Comparisons of minimally invasive esophagectomy and open esophagectomy in lymph node metastasis/dissection for thoracic esophageal cancer

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Abstract

Background: The study aimed to clarify the characteristics of lymph node metastasis (LNM) and to compare the oncologic outcomes of minimally invasive esophagectomy (MIE) with open esophagectomy (OE) in terms of lymph node dissection (LND) in thoracic esophageal cancer patients.

Methods: The data from esophageal cancer patients who underwent MIE or OE from January 2016 to January 2019 were retrospectively reviewed. The characteristics of LNM in thoracic esophageal cancer were discussed, and the differences in numbers of LND, LND rate, and LNM rate/degree of upper mediastinum between MIE and OE were compared.

Results: For overall characteristics of LNM in 249 included patients, the highest rate of LNM was found in upper mediastinum, while LNM rate in middle and lower mediastinum, and abdomen increased with the tumor site moving down. The patients were divided into MIE ($n = 204$) and OE groups ($n = 45$). In terms of number of LND, there were significant differences in upper mediastinum between MIE and OE groups (8 [5, 11] *vs.* 5 [3, 8], $P < 0.001$). The comparative analysis of regional lymph node showed there was no significant difference except the subgroup of upper mediastinal 2L and 4L group (3 [1, 5] *vs.* 0 [0, 2], $P < 0.001$ and 0 [0, 2] *vs.* 0, $P = 0.012$, respectively). Meanwhile, there was no significant difference in terms of LND rate except 2L (89.7% [183/204] *vs.* 71.1% [32/45], $P = 0.001$) and 4L (41.2% [84/204] *vs.* 22.2% [10/45], $P = 0.018$) groups. For LNM rate of T3 stage, there was no significant difference between MIE and OE groups, and the comparative analysis of regional lymph node showed that there was no significant difference except 2L group (11.1% [5/45] *vs.* 38.1% [8/21], $P = 0.025$). The LNM degree of OE group was significantly higher than that of MIE group (27.2% [47/173] *vs.* 7.6% [32/419], $P < 0.001$), and the comparative analysis of regional LNM degree showed that there was no significant difference except 2L (34.7% [17/49] *vs.* 7.7% [13/169], $P < 0.001$) and 4L (23.8% [5/21] *vs.* 3.9% [2/51], $P = 0.031$) subgroups.

Conclusion: MIE may have an advantage in LND of upper mediastinum 2L and 4L groups, while it was similar to OE in other stations of LND.

Keywords: Esophageal neoplasms; Lymph node; Minimally invasive esophagectomy; Open esophagectomy

Introduction

Cancer is the leading cause of deaths in China, seriously threatening human health and life expectancy.[1,2] Esophageal cancer is a common malignancy of the digestive tract with family clustering.[3] A high incidence of esophageal cancer has been reported in China, especially in Henan province among the highest mortality in the world.[4] Esophageal cancer can be divided into cervical and thoracic esophageal cancers according to tumor sites.[5,6] Cancer cases coded as thoracic esophagus include upper, middle, and lower esophageal carcinoma, and the carcinomas were predominantly located in the middle thoracic esophagus (51.6%).[7,8] Minimal invasive esophagectomy (MIE) and open esophagectomy (OE) are the main treatment methods for esophageal cancer.[9,10] Clinically, the surgical approaches include left thoracotomy (Sweet), right thoracotomy (McKeown or Ivor–Lewis), and transmediastinal and esophageal hiatus approaches.[11] The surgical treatment for esophageal cancer is relatively complicated, due to the special anatomical position of esophagus.[12] The potential advantage of MIE is the avoidance of thoracotomy, thus causing less surgical access-related trauma.

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Existing literature has shown that right/left thoracotomy approach has significant advantages in improving prognosis and long-term survival rate of esophageal cancer patients.[13-15] However, the 5-year overall survival rate of patients with esophageal cancer worldwide is still less than 20%,[16] which gradually decreases with the increasing of number and metastasis range of lymph nodes.[17,18] Therefore, reasonable lymph node dissection (LND) is very critical for long-term prognosis of esophageal cancer patients. Recently, despite many studies having made comparison between MIE and OE,[19] there are few reports on the characteristics of lymph node metastasis (LNM) and regional LND.

