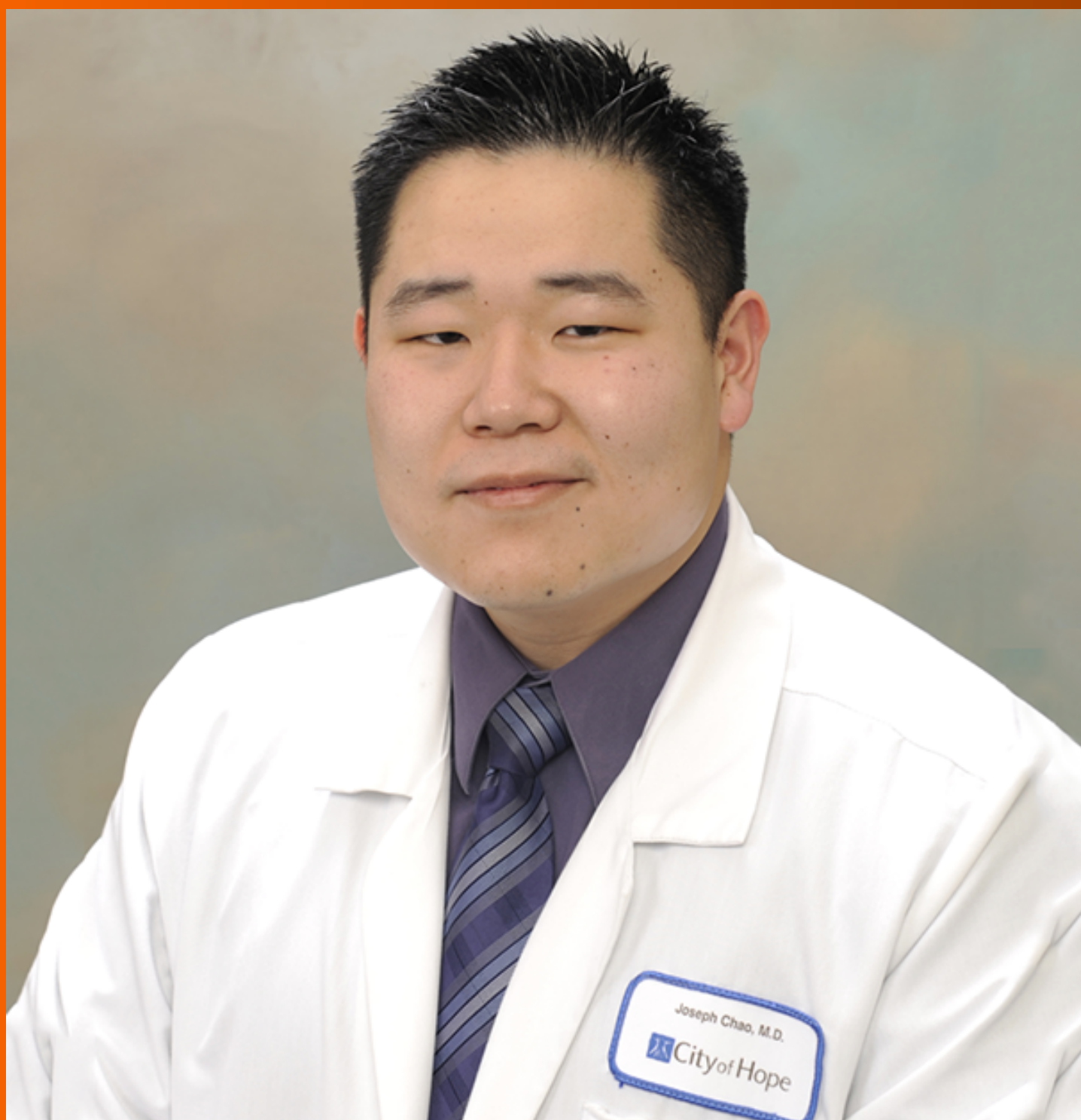


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Efficacy of hybrid minimally invasive esophagectomy vs open esophagectomy for esophageal cancer: A meta-analysis

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Abstract

BACKGROUND

The first line treatment regimen for esophageal cancer is still surgical resection and the choice of surgical scheme depends on surgeon. Now the efficacy comparison of hybrid minimally invasive esophagectomy (HMIE) and open esophagectomy (OE) is still controversial.

AIM

To compare the perioperative and postoperative outcomes of HMIE and OE in patients with esophageal cancer.

METHODS

PubMed, EMBASE, and Cochrane Library databases were searched for related articles. The odds ratio (OR) or standard mean difference (SMD) with a 95% confidence interval (CI) was used to evaluate the effectiveness of HMIE and OE.

