochrane Library, Wanfang Database, China National Knowledge Infrastructure (CNKI), and Chinese VIP Information, deposited on or before May 2019, were retrieved using the search strategies designed by the authors (Supplementary file 1). Only studies published in Chinese and English were included, regardless of the language of the country where the study was performed. To ensure that the retrieval is as comprehensive as possible, and to reduce the selection bias, all references listed in the included studies were retrieved and analyzed manually.

Study selection

The literature retrieval was carried out independently by two assessors (J Wang and J Hu) and the cohort studies that did not fulfill the inclusion criteria were screened out. First, studies that based on the title and the abstract were evidently unrelated to MIME or MILE were disregarded. Subsequently, the considered studies were downloaded in full-text format and assessed according to inclusion criteria. Inclusion criteria were as follows: (I) research type: cohort studies (including prospective cohort studies and retrospective cohort studies); (II) surgical procedures: clear description of the surgical procedures, ensuring that the surgical protocol complied with the criteria of minimally invasive surgery; and (II) research results: presence of the data on anastomotic leakage. Any disagreement during the retrieval and screening process was discussed with and resolved by the third assessor (Y Yang).

Data extraction

The data were extracted and exchanged for examination by two assessors (J Wang and J Hu) independently. Any disagreement was discussed with and resolved by the third assessor (Y Yang). The extracted information included: (I) paper information: name of the first author, publication year, duration of the study, study design, and country; (II) patient information: number of enrolled patients, age, gender, and tumor site; and (III) the outcome parameters. The primary outcome parameter was the occurrence of an anastomotic leakage, while secondary outcome parameters included operating time, blood loss, number of lymph nodes obtained, R0 resection rate, drainage duration, re-operation rate, blood transfusion rate, length of stay in intensive care unit (ICU), length of hospital stay, cost, in-hospital mortality, 30-day mortality, 90-day mortality, 1-year mortality, anastomotic stenosis, recurrent laryngeal nerve injury, chylothorax, pulmonary complications, arrhythmia, delayed gastric emptying and total complications.

Quality assessment

Quality assessment was performed using the Newcastle-Ottawa quality assessment scale (NOS). The scale comprises 8 items divided into three parts: selection (maximum score, 4), comparability (maximum score, 2), and outcome (maximum score, 3) and which in total can give a maximum score of 9 points. The total score of 7 or more points was considered to indicate a high quality of the study, 6 points medium quality, and less than 6 points indicate low quality. Only studies with high and medium quality were finally enrolled. The assessment process was carried out independently by two assessors (J Wang and J Hu). Any disagreement was discussed with the third assessor until an agreement was reached.

Statistical analysis

Statistical analysis of the data was conducted using the Review Manager 5.3 software. The heterogeneity between the studies was analyzed by the I^2 test, and I^2>50% was considered to indicate significant heterogeneity between the studies. When significant heterogeneity was present between the studies, DerSimonian and Laird random effects model or Mantel-Haenszel fixed effect model was chosen. For binary variable results, the odds ratio (OR) and 95% confidence interval (CI) were calculated. For continuous variables, the mean difference and 95% CI were computed. P<0.05 was considered as statistically significant. Sensitivity analysis was performed on variables with significant heterogeneity using the Stata 15 statistical package to identify the source of heterogeneity. The publication bias of variables with the number of studies >10 was tested using the Egger's test. The trim-and-fill method was used to further test the influence of publication bias on the results.

Results

Literature search and quality assessment

The retrieval and screening process of the references is shown in *Figure 1*. The retrieval strategy used identified 5,728 studies, of which 4,108 remained after removing duplicate publications. After reading the titles and abstracts, 4,028 studies that were evidently unrelated to the present analysis were eliminated. Full text of the remaining 80 studies was downloaded for further detailed reviews. Finally, the meta-analysis was conducted on the 23 studies that met the inclusion criteria. The characteristics and quality assessment scores of these 23 investigations are listed in *Table S1*. The quality assessment scores for all studies were above 6, meeting the inclusion criteria (8-30).

Results of meta-analysis

Primary outcome measures

Anastomotic leakage

A total of 23 publications reported the occurrence rate of anastomotic leakage. However, the report by Luketich *et al.* (21) provided only the incidence of anastomotic leakage requiring surgery, making it impossible to combine it with the other studies. This necessitated a separate meta-analysis of the occurrence rate of anastomotic leakage requiring surgery (see below). The 22 studies which listed the incidence of anastomotic leakage included 3,922 patients. The occurrence rate of anastomotic leakage was 14.7% in MIME, and 5.5% in MILE. The heterogeneity between the 22 studies was not statistically significant (P=0.09; I^2=30%). Therefore, the fixed-effect model was adopted to compare the outcomes of the two protocols. This analysis indicated that the occurrence rate of anastomotic leakage was higher in MIME than that in MILE (OR =2.97, 95% CI: 2.34–3.77), and this difference was statistically significant (P<0.00001) (*Figure 2*).