According to the standard of esophageal lymph node grouping formulated by American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC),[20] this study aimed to clarify the characteristics of LNM and to compare the outcomes of MIE with OE (McKeown or Ivor–Lewis) in terms of LND in thoracic esophageal cancer patients. This comparative study is expected to provide better guidance and a clearer set of objectives for LND in surgical treatment of esophageal cancer, so as to achieve a better survival prognosis.

Methods

Ethical approval

This study was approved by the Ethics Committee of the Fourth Hospital of Hebei Medical University hospital (No. 2020K-1183). Written informed consent was obtained from all patients.

Patients

A total of 427 primary thoracic esophageal cancer patients who underwent radical surgery from January 2016 to January 2019 in our hospital were retrospectively reviewed. Inclusion criteria were: (1) patients with complete clinical data; (2) tumors located in thoracic segment, no other malignancies history; (3) patients not received neoadjuvant therapies (including neoadjuvant chemotherapy, radiotherapy and other anti-tumor therapy) before surgery; (4) patients underwent OE (McKeown or Ivor–Lewis) or MIE; (5) patients underwent at least two regional (thoraco-abdominal) LND; (6) no distant metastasis detected by preoperative CT and other examinations; and (7) postoperative pathology confirmed R0 resection. Patients with multiple esophageal cancers, or postoperative pathology predicting positive resection margins were excluded. Then they were divided into two groups according to surgical methods: MIE and OE groups.

Surgical protocols

Preoperative preparation was the same for both groups. 150 mL olive oil was orally administered 4 to 8 h before surgery. The stomach was empty, and antibiotics were given 30 min before surgery to prevent infection. Intravenous-inhalation combined anesthesia was performed. The tri-incisional approach (McKeown) was adopted as the surgical approach for MIE with thoracoscope and laparoscope. The McKeown or Ivor–Lewis approach was used for OE, and the thoraco-abdominal two-field LND was required for both approaches.[21] All operations were performed by the same thoracic surgery team, avoiding the selection deviation caused by different surgeons' technology and experience. They are well-known experts in the industry, and have completed the surgical demonstration of esophageal cancer in provincial and domestic large conferences for many times, and their surgical technology has been unanimously recognized by the industry's peer experts.

Clinical evaluation

The invasion depth of postoperative pathological T stages and lymph node grouping criteria were according to the 8th edition of Tumor, Node, and Metastasis (TNM) staging standard of UICC and AJCC:[20] (1) LND rate = the number of cases of LND in each lymph node group/the total number of cases × 100%, to evaluate the degree and effect of LND; (2) LNM degree = the number of positive lymph nodes in each lymph node group/the total number of LND in this group × 100%, to evaluate the degree of LNM; and (3) LNM rate = the number of cases with LNM in each lymph node group/the total number of cases × 100%, to evaluate the probability of LNM in each lymph node group. Standards for grouping and subregion of lymph nodes are shown in Table 1.

Statistical analysis

All statistical analyses were performed with SPSS version 22 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as median (interquartile range). Mann–Whitney *U* test was used for continuous variables that did not meet a normal distribution. Comparison among groups was conducted by Student's *t*-test, and comparisons of categorical variables and sample composition ratio were conducted by chi-squared test or Fisher's exact test. $P < 0.05$ was considered statistically significant.

Results

Patients

A total of 249 patients were included and divided into MIE group ($n = 204$) and OE group ($n = 45$) [Figure 1]. There was no statistically significant difference in age, gender, body mass index (BMI), tumor sites (except middle thoracic), and LNM rates between the two groups [Table 2]. In thoracic upper, middle, and lower esophageal cancer, the differences in LNM rate among upper, middle, lower mediastinum and abdomen were all statistically significant ($P < 0.001$, $P < 0.001$, and $P = 0.019$, respectively; Table 3). LNM rate of upper mediastinum was the highest, while there was no statistically significant difference in tumor site ($P = 0.848$), indicating that LNM was not related to tumor location. The LNM rates of middle and lower mediastinum and abdomen were all increased with the

Table 1: Lymph nodes grouping and sub-regional standards in esophageal cancer.