RESULTS

Seventeen studies including a total of 2397 patients were selected. HMIE was significantly associated with less blood loss (SMD = -0.43, 95%CI: -0.66, -0.20; $P = 0.0002$) and lower incidence of pulmonary complications (OR = 0.72, 95%CI: 0.57, 0.90; $P = 0.004$). No significant differences were seen in the lymph node yield (SMD = 0.11, 95%CI: -0.08, 0.30; $P = 0.26$), operation time (SMD = 0.24, 95%CI: -0.14, 0.61; $P = 0.22$), total complications rate (OR = 0.68, 95%CI: 0.46, 0.99; $P = 0.05$), cardiac complication rate (OR = 0.91, 95%CI: 0.62, 1.34; $P = 0.64$), anastomotic leak rate (OR = 0.95, 95%CI: 0.67, 1.35; $P = 0.78$), duration of intensive care unit stay (SMD = -0.01, 95%CI: -0.21, 0.19; $P = 0.93$), duration of hospital stay (SMD = -0.13, 95%CI: -0.28, 0.01; $P = 0.08$), and total mortality rates (OR = 0.70, 95%CI: 0.47, 1.06; $P = 0.09$) between the two treatment groups.

CONCLUSION

Compared with the OE, HMIE shows less blood loss and pulmonary

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complications. However, further studies are necessary to evaluate the long-term oncologic outcomes of HMIE.

Key words: Hybrid minimally invasive esophagectomy; Open esophagectomy; Esophageal cancer

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Core tip: In this meta-analysis, hybrid minimally invasive esophagectomy (HMIE) was found to be associated with less blood loss and lower incidence of pulmonary complications compared to conventional open esophagectomy (OE). In the subgroup analysis, patients with HMIE using laparoscopic gastric mobilization-thoracotomy presented less blood loss, shorter hospital stay, lower incidence of total and pulmonary complications than those with OE. No significant difference was observed between the two groups in mortality. In conclusion, our study is the first meta-analysis confirming the priority of HMIE to OE.

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INTRODUCTION

Esophageal cancer is the eighth most common cancer worldwide, with nearly 17000 newly diagnosed cases and 15910 deaths recorded annually in the United States alone^[1]. Despite early diagnosis and advanced therapeutic modalities, including surgical resection, radiotherapy, and chemotherapy, the 5-year overall survival rate is a dismal 15% to 20%^[2]. Esophageal resection remains the major curative and palliative option for dysphagia. For middle- and lower-third esophageal cancer, the abdominal and right thoracic approach is selected due to good loco-regional control. However, post-esophagectomy morbidity and mortality rates are 30%-50% and 2%-10%, respectively^[3], mainly due to endocrinal and metabolic changes. The most frequent complications of esophagectomy are the major pulmonary complications (MPPCs), such as pneumonia and acute respiratory distress syndrome. Almost 50% of the postoperative deaths are attributed to MPPCs, which are indicative of poor prognosis.

Cuschieri *et al*^[4] introduced endoscopic esophagectomy in 1992, which was followed by the development of minimally invasive esophagectomy (MIE), which uses a thoraco-abdominal approach and a combination of laparoscopy, thoracoscopy, and transhiatal laparoscopy. MIE can reduce surgical stress response, decrease blood loss, shorten hospital stay, and lower the incidence of complications^[5-7]. However, only a few randomized controlled trials (RCTs) and low-quality meta-analysis have evaluated its clinical outcomes, in terms of tumor and lymph node clearance, and the safety profile. Hybrid MIE (HMIE) is performed using an Ivor-Lewis procedure, *via* a thoracoscopic-laparotomy and laparoscopic gastric mobilization-thoracotomy, for tumors of the mid-lower esophagus. A three stage McKeown's procedure, with an additional left cervical incision, has been developed for the upper third of the esophagus. Open esophagectomy is performed by starting with an open right thoracotomy to mobilize the esophagus, followed by an open laparotomy to mobilize and pull the stomach to the neck for anastomosis. Therefore, HMIE may improve perioperative outcomes. The aim of this study was to compare the efficacy of open esophagectomy (OE) and HMIE in esophageal cancer patients.

MATERIALS AND METHODS

Literature search

PubMed, EMBASE, and Cochrane Library databases were searched for studies published till February 1, 2019 using the following key words: Open esophagectomy, Hybrid minimally invasive esophagectomy, minimally invasive esophagectomy, and

esophageal cancer. In addition, the reference lists of the eligible studies were manually searched to include additional studies.

Study selection

The inclusion criteria for the studies were as follows: (1) RCTs and non-RCTs; (2) Including patients with esophageal cancer; (3) Comparing the outcomes of OE and HMIE; and (4) Evaluating intraoperative outcomes and postoperative outcomes of both modalities. The exclusion criteria were: (1) In languages other than English; (2) Lacking comparison of OE and HMIE; and (3) Case reports and duplicate publications.

