



RAPID COMMUNICATION

Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy for squamous cell carcinoma of the lower thoracic esophagus

Jie Wu, Ying Chai, Xing-Ming Zhou, Qi-Xun Chen, Fu-Lai Yan

Jie Wu, Xing-Ming Zhou, Qi-Xun Chen, Fu-Lai Yan, Department of Thoracoabdominal Surgery, Zhejiang Cancer Hospital, Hangzhou 310022, Zhejiang Province, China
Ying Chai, Department of Thoracic Surgery, 2nd Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, Zhejiang Province, China

Author contributions: Wu J and Chai Y designed the research; Wu J, Zhou XM, Chen QX and Yan FL performed the research; Wu J analyzed the data and wrote the paper.

Correspondence to: Jie Wu, MD, Department of Thoracoabdominal Surgery, Zhejiang Cancer Hospital, 38 Guangji Road, Bangshan, Hangzhou 310022, Zhejiang Province, China. wujiephd729@126.com

Telephone: +86-571-88122031 Fax: +86-571-88122508

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with two-field (total mediastinum) lymphadenectomy is a safe and appropriate operation for squamous cell carcinoma of the lower thoracic esophagus.

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Key words: Esophageal neoplasm; Ivor Lewis approach; Two-field lymphadenectomy

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Abstract

AIM: To evaluate the clinical outcome of Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy for patients with squamous cell carcinoma of the lower thoracic esophagus.

METHODS: From January 1998 to December 2001, 73 patients with lower thoracic esophageal carcinoma underwent Ivor-Lewis subtotal esophagectomy with two-field lymphadenectomy. Clinicopathological information, postoperative complications, mortality and long term survival of all these patients were analyzed retrospectively.

RESULTS: The operative morbidity and mortality was 15.1% and the mortality was 2.7%. Lymph node metastases were found in 52 patients (71.2%). Nodal metastases to the upper, middle, lower mediastini and upper abdomen were found in 13 (17.8%), 15 (20.5%), 30 (41.1%), and 25 (34.2%) patients, respectively. Postoperative staging was as follows: stage I in 5 patients, stage II in 34 patients, stage III in 32 patients, and stage IV in 2 patients, respectively. The overall 5-year survival rate was 23.3%. For N0 and N1 patients, the 5-year survival rate was 38.1% and 17.3%, respectively ($\chi^2 = 22.65, P < 0.01$). The 5-year survival rate for patients in stages II a, II b and III was 31.2%, 27.8% and 12.5%, respectively ($\chi^2 = 29.18, P < 0.01$).

CONCLUSION: Ivor Lewis subtotal esophagectomy

INTRODUCTION

Radical esophagectomy with lymphadenectomy remains the mainstay of curative therapy for esophageal carcinoma. Complete resection of esophagus and regional lymph node (R_0 resection) are essential to improve long-term survival^[1-3]. For carcinomas of the lower thoracic esophagus, different tumor characteristics between the Western and Eastern countries cause various attitudes on their surgical management^[4]. Depending on the attending surgeon's philosophy, surgical approaches to carcinomas of the lower thoracic esophagus vary from the conventional left thoraco-abdominal approach^[5,6] to the transhiatal approach without thoracotomy^[7-9], Ivor Lewis approach^[10-12], and recently reported thoracoscopic approach^[13-15]. On the other hand, controversy continues over the optimal extent of lymphadenectomy to be performed with esophagectomy. Some authors do not favor lymphadenectomy considering lymph node involvement as systemic disease with no hope for cure, and the primary goal of surgical intervention is palliative, with a low surgical morbidity and mortality^[8]. However, some authors prefer two-field lymphadenectomy and regard it as a standard surgical procedure^[10,12,16]. What is more, other authors, mainly from Japan, advocate three-field lymphadenectomy in order to obtain accurate staging,

control locoregional recurrence and improve long-term survival^[17-20].

At our hospital, the main surgical approach to lower thoracic esophageal carcinoma is the Ivor Lewis approach, instead of left thoraco-abdominal approach that is widely adopted in China, because Ivor Lewis approach provides a wider extent of lymphadenectomy than left thoraco-abdominal approach, and the chance of obtaining R₀ resection is greater. The aim of this study was to retrospectively assess our results of Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy for patients with squamous cell carcinoma of the lower thoracic esophagus.