Region	Group	Description
Upper mediastinum	2R	Lymph nodes near upper-right trachea
	2L	Lymph nodes near upper-left trachea
	8U	Lymph nodes near upper thoracic esophagus
	4R	Lymph nodes near bottom-right trachea
	4L	Lymph nodes near bottom-left trachea
	5	Lymph nodes under aortic arch
	6	Lymph nodes near anterior mediastinum
Middle mediastinum	7	Lymph nodes under the carina
	8M	Lymph nodes near middle thoracic esophagus
	10R	Lymph nodes near right tracheal bronchus
	10L	Lymph nodes near left tracheal bronchus
Lower mediastinum	$8L_0$	Lymph nodes near lower thoracic esophagus
	9L/R	Lymph nodes near lower pulmonary ligament
	15	Lymph nodes near diaphragm
Abdominal region	16	Lymph nodes near cardia
	17	Lymph nodes near left side of stomach
	18	Common hepatic artery lymph nodes
	19	Splenic lymph nodes
	20	Celiac lymph nodes

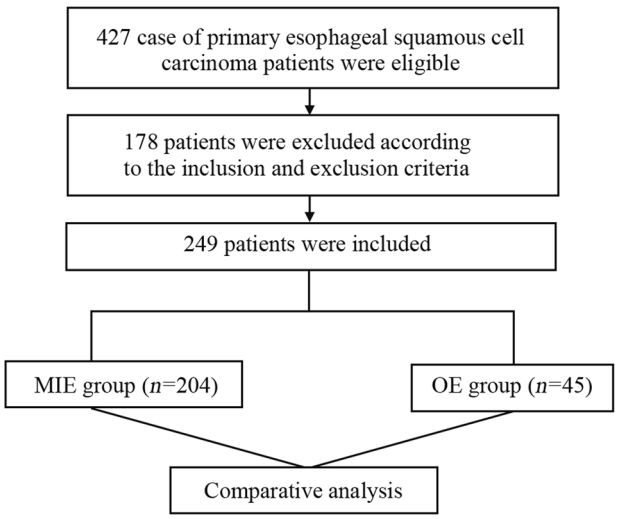

Figure 1: Patients selection for the comparisons of minimally invasive esophagectomy and open esophagectomy in lymph node metastasis/dissection for thoracic esophageal cancer.

tumor location moving down, showing significant differences ($P = 0.032$, $P = 0.019$, and $P < 0.001$, respectively) [Table 4].

LND of the two groups

There was significant difference in the total number of LND between MIE and OE groups (23 [18, 29] *vs.*19 [16, 25], $P = 0.008$) [Table 5]. The analysis of regional LND suggested significant differences in the number of upper mediastinal LND between the two groups (8 [5, 11] *vs.* 5 [3, 8], $P < 0.001$) [Table 5]. Furthermore, the subgroups of upper mediastinal (2R, 2L, 8U, 4R, and 4L) were stratified according to UICC lymph node grouping, and the results showed there were no significant differences in the number of LND between the two groups, except 2L and 4L subgroup (3 [1, 5] *vs.* 0 [0, 2], $P < 0.001$ and 0 [0, 2] *vs.* 0 [0, 0], $P = 0.012$, respectively) [Table 5]. In terms of LND rate in upper mediastinum, there were significant differences in 2L and 4L subgroups when comparing MIE and OE groups (89.7% [183/204] *vs.* 71.1% [32/45], $P = 0.001$; 41.2% [84/204] *vs.* 22.2% [10/45], $P = 0.018$, respectively) [Table 6].

Comparison of LNM rate and degree in the mediastinal region between MIE and OE groups with T3 middle esophageal carcinoma

In terms of LNM rate, there was no significant difference in the overall LNM rate of the upper mediastinum between MIE and OE groups (40.0% [18/45] *vs.* 61.9% [13/21], $P = 0.097$) [Table 7]. However, further stratification showed that there were significant differences in LNM rate of respective 2L groups in MIE and OE groups (11.1% [5/45] *vs.* 38.1% [8/21], $P = 0.025$). The overall LNM degree in upper mediastinum of OE group was significantly higher than that of MIE group (27.2% [47/173] *vs.* 7.6% [32/419], $P < 0.001$). The LNM degree of the respective 2L and 4L subgroups in MIE and OE groups was statistically significantly different (7.7% [13/169] *vs.* 34.7% [17/49], $P < 0.001$ and 3.9% [2/51] *vs.* 23.8% [5/21], $P = 0.031$, respectively) [Table 7].