Data extraction

Two authors (Jiao Yang and Ling Chen) evaluated the titles, abstracts, and the reference lists of the publications, and independently extracted the data of intraoperative outcomes (lymph node yield, blood loss, and operative time) and postoperative outcomes (the rates of total complications, pulmonary complications, cardiac complications, and anastomotic leak, the duration of intensive care unit (ICU) stay and hospital stay, and total 30-d and 90-d mortality). Any disagreements were resolved by discussion with a third investigator (Ke Ge). For case-control studies, the Newcastle-Ottawa Quality Assessment Scale was used to assess the quality of the eligible studies, and those with a score ≥ 6 were included. Quality of RCTs was evaluated using the risk bias of Cochrane Collaboration tool.

Statistical analysis

All analyses were performed with the RveMan5.3 tool (Nordic Cochrane Centre, Cochrane Collaboration). Study heterogeneity was assessed using χ^2 and I² tests. A fixed-effects model was used when I² was $< 50\%$ or $P > 0.1$, indicating no significant heterogeneity amongst the studies, and a random-effects model was used when I² was $> 50\%$ or $P < 0.1$. Odds ratio (OR), standard mean difference (SMD), and 95% confidence interval (CI) were used as effect measurements, and $P < 0.05$ was considered statistically significant. Publication bias was evaluated by funnel plots and sensitivity analysis was applied to assess the stability of results.

RESULTS

Characteristics of selected studies

A total of 17 studies, including 2 RCTs^[8,9] and 15 case-control studies^[10-24], were eligible for the meta-analysis. The studies included 2397 esophageal carcinoma patients, of which 1170 received HMIE and 1227 underwent OE. The detailed search strategy is shown in Figure 1. The baseline characteristics and quality of the included studies are summarized in Table 1, Table 2, Table 3, and Table 4.

Intraoperative outcomes

Lymph node yield: Nine studies reported the lymph node yield, with no significant difference between the HMIE with different approaches and OE groups (SMD = 0.11; 95%CI: -0.08, 0.30; $P = 0.26$; Table 5). Since significant heterogeneity (I² = 65% and $P = 0.004$) was observed amongst the studies, a random-effects model was utilized. Then, subgroup analysis was used to compare HMIE with laparoscopy and thoracotomy and OE. Patients with laparoscopy and thoracotomy (HMIE) presented no more lymph node yield compared to those with OE (SMD = 0.19; 95%CI: -0.00, 0.37; $P = 0.05$; Table 5).

Blood loss: Six trials evaluated blood loss, which was also analyzed using the random-effects model due to significant heterogeneity (I² = 58% and $P = 0.04$). HMIE with different strategies resulted in significantly lower blood loss compared to OE (SMD = -0.43; 95%CI: -0.66, -0.20; $P = 0.0002$; Table 5). In the subgroup analysis, HMIE using laparoscopy and thoracotomy showed priority to OE in decreasing the blood loss (SMD = -0.51; 95%CI: -0.74, -0.27; $P < 0.0001$; Table 5).

Operative time: Twelve studies involving 1630 patients recorded the operative time, and displayed significant heterogeneity in the outcome (I² = 92% and $P < 0.00001$). However, HMIE with different approaches or HMIE with laparoscopy and thoracotomy did not significantly decrease the duration of operation (SMD = 0.24; 95%CI: -0.14, 0.61; $P = 0.22$ and SMD = 0.10; 95%CI: -0.33, 0.52; $P = 0.65$, respectively; Table 5).