Three studies, reporting on 1,541 patients, included the data on the incidence of anastomotic leakage requiring surgery. The heterogeneity between the studies was not statistically significant (P=0.51; I^2=0%); therefore, the fixed-effect model was chosen for analysis, which indicated

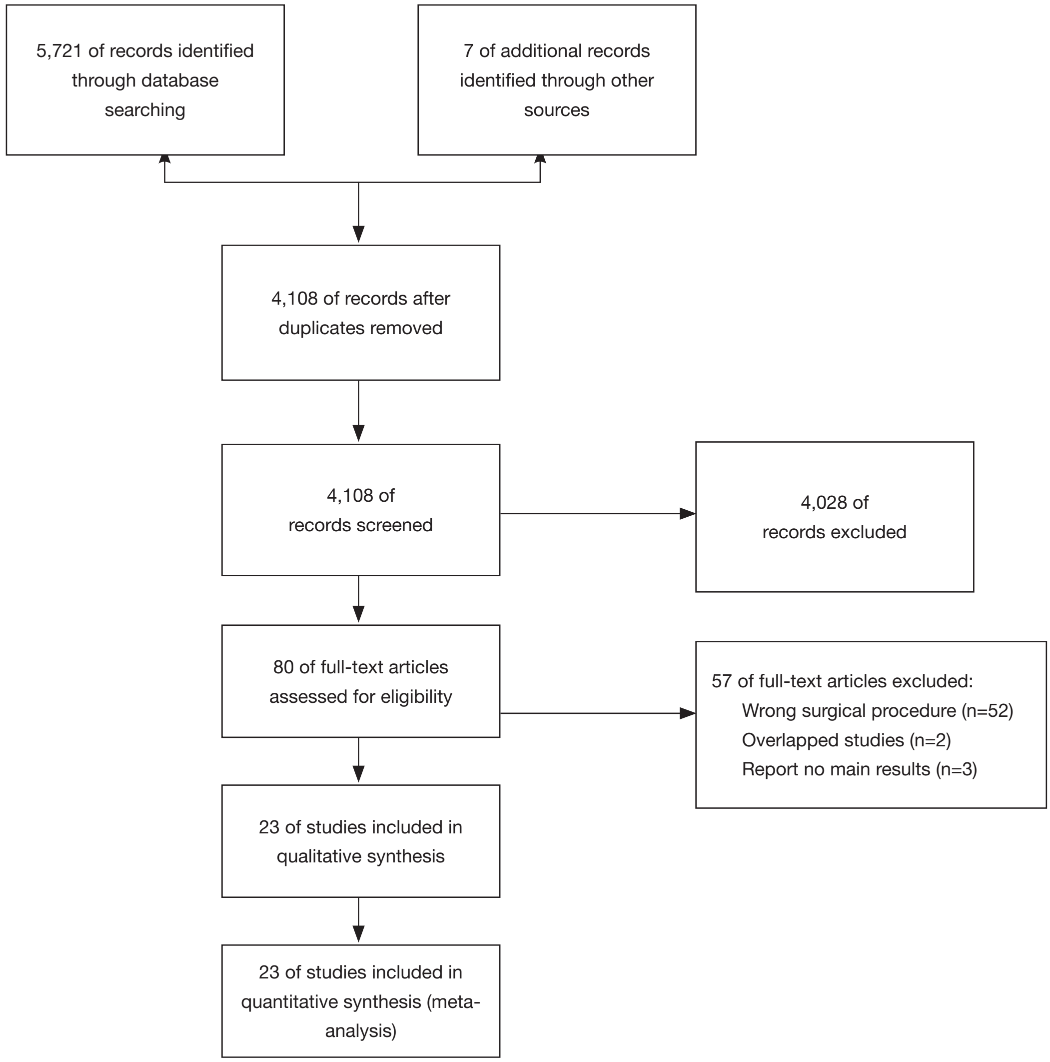

Figure 1 Summary of screening and selection process.

that the occurrence rate of anastomotic leakage requiring surgery was significantly higher in MIME than in MILE (OR =1.57, 95% CI: 1.02–2.43, P=0.04) (*Figure 3*).

Secondary outcome measures

Intraoperative data

The results of the meta-analysis of intraoperative data are shown in *Table 1*. The operating time was reported in 20 studies that included 3,478 patients. Meta-analysis documented that the operating time of MIME was longer than that of MILE [weighted mean difference (WMD) =23.69, 95% CI: 6.26–41.12, P=0.008]. There was no statistically significant difference between the two surgical procedures in terms of blood loss, the number of lymph nodes detected, transfusion rate, and R0 resection rate.

Postoperative data

The results of the meta-analysis of postoperative data are listed in *Table 2*. In comparison with MILE, MIME was associated with a longer length of hospital stay (WMD =1.13, 95% CI: 0.45–1.82, P=0.001), higher in-hospital mortality (OR =2.83, 95% CI: 1.35–5.93, P=0.006), higher 30-day mortality (OR =2.44, 95% CI: 1.33–4.50, P=0.004), higher 90-day mortality (OR =2.85, 95% CI: 1.55–5.23, P=0.0007), but the cost of MIME was lower (WMD =−0.40, 95% CI: −0.74 to 0.07, P=0.02). The re-operation rate, drainage duration, length of stay in the ICU, and 1-year mortality were not statistically different between the two surgical procedures.