Discussion

The incidence and mortality of esophageal cancer are high, with approximately 590,000 new cases and 548,000 deaths worldwide annually.[8,22] Radical surgical resection combined with systematic LND can not only remove tumor, but also prevent or reduce tumor recurrence and prolong survival of patients.[23,24] Traditional open surgeries have been widely recognized and applied in clinical practice.[19,25] Following the

Table 2: Characteristics of the MIE and OE groups of esophageal cancer.

Characteristic	MIE ($n = 204$)	OE ($n = 45$)	Statistics	*P*-value
Age (years)	62.8 ± 7.3	62.0 ± 8.1	0.59	0.557*
Gender (male/female)	137/67	35/10	1.95	0.163†
BMI (kg/cm^2)	23.34 ± 3.01	23.45 ± 3.10	0.21	0.833*
T stage			13.67	0.009‡
T1a	5 (2.5)	0		
T1b	53 (26.0)	7 (15.6)		
T2	29 (14.2)	1 (2.2)		
T3	105 (51.5)	30 (66.7)		
T4	12 (5.9)	7 (15.6)		
Tumor site			5.21	0.074†
Upper thoracic	33 (16.2)	4 (8.9)		
Middle thoracic	98 (48.0)	30 (66.7)		
Lower thoracic	73 (35.8)	11 (24.4)		
LNM			1.56	0.211†
Yes	106 (52.0)	28 (62.2)		
No	98 (48.0)	17 (37.8)		
ASA classification			5.59	0.094‡
1	1	1		
2	196	40		
3	6	4		
4	1	0		
NACT (yes/no)	21/183	8/37	2.01	0.157†
Co-existent diseases			1.66	0.678‡
Hypertension	59	18		
Diabetes	16	3		
Coronary heart disease	3	2		
Old cerebral infarction	4	1		

* Student's *t* test. † The chi-squared test. ‡ Fisher's exact test. Data are expressed as *n*, *n* (%), mean ± standard deviation. ASA: American Society of Anesthesiologists; BMI: Body mass index; LNM: Lymph node metastatic; MIE: Minimal invasive esophagectomy; NACT: Neo-adjuvant chemotherapy; OE: Open esophagectomy.

Table 3: Comparison of lymph node metastasis rates in different region of esophageal cancer, *n* (%).

Region	Upper mediastinum	Middle mediastinum	Lower mediastinum	Abdomen	χ^2	*P*-value
Upper thoracic ($n = 37$)					41.0	<0.001
Metastasis	17 (45.9)	2 (5.4)	1 (2.7)	1 (2.7)		
Not metastasis	20 (54.1)	35 (94.6)	36 (97.3)	36 (97.3)		
Middle thoracic ($n = 128$)					33.63	<0.001
Metastasis	53 (41.4)	27 (21.1)	14 (10.9)	30 (23.4)		
Not metastasis	75 (58.6)	101 (78.9)	114 (89.1)	98 (76.6)		
Lower thoracic ($n = 84$)					9.90	0.019
Metastasis	34 (40.5)	22 (26.2)	17 (20.2)	30 (35.7)		
Not metastasis	50 (59.5)	62 (73.8)	67 (79.8)	54 (64.3)		

progress and development of surgical techniques, the therapeutic protocols for esophageal cancer patients are diversified. Since the end of 20th century, MIE has been recognized by many scholars. Subsequently, thoracoscopy and laparoscopy have been applied in esophageal cancer surgery.[26] Every innovation and progress of esophageal surgery is closely related to LND. Presently, there are still some fundamental issues to be further explored, and one of them is the regularity and characteristics of LNM.

Analysis on different areas of LND suggested that the LNM rate of esophageal cancer in the middle and lower mediastinum and abdominal regions showed an increasing trend with the tumor location moving downward. However, the LNM rate of upper mediastinal did not significantly decrease, but was significantly higher than that in other regions. Tachimori *et al*[27] have reported that among patients with thoracic esophageal cancer, the upper mediastinum had the highest (51.1%) LNM rate, and our study has drawn a similar conclusion. This result is also consistent with the characteristics of esophageal LNM, that is, esophageal lymphatics crisscross in the mucosa and submucosa, and the longitudinal lymphatics are six times larger than the transverse lymphatics. The longitudinal lymphatics can not only directly penetrate the esophageal

Table 4: Comparison of lymph node metastasis rates in different tumor sites of esophageal cancer, *n* (%).