Postoperative outcomes

Table 1 Baseline characteristics of the eligible studies

Ref.	Time	Design	Area	Male/total		Age		Weight (kg/BMI)	
				HMIE	OE	HMIE	OE	HMIE	OE
Yun <i>et al</i> ^[11]	2017	Retrospective	South Korea	51/53	61/62	66 48-83	68 45-79	NA	NA
Scarpa <i>et al</i> ^[14]	2015	Retrospective	Italy	25/34	27/34	62 52-70	64 56-70	NA	NA
Briez <i>et al</i> ^[13]	2012	Retrospective	France	110/140	117/140	NA	NA	NA	NA
Mariette <i>et al</i> ^[8]	2019	RCT	France	88/103	87/104	59 23-75	62 41-78	26 16-37	25 18-35
Glatz <i>et al</i> ^[15]	2017	Retrospective	Germany	49/60	52/60	61 42-92	61 44-84	27 19-40	26 17-38
Rinieri <i>et al</i> ^[17]	2016	Retrospective	France	59/70	54/70	61.1 ± 9	61 ± 9	NA	NA
Paireder <i>et al</i> ^[9]	2018	RCT	Austria	10/14	10/12	64.5 40-75	62.5 49-77	24.08 18.07-41.45	26.96 17.53-35.26
Rolff <i>et al</i> ^[22]	2017	Retrospective	Denmark	50/56	125/160	66 39-86	65 28-88	25.8 18.8-31.2	26.6 15.6-43.7
Parameswaran <i>et al</i> ^[10]	2013	Prospective	United Kingdom	23/31	15/19	67 48-79	64 51-77	NA	NA
Smithers <i>et al</i> ^[12]	2007	Prospective	Australia	247/309	104/114	64 27-85	62.5 29-81	80 41-132	78.5 40-119
Lee <i>et al</i> ^[16]	2011	Prospective	Taiwan	43/44	61/64	59.7 44-78	56.58 30-90	NA	NA
Findlay <i>et al</i> ^[19]	2016	Retrospective	United States	84/95	69/87	67.76	65.54	NA	NA
Safranek <i>et al</i> ^[20]	2010	Prospective	United Kingdom	28/34	38/46	63 44-76	60 44-77	NA	NA
Shiraishi <i>et al</i> ^[21]	2006	Retrospective	Japan	32/38	31/37	62.1 ± 9	66.5 ± 9.3	NA	NA
Kubo <i>et al</i> ^[23]	2014	Retrospective	Japan	34/42	60/74	65.4 ± 9	62.2 ± 7.2	NA	NA
Yanasoot <i>et al</i> ^[24]	2017	Retrospective	Thailand	13/16	46/54	58.19 ± 7.78	61.02 ± 8.59	NA	NA
Khan <i>et al</i> ^[18]	2017	Retrospective	Pakistan	17/31	52/90	48.7 ± 13.1	56.5 ± 10.7	22.3 15-30.8	21.6 15-35

NA: Not available; HMIE: Hybrid minimally invasive esophagectomy; OE: Open esophagectomy.

Complications: Fourteen trials provided data of the total complications, and showed no significant differences between the HMIE with different approaches group and OE group (OR = 0.68; 95%CI: 0.46, 0.99; $P = 0.05$; Table 6). However, patients with HMIE using laparoscopy and thoracotomy presented less total complications than those with OE (OR = 0.62; 95%CI: 0.41, 0.94; $P = 0.02$; Table 6). Total HMIE and HMIE with laparoscopy and thoracotomy were associated with less pulmonary complications than OE (OR = 0.72; 95%CI: 0.57, 0.90; $P = 0.004$ and OR = 0.69; 95%CI: 0.53, 0.90; $P = 0.005$, respectively; Table 6), whereas the incidences of cardiac complications (OR = 0.91; 95%CI: 0.62, 1.34; $P = 0.64$ and OR = 0.97; 95%CI: 0.65, 1.43; $P = 0.86$, respectively; Table 6) and anastomotic leak (OR = 0.95; 95%CI: 0.67, 1.35; $P = 0.78$ and OR = 0.99; 95%CI: 0.67, 1.46; $P = 0.96$, respectively; Table 6) were similar.

Hospital and ICU stays: Thirteen studies reported duration of hospital stay with significant heterogeneity ($I^2 = 57\%$ and $P = 0.006$), and total HMIE was not associated with significantly reduced duration of hospital stay (SMD = -0.13; 95%CI: -0.28, 0.01; $P = 0.08$; Table 6). However, shorter hospital stay showed in patients with HMIE using laparoscopy and thoracotomy than those with OE (SMD = -0.37; 95%CI: -0.64, -0.09; $P = 0.009$; Table 6).

In addition, the duration of ICU stay was similar in total HMIE or HMIE with laparoscopy and thoracotomy group and OE group (SMD = -0.01; 95%CI: -0.21, 0.19; $P = 0.93$ and SMD = -0.05; 95%CI: -0.37, 0.27; $P = 0.76$, respectively; Table 6).

Mortality: No significant heterogeneity was detected amongst the studies reporting the total, 30-d, and 90-d mortality rates, which were similar in total HMIE or HMIE with laparoscopy and thoracotomy group and OE group (total mortality: OR = 0.70, 95%CI: 0.47, 1.06, $P = 0.09$ and OR = 0.65, 95%CI: 0.4, 1.07, $P = 0.09$, respectively; 30-d mortality: OR = 1.00, 95%CI: 0.45, 2.23, $P = 0.99$ and OR = 1.10, 95%CI: 0.47, 2.59, $P = 0.82$, respectively; 90-d mortality: OR = 0.80, 95%CI: 0.43, 1.48, $P = 0.47$ and OR = 0.80, 95%CI: 0.43, 1.48, $P = 0.47$, respectively; Table 6).

Publication bias: Publication bias was evaluated for the outcomes of pulmonary complications, cardiac complications, anastomotic leak, and total mortality and none was detected (Figure 2).

Sensitivity analysis

We removed any single trial, chose different effect models, and conducted subgroup analysis, and the outcomes presented no significant changes, suggesting that the results were stable.