MATERIALS AND METHODS

Patients

From January 1998 to December 2001, 73 patients with squamous cell carcinoma of the lower thoracic esophagus underwent Ivor Lewis subtotal esophagectomy with two-field lymph node dissection at Zhejiang Cancer Hospital, Hangzhou, China. There were 65 men and 8 women. Median age was 57 years (range, 39 to 78 years). Preoperative evaluation was performed for all patients with a barium swallow examination, endoscopy with biopsy, ultrasonography of the neck and upper abdominal compartment. Cardiac and pulmonary functions were also routinely performed for these patients to determine their ability to withstand the planned surgical procedure. Before treatment, diagnosis of all patients was established histologically. No patient received chemotherapy or radiotherapy before operation. Postoperative staging was based on the 2002 UICC-TNM classification^[21].

Duration of surgery, operative blood loss, and the number of lymph nodes were recorded. Postoperative complications were also recorded. Operative mortality was defined as any death during the first 30 d after operation or during the same hospital stay.

Surgical technique

All patients underwent Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy. In brief, all resections were carried out by initial abdominal exploration through an upper midline laparotomy. The stomach was mobilized on the right gastric and gastroepiploic arteries. The left gastric artery was divided at its origin, and all lymph nodes along the celiac axis and its three branches along the left aspect of the portal vein, in front of the inferior vena cava, along the diaphragmatic pillars, and in front of the left adrenal gland were *en bloc* resected. A pyloromyotomy was performed routinely for all the patients. No drainage procedure was done. After the abdominal stage, a right posterolateral thoracotomy was performed. The thoracic dissection included removal of azygous arch with its associated lymph nodes, thoracic duct, and the low paratracheal, subcarinal, paraesophageal, and parahial nodes in continuity with the resected esophagus. In addition, upper mediastinal, paratracheal lymphatic tissue

Table 1 Postoperative pathological staging in 73 patients with esophageal carcinoma

Stage	TNM	Patients, n (%)
I (n = 5)	T1N0M0	5 (6.8)
II a (n = 16)	T2N0M0	7 (9.6)
	T3N0M0	9 (12.3)
II b (n = 19)	T1N1M0	3 (4.1)
	T2N1M0	15 (20.5)
III (n = 32)	T3N1M0	29 (39.7)
	T4N1M0	3 (4.1)
IV (n = 2)	T3N1M1	2 (2.7)

including lymph nodes of the left and right recurrent laryngeal nerves were also removed. Denudation of the lesser curvature was usually performed in the pleural cavity. After resection of the specimen, an anastomosis was constructed between the stomach and esophagus. The anastomosis was located in the apex of the chest in all patients.

After surgery, all patients returned to the intensive care unit for 2 d on average. On day 5 after surgery, patients underwent contrast X-ray study for assessment of esophagogastric anastomosis and then received enteral feeding.

Follow-up

Postoperative data were collected at the outpatient clinic. Follow-up data were obtained by telephone. The follow-up time ranged 0-88 mo (median 47 mo). Survival time was defined as the period from the date of surgery until death or the most recent follow-up investigation (September 2005), with none lost to follow-up.

Statistical analysis

Survival analysis was carried out with the Kaplan-Meier method, and the log-rank test was used for comparisons. Estimates and 95% confidence intervals (CI₉₅) were given for 5 years. Fisher's exact two-tailed test was used to compare categorical data. *P* < 0.05 was considered statistically significant.

RESULTS

Pathological findings

All the 73 patients acquired complete resection (R₀ resection). The postoperative stage and TNM classification are shown in Table 1. Of the 8 patients with pathological T1 tumors, 2 had muscularis mucosae tumors and 6 had submucosal tumors. Nodal involvement was found in 3 of the 6 patients with submucosal tumors. Of the 3 patients with pathological T4 tumors, 2 had liver involvement and 1 had lung involvement. Combined resections were performed for the 3 patients. Metastases were found in celiac nodes of 2 patients with M1 disease.