Region	Upper thoracic ($n=37$)	Middle thoracic ($n=128$)	Lower thoracic ($n=84$)	χ^2	*P*-value
Upper mediastinum					
Metastasis	17 (45.9)	53 (41.4)	34 (40.5)	0.33	0.848
Not metastasis	20 (54.1)	75 (58.6)	50 (59.5)		
Middle mediastinum					
Metastasis	2 (5.4)	27 (21.1)	22 (26.2)	6.87	0.032
Not metastasis	35 (94.6)	101 (78.9)	62 (73.8)		
Lower mediastinum					
Metastasis	1 (2.7)	14 (10.9)	17 (20.2)	7.91	0.019
Not metastasis	36 (97.3)	114 (89.1)	67 (79.8)		
Abdomen					
Metastasis	1 (2.7)	30 (23.4)	30 (35.7)	15.29	<0.001
Not metastasis	36 (97.3)	98 (76.6)	54 (64.3)		

Table 5: Comparison of the number of lymph nodes dissection in different groups of esophageal cancer.

Region	MIE ($n=204$)	OE ($n=45$)	*Z*-value	*P*-value
Total	23 (18, 29)	19 (16, 25)	−2.651	0.008
Lymph nodes regions				
Upper mediastinum	8 (5, 11)	5 (3, 8)	−4.220	<0.001
Middle mediastinum	5 (3, 7)	5 (3, 7)	−0.321	0.748
Lower mediastinum	2 (1, 4)	2 (0, 4)	−1.321	0.186
Abdomen	6 (3, 10)	6 (3, 9)	−0.026	0.979
Upper mediastinum				
2R	3 (2, 5)	3 (2, 4)	−0.535	0.593
2L	3 (1, 5)	0 (0, 2)	−6.092	<0.001
8U	0 (0, 1)	0 (0, 1)	−0.657	0.511
4R	0 (0, 0)	0 (0, 0)	−1.281	0.200
4L	0 (0, 2)	0 (0, 0)	−2.524	0.012

Data were expressed as median (Q_1, Q_3). Lymph node grouping criteria were made according to the 8th edition TNM staging standard of the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC). MIE: Minimal invasive esophagectomy; OE: Open esophagectomy; TNM staging: Tumor, Node and Metastasis staging.

Table 6: Comparative analysis of lymph node dissection rate in upper mediastinum of esophageal cancer.

Group	MIE ($n=204$)	OE ($n=45$)	χ^2	*P*-value
2R	193 (94.6)	42 (93.3)	0.01	1.000
2L	183 (89.7)	32 (71.1)	10.81	0.001
8U	66 (32.4)	12 (26.7)	0.55	0.457
4R	19 (9.3)	6 (13.3)	0.29	0.591
4L	84 (41.2)	10 (22.2)	5.64	0.018

Lymph node grouping criteria were made according to the 8th edition TNM staging standard of the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC). MIE: Minimal invasive esophagectomy; OE: Open esophagectomy; TNM staging: Tumor, Node and Metastasis staging.

wall to the nearby regional lymph nodes, but also metastasize to the cervical or abdominal regional lymph nodes along the esophageal longitudinal direction. This metastasizing pattern makes it difficult to predict regional LNM by tumor location and invasion depth. In addition, this study showed that the upper mediastinal LNM rate of esophageal cancer in lower thorax was as high as 40.5% [34/84], which might be related to the regularity of lymphatic reflux. Most intrathoracic lymph nodes reflux into the thoracic duct and finally into the vein angle, which may significantly increase the probability of cancer cells' metastasis into the upper mediastinum. The above two characteristics of LNM in esophageal cancer suggests that lymph nodes of thoracic and abdominal areas in thoracic esophageal cancer should be dissected systematically and comprehensively, especially in the upper mediastinum to reduce the possibility of local recurrence and metastasis after esophagectomy.