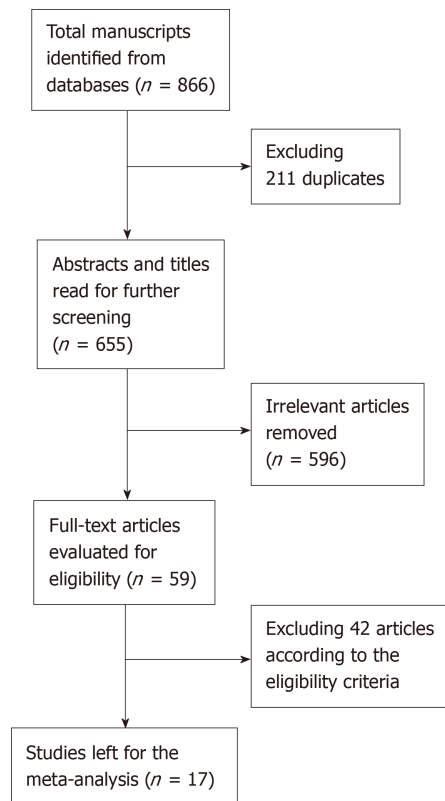


Figure 1 Flow diagram showing the selection process of relevant literature.

DISCUSSION

Esophageal cancer is the sixth leading cause of cancer-related deaths worldwide. Surgical resection is the first line of treatment, and includes OE, total MIE, and HMIE. Depending on the surgeon and the hospital, the choice and sequence of surgical approaches differ significantly (transthoracic *vs* transhiatal, intrathoracic *vs* cervical anastomosis, and the degree of lymphadenectomy). OE is associated with a significantly higher risk of surgical trauma, as well as higher morbidity and mortality compared to other surgeries^[25]. Sunpaweravong *et al.*^[25] conducted a meta-analysis to compare the efficacy of OE and MIE, and found that MIE resulted in fewer perioperative complications and less mortality. In addition, patients with MIE had better quality of life scores compared to those with OE in the global health, pain, and physical activity domains^[26]. Therefore, total MIE would be the ideal choice. But the technical difficulties, the long learning curve, and low reproducibility of the anastomosis limit its use. HMIE has a shorter learning curve while sharing the advantages of MIE. The transition from OE to HMIE may be acceptable. The above information of MIE does not distinguish between the total MIE and HMIE approaches, so whether HMIE is prior to OE is still controversial. In this meta-analysis, we first compared the intraoperative and postoperative outcomes of HMIE and OE in patients with esophageal cancer.

Many studies show that radical lymph node resection and greater extent of lymphadenectomy are closely associated with higher survival rates^[27-30]. In this study, there was no significant difference in terms of the number of harvested lymph nodes between total HMIE and OE groups, which is consistent with a previous RCT^[8]. But there was a trend for patients with HMIE using laparoscopy and thoracotomy with a high rate of lymphadenectomy. Some studies once reported a higher or lower number of lymph nodes harvested in MIE group^[31,32]. Those discrepancies may be explained by the inconsistency of Current Procedure Terminology codes reported by the operating surgeons.

Smithers *et al.*^[12] reported that patients who underwent HMIE had less blood loss than those undergoing OE, while Yanasoot *et al.*^[24] showed no significant difference. In our meta-analysis also, the total HMIE group and the HMIE with laparoscopy and thoracotomy group had less blood loss, which could be attributed to the relatively minimal trauma in HMIE.

Studies also report a longer operative duration of MIE compared to OE^[33-35], which

Table 2 Baseline characteristics

Ref.	Tumor location		Histological subtype		Pathological stage		ASA risk score	
	Upper/Middle/ Lower		ACA/SCC		0-I-II/ III-IV		1/2/3	
	HMIE	OE	HMIE	OE	HMIE	OE	HMIE	OE
Yun <i>et al</i> ^[11]	0/18/35	0/18/44	NA	NA	48/5	45/17	NA	NA
Scarpa <i>et al</i> ^[14]	0/25/9	0/29/5	24/10	24/10	29/5	29/5	5/22/7	4/17/13
Briez <i>et al</i> ^[13]	0/54/86	0/56/84	57/83	57/83	92/48	89/51	20/102/18	22/94/24
Mariette <i>et al</i> ^[8]	0/32/71	1/31/72	57/46	66/38	48/50	52/48	25/61/17	34/58/12
Glatz <i>et al</i> ^[15]	0/8/52	0/8/52	46/14	47/13	44/15	41/19	NA	NA
Rinieri <i>et al</i> ^[17]	60/10/0	63/7/0	50/20	55/15	52/18	49/21	9/48/13	14/40/16
Paireder <i>et al</i> ^[9]	NA	NA	10/4	11/1	7/7	8/4	NA	NA
Rolff <i>et al</i> ^[22]	NA	NA	NA	NA	NA	NA	17/28/12	41/80/39
Parameswaran <i>et al</i> ^[10]	NA	NA	27/3	16/3	18/31	8/11	NA	NA
Smithers <i>et al</i> ^[12]	8/68/208	0/3/47	199/74	100/7	183/108	36/75	12/200/98	6/68/38
Lee <i>et al</i> ^[16]	2/34/8	9/46/9	1/43	5/59	39/6	49/15	NA	NA
Findlay <i>et al</i> ^[19]	NA	NA	NA	NA	NA	NA	NA	NA
Safranek <i>et al</i> ^[20]	0/1/24	0/1/20	29/3	43/3	18/16	17/29	NA	NA
Shiraishi <i>et al</i> ^[21]	NA	NA	NA	NA	NA	NA	NA	NA
Kubo <i>et al</i> ^[23]	8/21/13	3/36/34	NA	NA	28/14	41/33	NA	NA
Yanasoot <i>et al</i> ^[24]	2/8/6	11/28/15	1/15	5/49	6/10	19/35	NA	A
Khan <i>et al</i> ^[18]	NA	NA	28/3	65/25	4/91	5/83	NA	NA