Operative outcomes

The operation time was 243 ± 40 min. The operative blood loss was 365 ± 230 mL. The number of lymph

Table 2 Postoperative complications in 73 patients with esophageal carcinoma *n* (%)

Complications	Patients	Patients died
Pneumonia	4 (5.5)	1 (1.4)
Vocal cord palsy	3 (4.1)	0 (0)
Arrhythmia	3 (4.1)	0 (0)
Anastomotic leakage	2 (2.7)	1 (1.4)
Postoperative bleeding	1 (1.4)	0 (0)
Wound infection	1 (1.4)	0 (0)

Table 3 Relation between depth of tumor infiltration (T) and lymph node metastasis (N)

T	N0	N1	Prevalence of nodal metastases (%)
T1 (<i>n</i> = 8)	5	3	37.5
T2 (<i>n</i> = 22)	7	15	68.2
T3 (<i>n</i> = 40)	9	31	77.5
T4 (<i>n</i> = 3)	0	3	100

$P = 0.888$.

nodes resected was 31 ± 11 (median, 27). Postoperative complications are listed in Table 2. Complications occurred in 11 patients (15.1%, CI_{95} 6.9%-23.3%). Of the 73 patients, 2 (2.7%, CI_{95} 0%-6.5%) died due to pneumonia and anastomotic leakage, respectively, within 30 d of the operation.

Tumor depth and lymph node metastases

Lymph node metastases were found in 52 patients and the prevalence of nodal metastasis was 71.2% (CI_{95} 60.8%-81.6%). As shown in Table 3, the prevalence of nodal metastases increased with increasing tumor depth, but the difference was not statistically significant. The prevalence of nodal metastases was 37.5% in T1 stage patients, 77.5% in T3 stage patients, which was statistically significant ($\chi^2 = 5.06$, $P = 0.025$). Other differences in the two stages were not statistically significant (T1 *vs* T2, T1 *vs* T4, T2 *vs* T3, T2 *vs* T4, T3 *vs* T4).

Distribution of metastatic lymph node

The frequencies of nodal metastases in different anatomical regions are shown in Table 4, which were statistically significant ($P = 0.004$). The frequency in lower mediastinum (41.1%) was higher than that in upper (17.8%, $\chi^2 = 9.53$, $P = 0.007$), and middle mediastini (20.5%, $\chi^2 = 7.23$, $P = 0.007$). The frequency in upper abdomen (34.2%) was higher than that in upper mediastinum (17.8%) ($\chi^2 = 5.12$, $P = 0.024$). Other differences in frequencies between the two regions were not statistically significant. Among the 52 patients with lymph node involvement, 13 (25.0%, CI_{95} 13.3%-36.7%) had skip nodal metastases without invasion of peritumoral nodes. Isolated lymph node involvement was observed in the upper mediastinum of 6 patients (4 with positive left recurrent laryngeal nerve nodes, 2 positive right left laryngeal nerve nodes) and in the upper abdomen of 7 patients with positive left gastric arterial nodes, respectively. These patients (17.8%, CI_{95}

Table 4 Distribution of lymph node metastatic locations

Metastatic location	Patients with negative lymph node (<i>n</i>)	Patients with positive lymph node (<i>n</i>)	Frequency of nodal metastases (%)
Upper mediastinum	60	13	17.8
Middle mediastinum	58	15	20.5
Lower mediastinum	43	30	41.1
Upper abdomen	48	25	34.2

$P = 0.004$.

9.0%-26.6%) did not undergo two-field lymphadenectomy but received incomplete resections (R_1 resection of microscopically residual tumors or R_2 resection of macroscopically residual tumors). Had upper mediastinal lymphadenectomy not been performed, six patients (8.2%, CI_{95} 1.9%-15.5%) would not have undergone upper mediastinal lymphadenectomy but received inaccurate staging.