Regarding to the comparison between MIE and traditional OE, previous studies mainly focused on level and ability

Table 7: Comparative analysis of the metastasis degree and rate of upper mediastinal lymph node of middle esophageal cancer in T3 stage.

Group	MIE ($n = 45$)	OE ($n = 21$)	χ^2	*P*-value
Metastasis rate, *n* (%)				
2R	13 (28.9)	8 (38.1)	0.56	0.455
2L	5 (11.1)	8 (38.1)	4.97	0.025
8U	2 (4.4)	4 (19.0)	2.14	0.144
4R	0	1 (4.8)	–	0.318
4L	2 (4.4)	2 (9.5)	0.06	0.801
Total	18 (40.0)	13 (61.9)	2.76	0.097
Metastasis degree*				
2R	15/174 (8.6)	20/82 (24.4)	11.74	0.001
2L	13/169 (7.7)	17/49 (34.7)	23.34	<0.001
8U	2/25 (8.0)	4/18 (22.2)	0.78	0.378
4R	0/22 (0)	1/3 (33.3)	–	0.120
4L	2/51 (3.9)	5/21 (23.8)	4.63	0.031
Total	32/419 (7.6)	47/173 (27.2)	40.39	<0.001

* Data were expressed as number of lymph node dissection for T3 stage/total lymph node dissection number (%). Lymph node grouping criteria were made according to the 8th edition TNM staging standard of Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC). –: Not applicable. MIE: Minimal invasive esophagectomy; OE: Open esophagectomy; TNM staging: Tumor, Node and Metastasis staging.

of tumor resection, so as to ascertain the long-term prognosis of patients.[28,29] Ye *et al*[30] have reported the differences of LND between MIE and OE groups, while the characteristics of LNM and regional LND were not studied, which were carried out by us. We found a higher trend in total number of LND in the upper mediastinum in MIE group than that in OE group. Further analysis on the results of LND in upper mediastinum showed that the number of LND in 2L and 4L subgroups of MIE group was higher than that of OE group ($P < 0.001$ and $P = 0.012$, respectively). LND rates of 2L and 4L subgroups in MIE group were significantly higher than those in OE group ($P = 0.001$ and $P = 0.018$, respectively). It is speculated that it is difficult to expose the lymph nodes of upper mediastinum to the operative field, especially for the 2L and 4L subgroups, since they are located at the left side of the recurrent laryngeal nerve chain and adjacent to the tracheal membrane and arterial wall. Due to the magnifying effect of endoscopy and good surgical field of vision, and the use of auxiliary artificial pneumothorax to expand the mediastinal space, MIE surgery makes the anatomical level clearer. Meanwhile, endoscopic instruments are more suitable for fine operation in some narrow spaces, and the protection of surrounding normal tissues is better than open surgery,[31] so as to minimize the injury of recurrent laryngeal nerve in the operation process.

To better determine whether different surgical methods have an impact on LNM degree and LND rate in the upper mediastinal, patients with T3 stage esophageal cancer in the middle thoracic segment were selected for further comparative analysis. The results showed that there was no significant difference in LNM rate of the upper mediastinal between the two groups, but the grouping analysis showed that the LNM rate of the 2L subgroup in OE group was significantly higher than that in MIE group. In addition, the LNM degree of the upper mediastinal lymph nodes in OE group was significantly higher than that of MIE group, and the differences in the 2L and the 4L subgroups were statistically significant. The reason for those results might be due to the different number and rate of LND, and the real metastatic status of esophageal cancer patients can be reflected more accurately and objectively by the degree and rate of LNM in MIE group.

This study has its inherent limitations as a retrospective analysis. First, it was a single-center study, with a small sample size. Second, the follow-up period was shorter, so there was no comparison of survival. Third, the choice of clinical operation cases was influenced by subjective factors. For cases with large tumor and late pathological stage, surgeons tend more to OE, which will also lead to selective bias. Therefore, further studies with larger samples are necessary to confirm those findings.

In conclusion, in esophageal cancer, the LNM rate in the middle, lower mediastinum and abdomen increased with the tumor site moving down. MIE has certain advantages in LND of upper mediastinum of 2L and 4L subgroups, while it is similar to OE in other regions of LND.