NA: Not available; ACA: Adenocarcinoma; SCC: Squamous cell carcinoma; ASA: American Society of Anesthesiologists; HMIE: Hybrid minimally invasive esophagectomy; OE: Open esophagectomy.

can result in atelectasis and pneumonia. In our meta-analysis, the operative time was similar for both surgeries.

Postoperative complications, especially pulmonary complications, significantly influence the survival of esophageal cancer patients. The incidences of total complications in patients with total HMIE and OE were 50.2% and 60.1%, respectively, although the lower occurrence after HMIE was not statistically significant. In the subgroup analysis, HMIE with laparoscopy and thoracotomy could largely lower the incidence of total complications than OE (46.55% vs 57.74%). The TIME trial showed that MIE resulted in a 70% lower incidence of pneumonia at 2 weeks post-surgery compared to OE^[36], which is consistent with our slightly higher incidence of pulmonary complications in OE compared to total HMIE or HMIE with laparoscopy and thoracotomy (25.37% vs 32.08% or 24.59% vs 31.23%). In contrast, the incidence of cardiac complications and anastomotic leak was not affected by the type of surgery.

Less pulmonary complications in the total HMIE group did not translate into a significant reduction in the duration of ICU and hospital stay. But HMIE with laparoscopy and thoracotomy presented a more reduction in the duration of hospital stay on the basis of its lower total complications and pulmonary complications.

Some studies indicate that the prolonged survival associated with HMIE is due to the lower incidence of postoperative complications^[37-39]. In our meta-analysis, the overall, 30-d, and 90-d mortality rates in the total HMIE group were 4.16%, 2.52%, and 4.00%, respectively vs 6.02%, 2.40%, and 4.70% in the OE group, indicating a lack of short-term survival benefit with total HMIE. Patients with HMIE using laparoscopy and thoracotomy presented no priority in short-term survival compared to those with OE. Wang *et al* reported that 6-year overall survival and disease-free survival were 44.7% and 46.1%, respectively, for MIE, indicating that MIE is safe^[40]. A score-matched study showed that the 2-year overall survival rates based on same pathologic stage were similar between MIE and OE^[41]. But further studies are still needed to clarify the long-term survival outcomes.

Our study has several limitations that need to be addressed. First, only two out of the 17 studies were RCTs and the remaining were case-control studies which might have influenced the reliability of the results, although they were consistent with that of one eligible RCT. Second, the studies had variable follow-up duration, neoadjuvant chemoradiotherapy, operating surgeons, pathological stages, histological types and

Table 3 Quality assessment of the eligible studies: Newcastle-Ottawa Scale for case control studies

Ref.	Selection				Comparability	Exposure		Total Score
	1	2	3	4	5	6	7 8	
Parameswaran <i>et al</i> ^[10]	Y	Y	Y	Y	Y	Y	Y Y	8
Yun <i>et al</i> ^[11]	Y	Y	Y	Y	Y	Y		6
Smithers <i>et al</i> ^[12]	Y	Y	Y	Y	Y	Y	Y	7
Briez <i>et al</i> ^[13]	Y	Y	Y	Y	Y	Y	Y	7
Scarpa <i>et al</i> ^[14]	Y	Y	Y	Y	Y	Y		6
Glatz <i>et al</i> ^[15]	Y	Y	Y	Y	Y	Y		6
Lee <i>et al</i> ^[16]	Y	Y	Y	Y	Y	Y	Y	7
Rinieri <i>et al</i> ^[17]	Y	Y	Y	Y	Y	Y	Y	7
Khan <i>et al</i> ^[18]	Y	Y	Y	Y	Y	Y		6
Findlay <i>et al</i> ^[19]	Y	Y	Y	Y	Y	Y	Y	7
Safranek <i>et al</i> ^[20]	Y	Y	Y	Y	Y	Y		6
Shiraishi <i>et al</i> ^[21]	Y	Y	Y	Y	Y	Y		6
Rolff <i>et al</i> ^[22]	Y	Y	Y	Y	Y	Y		6
Yanasoot <i>et al</i> ^[24]	Y	Y	Y	Y	Y	Y		6
Kubo <i>et al</i> ^[23]	Y	Y	Y	Y	Y	Y		6