Survival rate

The 5-year survival rate was 23.3% (CI_{95} 13.5%-32.9%) for all patients (Figure 1A). The 5-year survival rate was 38.1% (CI_{95} 17.4%-58.8%) and 17.3% (CI_{95} 7.0%-27.6%) for N0 and N1 patients, respectively ($\chi^2 = 22.65$, $P < 0.01$, Figure 1B). The 5-year survival rate for patients in stages IIa, IIb, and III was 31.2% (CI_{95} 8.9%-53.5%), 27.8% (CI_{95} 7.1%-48.5%) and 12.5% (CI_{95} 1.0%-24.0%), respectively ($\chi^2 = 29.18$, $P < 0.01$, Figure 1C).

DISCUSSION

Studies demonstrated that extensive submucosal lymphatic drainage to the esophageal wall causes a unique pattern of nodal metastases^[1,2,4]. It was reported that the prevalence of nodal metastases of lower thoracic esophageal carcinoma is up to 70%^[1-3]. Lymphatic dissemination is an early event of esophageal carcinoma, and involved nodes are found in 30%-40% of submucosal tumors^[2,3]. These data are consistent with our results (71.2% and 50%, respectively). It has been documented that the likelihood of nodal metastases of esophageal carcinoma depends on the depth of tumor invasion of the esophageal wall^[2,3]. The prevalence of nodal metastases increased with the increasing tumor invasion depth in this study. The prevalence of nodal metastases had no difference between the two groups according to their T status, suggesting that it may be related to the small sample size. Unlike squamous cell carcinoma of the upper thoracic esophagus, which shows lymphatic flow is mainly in the upward direction along the esophageal wall, squamous cell carcinoma of the lower thoracic esophagus, which shows lymphatic spread is mainly in the downward direction along the esophageal wall^[2,4], which is consistent with our findings. Although to some degree, the frequencies of lower mediastinal and upper abdominal metastases were higher than those of upper and middle mediastinal metastases, the frequency of upper mediastinal metastases (17.8%) was still not as low as that of middle mediastinal