Conflicts of interests

None.

References

1. Xia C, Dong X, Li H, Cao M, Sun D, He S, *et al*. Cancer statistics in China and United States 2022 profiles, trends, and determinants. Chin Med J 2022;135:584–590. doi: 10.1097/CM9.0000000000002108.
2. Wang YQ, Li HZ, Gong WW, Chen YY, Zhu C, Wang L, *et al*. Cancer incidence and mortality in Zhejiang Province Southeast China 2016: a population-based study. Chin Med J 2021;134:1959–1966. doi: 10.1097/CM9.0000000000001666.
3. Zhou JC, Sun KX, Wang SM, Chen R, Li MJ, Gu JH, *et al*. Associations between cancer family history and esophageal cancer and precancerous lesions in high-risk areas of China. Chin Med J 2022;135:813–819. doi: 10.1097/CM9.0000000000001939.
4. Hu N, Wang K, Zhang L, Liu ZJ, Jin Z, Cui RL, *et al*. Epidemiological and clinical features of functional dyspepsia in a region with a high incidence of esophageal cancer in China. Chin Med J 2021;134:1422–1430. doi: 10.1097/CM9.0000000000001584.

5. Fox M, Farmer R, Scoggins CR, McMasters KM, Martin RC 2nd. Lymph node ratio is a significant predictor of disease-specific mortality in patients undergoing esophagectomy for cancer. Am Surg 2012;78:528–534. doi: 10.1016/s0016-5085(11)64369-2.
6. Huang FL, Yu SJ. Esophageal cancer: risk factors, genetic association, and treatment. Asian J Surg 2018;41:210–215. doi: 10.1016/j.asjsur.2016.10.005.
7. Lagergren J, Lagergren P. Recent developments in esophageal adenocarcinoma. CA Cancer J Clin 2013;63:232–248. doi: 10.3322/caac.21185.
8. Short MW, Burgers KG, Fry VT. Esophageal cancer. Am Fam Physician 2017;95:22–28. doi: 10.1093/oso/9780190238667.003.0030.
9. Fujita H. History of lymphadenectomy for esophageal cancer and the future prospects for esophageal cancer surgery. Surg Today 2015;45:140–149. doi: 10.1007/s00595-014-0841-4.
10. Murakawa K, Ono K, Yamamura Y, Niwa H, Yamamoto H, Muto J, *et al*. Minimally invasive surgery for esophageal cancer after esophageal perforation. Asian J Endosc Surg 2017;10:407–410. doi: 10.1111/ases.12379.
11. Paul S, Altorki N. Outcomes in the management of esophageal cancer. J Surg Oncol 2014;110:599–610. doi: 10.1002/jso.23759.
12. Graham-Wisener L, Dempster M. Peer advice giving from posttreatment to newly diagnosed esophageal cancer patients. Dis Esophagus 2017;30:1–7. doi: 10.1093/dote/dox089.
13. Mentessidou A, Avgerinos I, Avgerinos N, Skandalakis PN, Mirilas P. Right or left thoracotomy for esophageal atresia and right aortic arch? Systematic review and surgicoanatomic justification. J Pediatr Surg 2018;53:2128–2135. doi: 10.1016/j.jpedsurg.2018.06.015.
14. Ariyaratnam P, Alibhai A, Saleh A, Rusling L, Cowen ME. The left thoracotomy approach for oncologic esophageal resection is still relevant for the modern surgical trainee. Ann Thorac Surg 2015;100:1515–1516. doi: 10.1016/j.athoracsur.2015.04.008.
15. Guillem P, Fontaine C, Triboulet JP. Esophageal cancer resection and right aortic arch: successful approach through left thoracotomy. Dis Esophagus 1999;12:212–215. doi: 10.1046/j. 1442-2050.1999.00024.x.
16. Palladino-Davis AG, Mendez BM, Fisichella PM, Davis CS. Dietary habits and esophageal cancer. Dis Esophagus 2015;28:59–67. doi: 10.1111/dote.12097.
17. Li H, Yang S, Xiang J, Chen H. The number of lymph node metastases influences survival and International Union Against Cancer tumor-node-metastasis classification for esophageal squamous cell carcinoma: does lymph node yield matter. Dis Esophagus 2011;24:108. doi: 10.1111/j. 1442-2050 2010.01108 x.