1: Is the case definition adequate; 2: Representativeness of the cases; 3: Selection of controls; 4: Definition of controls; 5: Comparability of cases and controls on the basis of the design or analysis; 6: Assessment of exposure; 7: Same method of ascertainment for cases and controls; 8: Non-response rate; Y: Yes.

location of the tumor, and baseline characteristics of the recruited population. Third, the meta-analysis did not compare the long-term oncological outcomes between HMIE and OE. Last but not the least, we made subgroup analysis between HMIE with laparoscopy and thoracotomy and OE group. But the information associated with HMIE using thoracoscopic-laparotomy approach is little and ambiguous. Therefore, the real impact of laparoscopy compared to thoracoscopy is unclear, and data that can confirm which part of esophagectomy would play an important role in MIE is lacking.

Taken together, HMIE, especially HMIE with laparoscopy and thoracotomy, has the advantages of reduced blood loss and lower incidence of pulmonary complications compared to OE for patients with esophageal cancer. However, there is no significant difference in overall survival in the two groups. These findings should be explained with caution because our study doesn't provide the data associated with cancer-specific survival and recurrence.

Table 4 Quality assessment of the eligible studies: Risk bias of Cochrane Collaboration tool for randomized controlled trials

Ref.	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Paireder <i>et al</i> ^[9]	Low risk	High risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk
Mariette <i>et al</i> ^[8]	Low risk	Low risk	Low risk	High risk	Unclear risk	Unclear risk	Unclear risk

Table 5 Comparison of perioperative outcomes between hybrid minimally invasive esophagectomy and open esophagectomy groups

Perioperative outcomes	SMD and 95%CI	P value
Lymph node yield	Total HMIE <i>vs</i> OE	0.11 (-0.08, 0.30)
	HMIE with A <i>vs</i> OE	0.19 (-0.00, 0.37)
Blood loss	Total HMIE <i>vs</i> OE	-0.43 (-0.66, -0.20)
	HMIE with A <i>vs</i> OE	-0.51 (-0.74, -0.27)
Operative time	Total HMIE <i>vs</i> OE	0.24 (-0.14, 0.61)
	HMIE with A <i>vs</i> OE	0.1 (-0.33, 0.52)

A: Laparoscopy and thoracotomy; SMD: Standard mean difference; CI: Confidence interval; HMIE; Hybrid minimally invasive esophagectomy; OE: Open esophagectomy.

Table 6 Postoperative outcomes between hybrid minimally invasive esophagectomy group and open esophagectomy groups

Postoperative outcomes	OR or SMD, 95%CI	P value
ICU stay	Total HMIE <i>vs</i> OE	-0.01 (-0.21, 0.19)
	HMIE with A <i>vs</i> OE	-0.05 (-0.37, 0.27)
Hospital stay	Total HMIE <i>vs</i> OE	-0.13 (-0.28, 0.01)
	HMIE with A <i>vs</i> OE	-0.37 (-0.64, -0.09)
Total complications	Total HMIE <i>vs</i> OE	0.68 (0.46, 0.99)
	HMIE with A <i>vs</i> OE	0.62 (0.41, 0.94)
Pulmonary complications	Total HMIE <i>vs</i> OE	0.72 (0.57, 0.90)
	HMIE with A <i>vs</i> OE	0.69 (0.53, 0.90)
Cardiac complications	Total HMIE <i>vs</i> OE	0.91 (0.62, 1.34)
	HMIE with A <i>vs</i> OE	0.97 (0.65, 1.43)
Anastomotic leak	Total HMIE <i>vs</i> OE	0.95 (0.67, 1.35)
	HMIE with A <i>vs</i> OE	0.99 (0.67, 1.46)
Total mortality	Total HMIE <i>vs</i> OE	0.7 (0.47, 1.06)
	HMIE with A <i>vs</i> OE	0.65 (0.4, 1.07)
30-d mortality	Total HMIE <i>vs</i> OE	1.00 (0.45, 2.23)
	HMIE with A <i>vs</i> OE	1.10 (0.47, 2.59)
90-d mortality	Total HMIE <i>vs</i> OE	0.80 (0.43, 1.48)
	HMIE with A <i>vs</i> OE	0.80 (0.43, 1.48)

A: Laparoscopy and thoracotomy; OR: Odds ratio; SMD: Standard mean difference; CI: Confidence interval; ICU: Intensive care unit; HMIE; Hybrid minimally invasive esophagectomy; OE: Open esophagectomy.