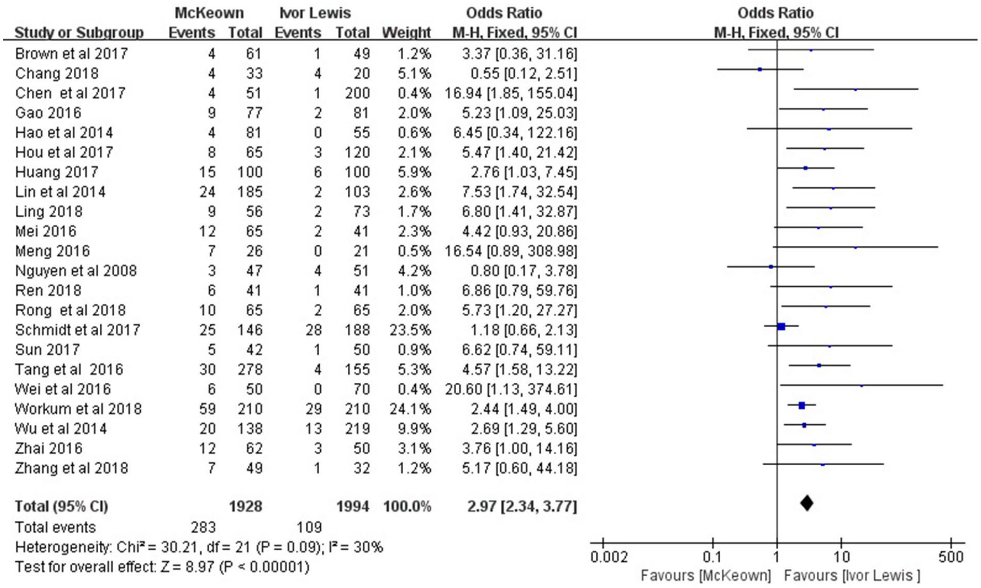

Figure 2 Forest plot anastomotic leakage. CI, confidence interval; M-H, Mantel-Haenszel.

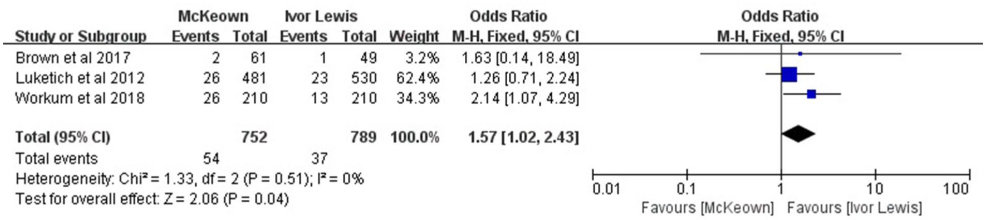

Figure 3 Forest plot anastomotic leakage requiring surgery. CI, confidence interval; M-H, Mantel-Haenszel.

Complications

The results of the meta-analysis of complications are presented in *Table 3*. Patients undergoing MIME had a higher morbidity associated with anastomotic stricture (OR =2.89, 95% CI: 1.97–4.24, P<0.00001), recurrent laryngeal nerve (RLN) injury (OR =5.63, 95% CI: 3.99–7.94, P<0.00001), chylothorax (OR =1.55, 95% CI: 1.01–2.38, P=0.04), pulmonary complications (OR =1.89, 95% CI: 1.54–2.32, P<0.00001) and overall complications (OR =1.90, 95% CI: 1.34–2.71, P=0.0004). There were no statistical differences in morbidity related to lung infection, cardiac arrhythmia and delayed gastric emptying between MIME and MILE.

Sensitivity analysis

Evident heterogeneity was present in the nine groups of studied variables, including operating time (I^2=98%, P<0.00001), blood loss (I^2=71%, P<0.00001), number of detected lymph nodes (I^2=87%, P<0.00001), drainage duration (I^2=94%, P<0.00001), length of hospital stay (I^2=82%, P<0.00001), length of the stay in ICU (I^2=95%, P<0.00001), cost (I^2=87%, P<0.00001), lung infection (I^2=52%, P=0.04), and total complications (I^2=74%, P<0.00001). The sensitivity analysis for blood loss, drainage duration, length of hospital stay, length of the stay in ICU, cost and lung infection produced stable results, indicating that there was no source of heterogeneity. The sensitivity analysis of operating time showed that studies by Tang *et al.* (16) and van Workum *et al.* (18) significantly influenced the combined OR and CI. However, when these studies were removed, there was no evident change in heterogeneity (I^2=98%, P<0.00001). The sensitivity analysis of the number of detected lymph nodes suggested

Table 1 Meta-analysis for intraoperative data

Outcomes	No. of studies	No. of patients	McKeown's events incidence (%)	Ivor Lewis's events incidence (%)	WMD/OR (95% CI)	Heterogeneity	Test for overall effect	Favors group
Operating time	20	3,478	–	–	23.69 (6.26, 41.12)	I^2=98%, P<0.00001	Z=2.66, P=0.008	Ivor Lewis
Blood loss	18	3,005	–	–	7.73 (–2.21, 17.59)	I^2=71%, P<0.00001	Z=1.54, P=0.12	–
Examined lymph nodes	17	4,231	–	–	0.69 (–0.62, 2.01)	I^2=87%, P<0.00001	Z=1.03, P=0.30	–
R0 resection	5	2,095	97.2%	96.8%	1.07 (0.63, 1.80)	I^2=0%, P=0.67	Z=0.24, P=0.81	–
Conversion to open	3	1,616	4.5%	3.6%	1.32 (0.80, 2.18)	I^2=0%, P=0.92	Z=1.08, P=0.28	–
Blood transfusion	5	984	3.5%	5.0%	0.79 (0.41, 1.50)	I^2=0%, P=0.54	Z=0.73, P=0.46	–

WMD, weighted mean difference; OR, odds ratio; CI, confidence interval.