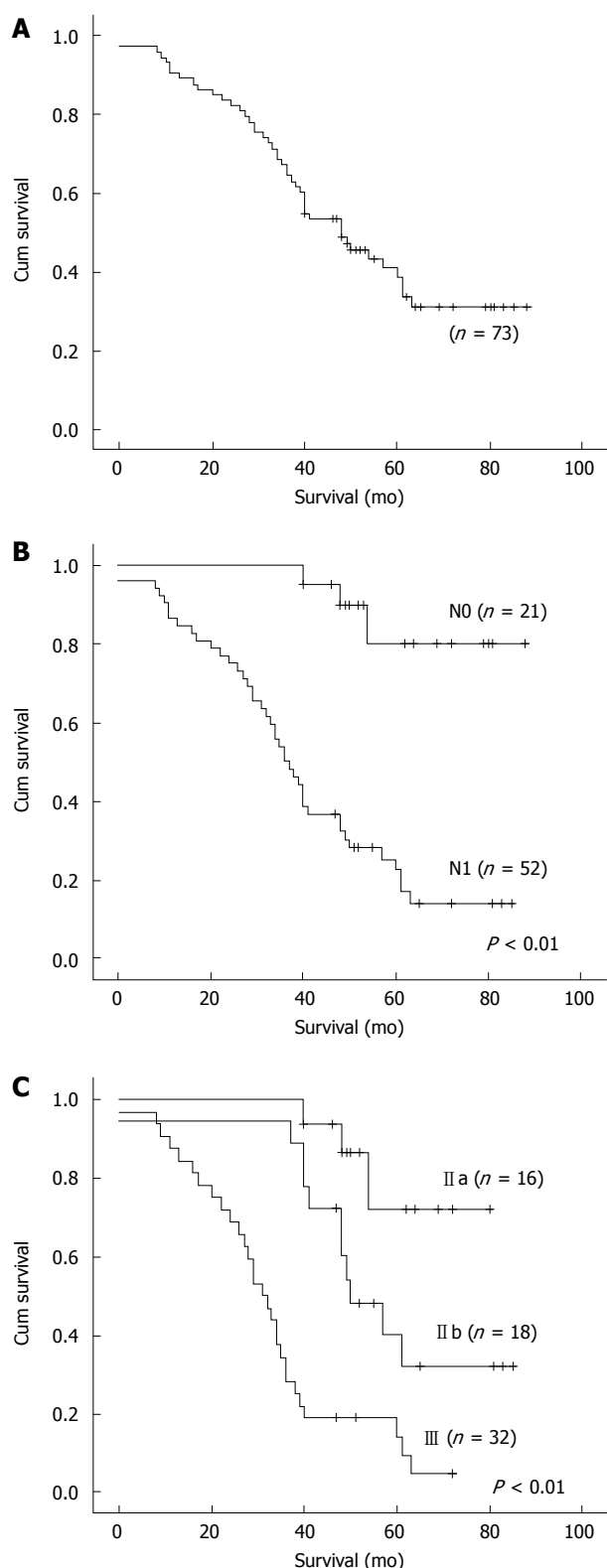


Figure 1 Survival curves for the 73 patients with squamous cell carcinoma of the lower thoracic esophagus (A), according to the N status (B), and the TNM stage (C).

metastases (20.5%) in the patients with lower thoracic esophageal carcinoma. An even higher frequency of upper and/or middle mediastinal metastases (30%-40%) has been reported^[2,4]. In our study, skip nodal metastases were found in 25% of nodal positive patients. Of the 52 patients, 6 (11.5%) and 7 (13.5%) had positive nodes in

the upper mediastinum and abdomen, respectively. Hosch *et al*^[22] reported that skip metastases nodal positive patients and a frequent event in esophageal cancer. Based on these nodal metastatic features, in order to obtain R₀ resection, lymphadenectomy with upper mediastinal dissection should be performed for squamous cell carcinoma of the lower esophagus.

The greater the number of lymph nodes is removed, the greater the chance of obtaining a R₀ resection, and the more precisely the disease can be staged^[1-3,11]. The extent of lymphadenectomy for a cancer in the thoracic esophagus has been classified by the Consensus Conference of the International Society for Diseases of the Esophagus (ISDE) as a standard, extended, total, or three-field lymphadenectomy^[23]. The optimal lymphadenectomy for squamous cell carcinoma of the lower thoracic esophagus is still debatable. Of the 4 types of lymphadenectomy, three-field lymphadenectomy can, most likely, achieve a R₀ resection and accurate staging. The question is whether it definitely improves the long-term survival of patients. However, most data are available from nonrandomized retrospective historical studies in Japan. Igaki *et al*^[4] reported that three-field lymphadenectomy could prolong the survival time of patients with squamous cell carcinoma of the lower thoracic esophagus compared to 2-field lymphadenectomy for nodal metastases present in the upper and/or middle mediastinum. Fujita *et al*^[24] reported that there is no difference in survival rate for patients with lower thoracic esophageal cancer between the two procedures of lymphadenectomy. Three-field lymphadenectomy has its obvious advantages and disadvantages^[16,18]. Hence, two field lymphadenectomy seems to be a more reasonable choice of treatment for squamous cell carcinoma of the lower thoracic esophagus. This viewpoint is far out weighed by the fact that the emphasis on three-field lymphadenectomy has shifted to lymphadenectomy along the recurrent laryngeal nerve chains, where lymph nodes could be dissected through two-field lymphadenectomy^[16]. Among the other three types of lymphadenectomy, total (mediastinal) lymphadenectomy which was applied in this study, provides more chances to obtain a R₀ resection and accurate staging than the other two types of lymphadenectomy. As our data show, if a standard lymphadenectomy was performed, positive nodes would be left intact, thus only R₁ or R₂ resection could be achieved, leading to stage migration from N₀ to N₁ in 6 patients (8.2%). If an extended lymphadenectomy was performed, stage migration from N₀ to N₁ would occur in 4 patients (5.5%), which can be explained by the fact that the extent of standard lymphadenectomy does not cover the upper and left upper mediastini. Total (mediastinal) lymphadenectomy is therefore an alternative for squamous cell carcinoma of the lower thoracic esophagus. Then, which surgical approach could satisfy the demand for total lymphadenectomy? Transhiatal approach without thoracotomy is unlikely to be chosen. In the left thoraco-abdominal approach we used previously, upper mediastinal lymph nodes are