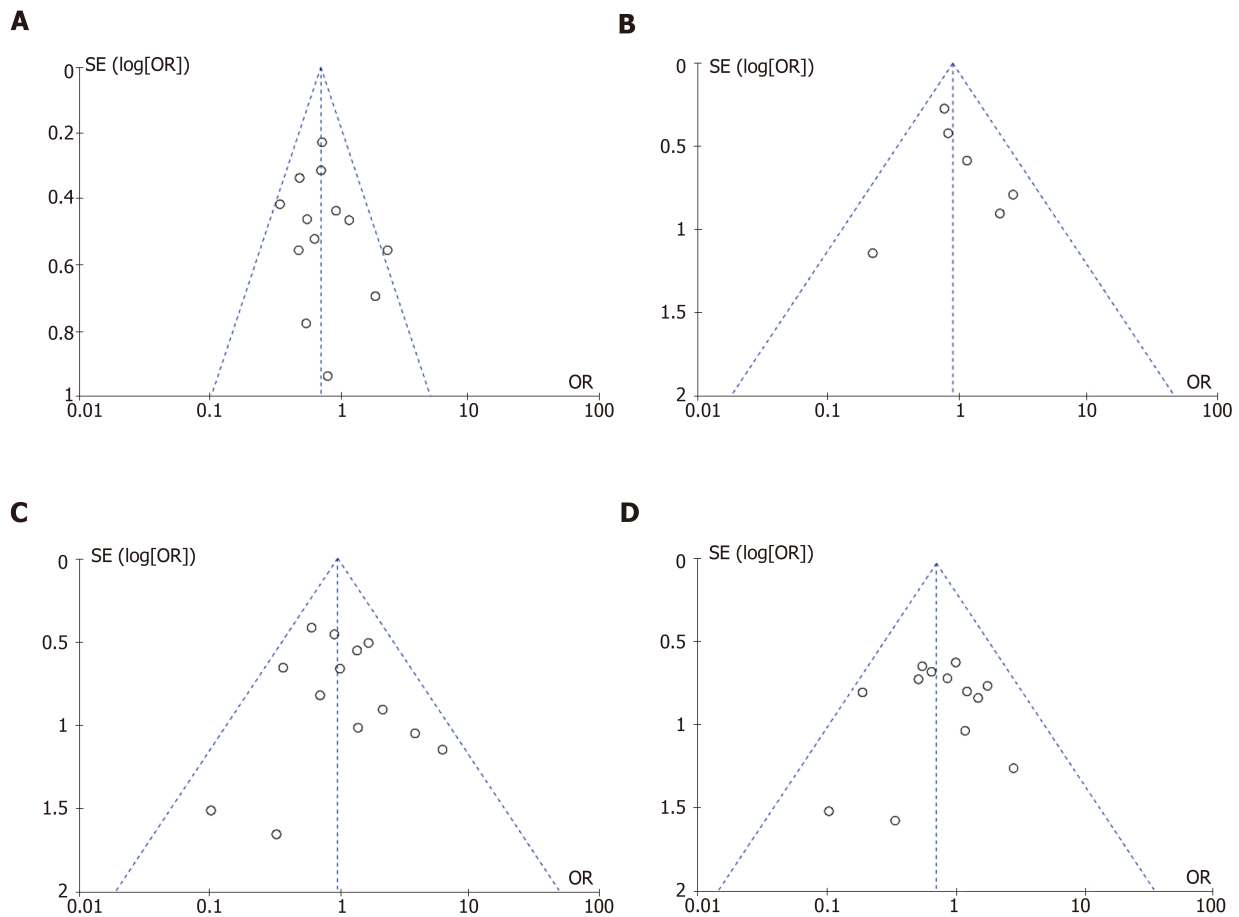


Figure 2 Funnel plots of eligible studies. A: Incidence of pulmonary complications; B: Incidence of cardiac complications; C: Incidence of anastomotic leak; D: Total mortality.

ARTICLE HIGHLIGHTS

Research background

The first line treatment regimen for esophageal cancer is still surgical resection and the choice of surgical scheme depends on the surgeon.

Research motivation

Now the efficacy comparison of hybrid minimally invasive esophagectomy (HMIE) and open esophagectomy (OE) is still controversial.

Research objectives

To compare the perioperative and postoperative outcomes of HMIE and OE in patients with esophageal cancer.

Research methods

PubMed, EMBASE, and Cochrane Library databases were searched for related articles.

Research results

Seventeen studies including a total of 2397 patients were selected. HMIE was significantly associated with less blood loss (SMD = -0.43, 95%CI: -0.66, -0.20; $P = 0.0002$) and lower incidence of pulmonary complications (OR = 0.72, 95%CI: 0.57, 0.90; $P = 0.004$).

Research conclusions

Compared with OE, HMIE shows less blood loss and pulmonary complications.

Research perspectives

Further studies are necessary to evaluate the long-term oncologic outcomes of HMIE.

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