Table 2 Meta-analysis for postoperative data

Outcomes	No. of studies	No. of patients	McKeown's events incidence (%)	Ivor Lewis's events incidence (%)	WMD/OR (95% CI)	Heterogeneity	Test for overall effect	Favors group
Reoperations	4	836	14.0%	6.9%	1.57 (0.98, 2.53)	I^2=26%, P=0.25	Z=1.87, P=0.06	–
Drainage time	12	2,093	–	–	–0.41 (–1.33, 0.52)	I^2=94%, P<0.00001	Z=0.87, P=0.39	–
Hospital LOS	20	4,331	–	–	1.13 (0.45, 1.82)	I^2=82%, P<0.00001	Z=3.23, P=0.001	Ivor Lewis
ICU LOS	5	1,916	–	–	0.17 (–1.07, 1.41)	I^2=95%, P<0.00001	Z=0.27, P=0.79	–
Cost	9	1,817	–	–	–0.40 (–0.74, –0.07)	I^2=87%, P<0.00001	Z=2.37, P=0.02	McKeown
In-hospital mortality	10	2,316	2.4%	0.9%	2.83 (1.35, 5.93)	I^2=0%, P=0.80	Z=2.75, P=0.006	Ivor Lewis
30-day mortality	6	2,179	3.4%	1.2%	2.44 (1.33, 4.50)	I^2=2%, P=0.40	Z=2.86, P=0.004	Ivor Lewis
90-day mortality	4	919	8.9%	3.2%	2.85 (1.55, 5.23)	I^2=0%, P=0.97	Z=3.39, P=0.0007	Ivor Lewis
1-year mortality	3	294	9.8%	9.3%	1.04 (0.48, 2.27)	I^2=0%, P=0.56	Z=0.11, P=0.92	–

WMD, weighted mean difference; OR, odds ratio; CI, confidence interval; LOS, length of stay.

that the study by Luketich *et al.* (21) significantly affected the final result. After eliminating this study, significant heterogeneity continued to be present (I^2=75%, P<0.00001). Sensitivity analysis pointed to the publication of Tang *et al.* as the source of heterogeneity in meta-analysis of total complications. After removing this study, the heterogeneity of the results disappeared (I^2=0%, P<0.66), and the results were: OR =1.55, 95% CI: 1.30–1.85, Z=4.83, P<0.00001.

Publication bias

The Egger's test revealed that there was publication bias affecting the results of operating time, length of hospital stay, anastomotic stenosis, and anastomotic leakage.

Table 3 Meta-analysis for complications data

Outcomes	No. of studies	No. of patients	McKeown's events incidence (%)	Ivor Lewis's events incidence (%)	WMD/OR (95% CI)	Heterogeneity	Test for overall effect	Favors group
Anastomotic stricture	11	2,102	10.0%	4.1%	2.89 (1.97, 4.24)	I^2=25%, P=0.21	Z=5.43, P<0.00001	Ivor Lewis
RLN trauma	20	4,365	9.7%	1.7%	5.63 (3.99, 7.94)	I^2=0%, P=0.85	Z=9.86, P<0.00001	Ivor Lewis
Chylothorax	12	2,352	4.9%	3.1%	1.55 (1.01, 2.38)	I^2=0%, P=0.70	Z=2.03, P=0.04	Ivor Lewis
Pulmonary complications	14	2,736	25.4%	15.1%	1.89 (1.54, 2.32)	I^2=36%, P=0.09	Z=6.11, P<0.00001	Ivor Lewis
Lung infection	8	971	11.9%	7.7%	1.44 (0.69, 3.00)	I^2=52%, P=0.04	Z=0.96, P=0.34	–
Cardiac arrhythmia	10	1,789	6.0%	4.3%	1.39 (0.89, 2.18)	I^2=0%, P=0.69	Z=1.44, P=0.15	–
Delayed gastric emptying	9	1,537	4.8%	3.9%	1.33 (0.80, 2.23)	I^2=36%, P=0.13	Z=1.09, P=0.28	–
Overall complications	13	2,861	43.8%	29.7%	1.90 (1.34, 2.71)	I^2=74%, P < 0.00001	Z=3.57, P=0.0004	Ivor Lewis

WMD, weighted mean difference; OR, odds ratio; CI, confidence interval; RLN, recurrent laryngeal nerve.

However, the trim-and-fill analysis indicated that the publication bias did not affect significantly the conclusions.