18. Kayani B, Zacharakis E, Ahmed K, Hanna GB. Lymph node metastases and prognosis in oesophageal carcinoma— a systematic review. Eur J Surg Oncol 2011;37:747–753. doi: 10.1016/j.ejso.2011.06.018.
19. Yibulayin W, Abulizi S, Lv HB, Sun W. Minimally invasive oesophagectomy versus open esophagectomy for resectable esophageal cancer: a meta-analysis. World J Surg Oncol 2016;14:304. doi: 10.1186/s12957-016-1062-7.
20. Rice TW, Gress DM, Patil DT, Hofstetter WL, Kelsen DP, Blackstone EH. Cancer of the esophagus and esophagogastric junction-major changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA Cancer J Clin 2017;67:304–317. doi: 10.3322/caac.21399.
21. van Workum F, Berkelmans GH, Klarenbeek BR, Nieuwenhuijzen GAP, Luyer MDP, Rosman C. McKeown or Ivor Lewis totally minimally invasive esophagectomy for cancer of the esophagus and gastroesophageal junction: systematic review and meta-analysis. J Thorac Dis 2017;9 (Suppl 8):S826–S833. doi: 10.21037/jtd.2017.03.173.
22. Wang MM, Guo CH, Li FL, Xu RP, Liu Z, Pan YQ, *et al*. Family history of esophageal cancer modifies the association of serum lipids and malignant esophageal lesions: a nested case-control study from the "ndoscopic Screening for Esophageal Cancer in China" trial. Chin Med J 2021;134:1079–1086. doi: 10.1097/CM9.0000000000001432.
23. Bollschweiler E, Plum P, Mönig SP, Hölscher AH. Current and future treatment options for esophageal cancer in the elderly. Expert Opin Pharmacother 2017;18:1001–1010. doi: 10.1080/14656566.2017.1334764.
24. Domper Arnal MJ, Ferrández Arenas Á, Lanas Arbeloa Á. Esophageal cancer: risk factors, screening and endoscopic treatment in Western and Eastern countries. World J Gastroenterol 2015;21:7933–7943. doi: 10.3748/wjg.v21.i26.7933.
25. Sohda M, Kuwano H. Current status and future prospects for esophageal cancer treatment. Ann Thorac Cardiovasc Surg 2017;23:1–11. doi: 10.5761/atcs.ra.16-00162.
26. Giugliano DN, Berger AC, Rosato EL, Palazzo F. Total minimally invasive esophagectomy for esophageal cancer: approaches and outcomes. Langenbecks Arch Surg 2016;401:747–756. doi: 10.1007/s00423-016-1469-1.
27. Tachimori Y, Nagai Y, Kanamori N, Hokamura N, Igaki H. Pattern of lymph node metastases of esophageal squamous cell carcinoma based on the anatomical lymphatic drainage system. Dis Esophagus 2011;24:33–38. doi: 10.1111/j. 1442-2050 2010.01086 x.
28. Nakagawa S, Nishimaki T, Kosugi S, Ohashi M, Kanda T, Hatakeyama K. Cervical lymphadenectomy is beneficial for patients with carcinoma of the upper and mid-thoracic esophagus. Dis Esophagus 2003;16:4–8. doi: 10.1046/j. 1442-2050 2003.00286 x.28.
29. Shim YM, Kim HK, Kim K. Comparison of survival and recurrence pattern between two-field and three-field lymph node dissections for upper thoracic esophageal squamous cell carcinoma. J Thorac Oncol 2010;5:707–712. doi: 10.1097/JTO.0b013e3181d3ccb2.
30. Ye B, Zhong CX, Yang Y, Fang WT, Mao T, Ji CY, *et al*. Lymph node dissection in esophageal carcinoma: minimally invasive esophagectomy vs. open surgery. World J Gastroenterol 2016;22:4750–4756. doi: 10.3748/wjg.v22.i19.4750.
31. Wen J, Lu ZS, Liu CH, Bian XQ, Huang J. Predictive factors of endoscopic submucosal dissection procedure time for early esophageal cancer. Chin Med J 2021;134:1373–1375. doi: 10.1097/CM9.0000000000001355.

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