Discussion

This systematic review and meta-analysis compare the short-term effects of MIME and MILE. The present study reveals for the first time that MILE is superior to MIME in in-hospital mortality, 30-day mortality, 90-day mortality, the incidence of chylothorax, severe anastomotic leakage, and total complications, but is associated with a higher cost. The analysis confirmed previous findings that MILE provides better outcomes of operating time, length of hospital stay, anastomotic leakage, anastomotic stenosis, RLN injury, pulmonary complications.

In the comparison of intra-operative data, only identified difference between the two surgical procedures was the shorter operating time in MILE, since the neck incision is not necessary with this protocol. Among the postoperative complications, the lifted length of the tubular stomach was shorter in MILE, reducing the tension of anastomotic stoma and providing a better blood supply. Additionally, the anastomotic stoma inside the thorax was less compressed than the anastomotic stoma in the narrow cervical region, decreasing the likelihood of anastomotic leakage and anastomotic stenosis. Since the neck incision was not required for MILE, the exposure of the recurrent cervical laryngeal nerve was avoided, decreasing the morbidity associated with RLN injury. The morbidity of pulmonary complications after MILE was also lower, likely due to the shorter operating and RLN injury (31,32). MILE dissociated the proximal esophagus, which was lower than that in MIME, so it had less chance to damage the thoracic duct and reduced the morbidity of chylothorax (10). The meta-analysis of postoperative data indicated that MILE had lower morbidity associated with postoperative complications, resulting in a shorter length of hospital stay, and lower in-hospital mortality, 30-day mortality, and 90-day mortality. In MILE, anastomat was used for intrathoracic esophageal anastomosis, which may increase the cost (12). Importantly, all the relevant data were from Chinese research.

A remarkable aspect of the present analysis is the demonstration of the survival benefit of MILE. Mortality is an important indicator of the outcome of the surgery mode, highlighting the significance of the comparison of MILE and MIME. The absence of a statistically significant difference in 1-year mortality may reflect the small number of enrolled studies and cases was.

In comparison with previously published meta-analyses, more perfect improved strategies were developed, which not only enhanced the effectiveness of the search, but also retrieved the Chinese database. As a result, 23 medium and high-quality studies with 4,933 patients were enrolled in the meta-analysis. More outcome indexes were collected and analyzed, and the differences between the two procedures were analyzed in a more comprehensive way. The current meta-analysis detected also more differences between the two surgical approaches than previously published studies. Of note, a sensitivity analysis was performed for the results with significant heterogeneity, and the sources of heterogeneity were identified.

Some limitations of the present study should be acknowledged: (I) The analysis included only cohort studies so that the selection bias was unavoidable. (II) Long-term survival data were not available in the enrolled studies, making the assessment of the difference in long-term prognosis between MILE and MIME impossible. This limitation emphasized the need for new relevant clinical studies to determine the long-term survival after these two surgical protocols. (III) The homogeneity test of continuous variables demonstrated a significant heterogeneity. It may be caused by differences in experience and skills among the surgeons, and variations in the diagnosis and treatment protocols between different geographic regions. (IV) Among the 23 studies enrolled in the research, 18 were performed in China. Thus, the results of the present study may not serve as a reference for other countries and regions of the world.

Conclusions

MILE is superior to MIME in operating time, length of hospital stay, in-hospital mortality, 30-day mortality, 90-day mortality, anastomotic leakage, anastomotic leakage requiring surgery, anastomotic stenosis, RLN injury, chylothorax, pulmonary complications, total complications. However, MILE is associated with a higher cost. Therefore, MILE may represent a better option for MIE if economic conditions are not a limiting factor. It is worth noting that presented the meta-analysis is based on nonrandom cohort studies that have inherent selection bias and, therefore, should be interpreted cautiously. A large number of high-quality randomized controlled trials should be done to verify the results.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2020.01.45). The authors have no conflicts of interest to declare.

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.

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PubMed and Medline search strategy

#1, "Esophageal Neoplasms"[Mesh]
#2, Esophageal Neoplasm
#3, Neoplasm, Esophageal
#4, Esophagus Neoplasm
#5, Esophagus Neoplasms
#6, Neoplasm, Esophagus
#7, Neoplasms, Esophagus
#8, Neoplasms, Esophageal
#9, "Cancer of Esophagus"
#10, "Cancer of the Esophagus"
#11, Esophagus Cancer
#12, Cancer, Esophagus
#13, Cancers, Esophagus
#14, Esophagus Cancers
#15, Esophageal Cancer
#16, Cancer, Esophageal
#17, Cancers, Esophageal
#18, Esophageal Cancers
#19, "Esophagectomy"[Mesh]
#20, Esophagectomies
#21, Oesophagectomy
#22, Oesophagectomies
#23, #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
#24, "Video-Assisted Surgery"[Mesh]
#25, Surgeries, Video-Assisted
#26, Video Assisted Surgery
#27, Video-Assisted Surgeries
#28, Surgery, Video-Assisted
#29, Surgery, Video Assisted
#30, "Thoracic Surgery, Video-Assisted"[Mesh]
#31, Surgeries, Video-Assisted Thoracic
#32, Surgery, Video-Assisted Thoracic
#33, Thoracic Surgeries, Video-Assisted
#34, Thoracic Surgery, Video Assisted
#35, Video-Assisted Thoracic Surgeries
#36, Video-Assisted Thoracoscopic Surgery
#37, Surgeries, Video-Assisted Thoracoscopic
#38, Surgery, Video-Assisted Thoracoscopic
#39, Thoracoscopic Surgeries, Video-Assisted
#40, Thoracoscopic Surgery, Video-Assisted
#41, Video Assisted Thoracoscopic Surgery
#42, Video-Assisted Thoracoscopic Surgeries
#43, Video-Assisted Thoracic Surgery
#44, Video Assisted Thoracic Surgery
#45, Surgery, Thoracic, Video-Assisted
#46, VATS
#47, VATSs
#48, "Minimally Invasive Surgical Procedures"[Mesh]
#49, Surgical Procedures, Minimal
#50, Surgical Procedures, Minimal Access
#51, Surgical Procedures, Minimally Invasive
#52, Minimal Access Surgical Procedures
#53, Minimal Surgical Procedure
#54, Procedures, Minimally Invasive Surgical
#55, Minimally Invasive Surgery
#56, Surgeries, Minimally Invasive
#57, Surgery, Minimally Invasive
#58, Procedure, Minimal Surgical
#59, Procedures, Minimal Access Surgical
#60, Procedures, Minimal Surgical
#61, Surgical Procedure, Minimal
#62, Minimal Surgical Procedures
#63, #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62
#64, #23 AND #63
#65, #64 OR McKeown OR Ivor Lewis
#66, "Cohort Studies"[Mesh]
#67, Cohort Study
#68, Studies, Cohort
#69, Study, Cohort
#70, Concurrent Studies
#71, Studies, Concurrent
#72, Concurrent Study
#73, Study, Concurrent
#74, Closed Cohort Studies
#75, Cohort Studies, Closed
#76, Closed Cohort Study
#77, Cohort Study, Closed
#78, Study, Closed Cohort
#79, Studies, Closed Cohort
#80, Analysis, Cohort
#81, Cohort Analysis
#82, Analyses, Cohort

#83, Cohort Analyses
#84, Historical Cohort Studies
#85, Cohort Study, Historical
#86, Historical Cohort Study
#87, Study, Historical Cohort
#88, Incidence Studies
#89, Incidence Study
#90, Studies, Incidence
#91, Study, Incidence
#92, #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91
#93, #65 AND #92

Embase search strategy

#1, 'esophagus tumor'/exp
#2, 'esophageal neoplasms'
#3, 'esophageal tumor'
#4, 'esophagus tumor'
#5, 'esophagus tumour'
#6, 'oesophageal neoplasms'
#7, 'oesophageal tumor'
#8, 'oesophageal tumour'
#9, 'oesophagus tumor'
#10, 'oesophagus tumour'
#11, 'tumor, esophagus'
#12, 'tumour, esophagus'
#13, #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12
#14, 'endoscopic surgery'/exp
#15, 'endoscopic resection'
#16, 'endoscopic surgery'
#17, 'resection, endoscopic'
#18, 'surgery, endoscopic'
#19, 'surgery, video assisted'
#20, 'surgical procedures, endoscopic'
#21, 'video-assisted surgery'
#22, 'video assisted thoracoscopic surgery'/exp
#23, 'vats'
#24, 'thoracic surgery, video-assisted'
#25, 'video assisted thoracic surgery'
#26, 'video assisted thoracoscopic surgery'
#27, 'videothoracoscopic surgery'
#28, 'minimally invasive surgery'/exp
#29, 'mini-invasive surgery'
#30, 'mini-invasive surgical procedure'
#31, 'mini-invasive surgical procedures'
#32, 'minimally invasive surgery'
#33, 'minimally invasive surgical method'
#34, 'minimally invasive surgical methods'
#35, 'minimally invasive surgical procedure'
#36, 'minimally invasive surgical procedures'
#37, 'minimally invasive surgical technique'
#38, 'minimally invasive surgical techniques'
#39, 'surgery, minimally invasive'
#40, 'surgical procedures, minimally invasive'
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#42, #13 AND #41
#43, #42 OR 'McKeown' OR 'ivor lewis'
#44, 'cohort analysis'/exp
#45, 'analysis, cohort'
#46, 'cohort analysis'
#47, 'cohort fertility'
#48, 'cohort life cycle'
#49, 'cohort studies'
#50, 'cohort study'
#51, 'fertility, cohort'
#52, #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51
#53, #43 AND #52

The Cochrane Library search strategy

#1, MeSH descriptor: [Esophageal Neoplasms] explode all trees
#2, MeSH descriptor: [Esophagectomy] explode all trees
#3, Oesophagectomy
#4, Oesophagectomies
#5, #1 OR #2 OR #3 OR #4
#6, MeSH descriptor: [Video-Assisted Surgery] explode all trees

#7, MeSH descriptor: [Thoracic Surgery, Video-Assisted] explode all trees
#8, MeSH descriptor: [Minimally Invasive Surgical Procedures] explode all trees
#9, #6 OR #7 OR #8
#10, #5 AND #9
#11, #10 OR McKeown OR Ivor Lewis

Wanfang Databases, China National Knowledge Infrastructure (CNKI) and Chinese VIP Information search strategy

#1, McKeown
#2, Ivor Lewis
#3, Ivor-Lewis
#4, #1 OR #2 OR #3

Table S1 The characteristics and quality assessment scores of included studies

Study	Study interval	Study type	Country	Total cases	Group	Number	Sex (M/F)	Age (mean ± SD)	Location of cancer	Outcome parameters	Quality score
Brown *et al*., 2018	June 2011 to May 2016	Prospective cohort	USA	110	McKeown	61	51/10	63±8.7	All segments	Duration of surgery, blood loss, examined LN, examined LN positive, R0 resection, hospital length of stay, cost, in-hospital mortality, 30-day mortality, anastomotic leakage, RLN injury, chylothorax, cardiac complications, pulmonary complications, delayed gastric emptying, thromboembolism, urinary tract complications, wound infection, 90 days, 180 days of serious complications	7
					Ivor Lewis	49	40/9	60.9±9.0			
Chang, 2018	January to December 2015	Retrospective cohort	China	53	McKeown	33	NA	NA	All segments	Reoperations, ICU length of stay, hospital length of stay, 30-day mortality, 90-day mortality, anastomotic leakage, anastomotic stenosis, RLN injury, cardiac arrhythmia, pulmonary complications	6
					Ivor Lewis	20	NA	NA			
Chen *et al*., 2017	2014–2016	Prospective cohort	China	251	McKeown	51	38/13	61.4±9.1	All segments	Duration of surgery, blood loss, examined LN, conversion to open, R0 resection, hospital length of stay, reoperations, 30-day mortality, ICU stay, anastomotic leakage, anastomotic stenosis, chylothorax, cardiac arrhythmia, RLN injury	7
					Ivor Lewis	200	169/31	59.9±8.4			
Gao, 2016	February 2012 to January 2015	Retrospective cohort	China	158	McKeown	77	41/36	57.3±5.9	All segments	Duration of surgery, blood loss, examined LN, drainage time, 6-month tumor recurrence, anastomotic leakage, RLN injury, cardiac arrhythmia, pulmonary infection	8
					Ivor Lewis	81	44/37	59.6±6.8			
Hao *et al*., 2014	June 2008 to June 2012	Retrospective cohort	China	136	McKeown	81	NA	NA	All segments	Duration of surgery, blood loss, examined LN, hospital length of stay, in-hospital mortality, anastomotic leakage	6
					Ivor Lewis	55	NA	NA			
Hou *et al*., 2017	2014 l January to May 2016	Retrospective cohort	China	185	McKeown	65	41/24	56.7±11.6	All segments	Duration of surgery, blood loss, examined LN, serious intraoperative complications, conversion to open, R0 resection, hospital length of stay, cost, in-hospital mortality, anastomotic leakage, RLN injury, respiratory complications, cardiovascular complications, postoperative bleeding, other complications, postoperative pain, quality of life score	8
					Ivor Lewis	120	82/38	57.2±13.0			
Huang, 2017	January 2015 to December 2016	Prospective cohort	China	200	McKeown	100	59/41	56.2±6.3	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, hospital length of stay, cost, in-hospital mortality, tumor recurrence, anastomotic leakage, anastomotic stenosis, RLN injury, chylothorax, cardiac arrhythmia, pulmonary complications, delayed gastric emptying, esophageal reflux, incision infection	7
					Ivor Lewis	100	61/39	57.5±7.1			
Lin *et al*., 2014	December 2010 to March 2014	Retrospective cohort	China	288	McKeown	185	142/43	58.3±8.7	Middle and low segments	Duration of surgery, blood loss, examined LN, blood transfusion, drainage time, postoperative feeding time, ICU stay, hospital length of stay, cost, in-hospital mortality, anastomotic leakage, anastomotic stenosis, RLN injury, chylothorax, cardiac arrhythmia, pulmonary complications, delayed gastric emptying, incision bleeding	8
					McKeown	103	80/23	59.1±8.4			
Ling, 2018	January 2014 to April 2017	Retrospective cohort	China	129	McKeown	56	43/13	61.5±18.1	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, hospital length of stay, cost, 6-months tumor recurrence, anastomotic leakage, anastomotic stenosis, RLN injury, chylothorax, pulmonary infection, atelectasis, delayed gastric emptying	8
					Ivor Lewis	73	55/18	63.2±17.8			
Luketich *et al*., 2012	August 1996 to March 2011	Retrospective cohort	USA	1,011	McKeown	481	392/89	65 [56–72]	All segments	Examined LN, conversion to open, R0 resection, ICU length of stay, hospital length of stay, ICU length of stay, 30-day mortality, anastomotic leakage, RLN injury, cardiac complications, ARDS, empyema, gastric tube necrosis	7
					Ivor Lewis	530	415/115	64 [56–72]			
Mei, 2016	January 2012 to September 2015	Retrospective cohort	China	106	McKeown	65	49/16	63.56±5.09	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, hospital length of stay, cost, anastomotic leakage, anastomotic stenosis, RLN injury, chylothorax, pulmonary infection, incision infection	8
					Ivor Lewis	41	32/9	62.71±5.04			
Meng, 2016	March 2011 to June 2014	Retrospective cohort	China	47	McKeown	26	16/10	56.8±7.2	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, hospital length of stay, in-hospital mortality, anastomotic leakage, anastomotic stenosis, RLN injury, pulmonary infection, esophageal reflux	8
					Ivor Lewis	21	13/8	57.3±6.4			
Nguyen *et al*., 2008	August 1998 to September 2007	Prospective cohort	USA	98	McKeown	47	39/8	65±10	All segments	Duration of surgery, blood loss, blood transfusion, ICU length of stay, hospital length of stay, 30-Day mortality, anastomotic leakage, anastomotic stenosis, major complications	6
					Ivor Lewis	51	33/18	64±12			
Ren, 2018	March 2013 to July 2016	Prospective cohort	China	82	McKeown	41	31/10	59.0±7.5	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, hospital length of stay, cost, 1-year mortality, 1-year tumor recurrence, anastomotic leakage, RLN injury, cardiac arrhythmia, pulmonary complications, delayed gastric emptying, incision bleeding	9
					Ivor Lewis	41	31/10	57.2±8.0			
Rong *et al*., 2018	March to November 2017	Retrospective cohort	China	130	McKeown	65	46/19	NA	Middle segments	Duration of surgery, blood loss, examined LN, R0 resection, ICU stay, hospital length of stay, cost, in-hospital mortality, anastomotic leakage, RLN injury, chylothorax, pulmonary infection	6
					Ivor Lewis	65	52/13	NA			
Schmidt *et al*., 2017	June 2011 to May 2016	Retrospective cohort	Switzerland	334	McKeown	146	NA	NA	All segments	Examined LN, R0 resection, hospital length of stay, 30-day mortality, 90-day mortality, ICU length of stay, hospital readmission, anastomotic leakage, cardiac complications, pulmonary complications	7
					Ivor Lewis	188	NA	NA			
Sun, 2017	May 2014 to May 2015	Retrospective cohort	China	92	McKeown	42	NA	NA	Middle and low segments	Duration of surgery, blood loss, examined LN, examined LN positive, drainage time, hospital length of stay, cost, 1-year mortality, 1-year tumor metastasis, anastomotic leakage, RLN injury, pulmonary complications, cardiac arrhythmia, delayed gastric emptying, incision bleeding	8
					Ivor Lewis	50	NA	NA			
Tang *et al*., 2016	December 2013 to April 2015	Retrospective cohort	China	433	McKeown	278	201/77	57.1±6.9	Middle and low segments	Duration of surgery, blood loss, examined LN, blood transfusion, drainage time, postoperative feeding time, hospital length of stay, cost, in-hospital mortality, anastomotic leakage, anastomotic stenosis, RLN injury, chylothorax, cardiac arrhythmia, pulmonary complications, delayed gastric emptying	8
					Ivor Lewis	155	103/52	55.8±7.1			
Wei *et al*., 2016	January 2013 to June 2015	Prospective cohort	China	120	McKeown	50	31/19	59.69±8.31	Middle and low segments	Duration of surgery, blood loss, examined LN, conversion to open, drainage time, hospital length of stay, in-hospital mortality, 1-year mortality, anastomotic leakage, RLN injury, chylothorax, cardiac arrhythmia, pulmonary complications, delayed gastric emptying, incision bleeding, pain score 24 hours after surgery, pain score 72 hours after surgery, time to get out of bed, anal exhaust time	9
					Ivor Lewis	70	47/23	55.69±6.15			
Workum *et al*., 2018	November 2009 to April 2017	Retrospective cohort	The Nether-lands	420	McKeown	210	169/41	NA	Low segment and gastroesophageal junction	Duration of surgery, examined LN, conversion to open, R0 resection, reintervention, ICU length of stay, hospital length of stay, in-hospital mortality, 30-day mortality, 90-day mortality, anastomotic leakage, RLN injury, chylothorax, cardiac complications, pulmonary complications, jejunostomy-related complications, overall complications, 30-day hospital readmission	8
					Ivor Lewis	210	176/34	NA			
Wu *et al*., 2014	October 2011 to March 2014	Retrospective cohort	China	357	McKeown	138	106/32	63.52±17.6	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, hospital length of stay, cost, In-hospital mortality, tumor recurrence, anastomotic leakage, anastomotic stenosis, RLN injury	8
					Ivor Lewis	219	169/50	61.8±18.5			
Zhai, 2016	January 2013 to June 2015	Retrospective cohort	China	112	McKeown	62	56/6	60.8±1.3	Middle and low segments	Duration of surgery, blood loss, examined LN, blood transfusion, ICU stay, hospital length of stay, reoperations, 90-day mortality, anastomotic leakage, anastomotic stenosis, RLN injury, chylothorax, pulmonary complications, delayed gastric emptying	8
					Ivor Lewis	50	46/4	59.3±1.2			
Zhang *et al*., 2018	October 2015 to September 2017	Retrospective cohort	China	81	McKeown	49	26/23	49.41±9.63	Middle and low segments	Duration of surgery, blood loss, examined LN, drainage time, drainage volume, hospital length of stay, anastomotic leakage, anastomotic stenosis, RLN injury, pulmonary infection, delayed gastric emptying	7
					Ivor Lewis	32	17/15	51.76±6.98			

NA, not available; M/F, male/female; SD, standard deviation; LN, lymph nodes; RLN, recurrent laryngeal nerve; ICU, intensive care unit.