not available. In the McKeown approach (anterolateral right thoracotomy), a radical lymphadenectomy is more difficult to achieve than the Ivor Lewis approach^[5,12]. Thoracoscopic approach to esophageal carcinoma remains to be investigated and no systemic data are available to support its advantages over the minimally invasive approach to esophagectomy^[25]. Ivor Lewis approach which allows complete visualization of mediastinum, especially upper mediastinum, seems to be most appropriate for squamous cell carcinoma of the lower thoracic esophagus.

Morbidity increases with the extent of lymphadenectomy but does not lead to a higher mortality^[11]. Pneumonia was the most common complication in this study, which is consistent with previous reports^[10-12]. Vocal cord palsy caused by lymphadenectomy around recurrent laryngeal nerves also occurs occasionally. Functional mediastinal lymphadenectomy can preserve the bronchial artery and bronchial branches of the vagus nerve, thus reducing the respiratory complications^[20,26]. To prevent vocal cord palsy, electrocautery close to the recurrent laryngeal nerve and drawing the nerve with a vessel tape should be avoided during lymphadenectomy^[19].

The overall 5-year survival rate of our patients was only 23.3%, which may be due to the small sample size in our study. On the other hand, the survival of patients was ascertained in September 2005 when 15 patients were alive at the most recent follow-up. Accordingly, this overall survival rate could not completely explain the effect of treatment since we did not make comparisons with others. However, there was a significant difference in the survival rate between the two groups of patients with different N status and different stages. This series were proved to be more homogenous with regard to the clinical variables, such as tumor site and pathological type. The surgical procedure performed in this series revealed more R₀ resection and staging information than other surgical procedures (except three-field lymphadenectomy). Compared to other surgical procedures, Ivor Lewis esophagectomy with two-field (total mediastinal) lymphadenectomy could achieve better results in patients with squamous cell carcinoma of the lower thoracic esophagus. Because of the small sample size used in this study, further studies are needed to confirm our results.

In conclusion, Ivor Lewis subtotal esophagectomy with two-field (total mediastinal) lymphadenectomy is a safe and appropriate surgical procedure for squamous cell carcinoma of the lower esophagus.

COMMENTS

Background

Radical esophagectomy with lymphadenectomy is still the mainstay of curative therapy for esophageal carcinoma. This study retrospectively analyzed the clinical outcome of Ivor Lewis subtotal esophagectomy with two-field lymphadenectomy for squamous cell carcinoma of the lower thoracic esophagus.

Research frontiers

Adenocarcinoma of the lower thoracic esophagus is a common pathological type in Western countries, while squamous cell carcinoma is the main type in Eastern countries. The attitudes to the surgical approach and the extent of the lymphadenectomy for the lower thoracic esophageal carcinoma are different in

Western and Eastern countries. Western general thoracic surgeons prefer the transhiatal approach and limited extent of lymphadenectomy, whereas Eastern general thoracic surgeons prefer the transthoracic approach and 2-field or 3-field lymphadenectomy.

Innovations and breakthroughs

In China, the left thoracoabdominal approach and standard 2-field lymphadenectomy are widely performed for lower thoracic esophageal carcinoma. In our clinical practice, however, they are widely performed as upper mediastinal lymphadenectomy. Furthermore, the prevalence of upper mediastinal nodal involvement is not low. 3-field lymphadenectomy is still controversial. This type of lymphadenectomy is not routinely performed in our institution. We prefer the Ivor Lewis approach with total mediastinal 2-field lymphadenectomy in the treatment of this disease.

Applications

Ivor Lewis subtotal esophagectomy with 2-field lymphadenectomy is a safe surgical procedure for squamous cell carcinoma of the lower thoracic esophagus.

Terminology

Ivor Lewis subtotal esophagectomy is a laparotomy followed by a right thoracotomy. Two-field total mediastinal lymphadenectomy involves resection of bilateral upper mediastinum in addition to a standard lymphadenectomy.

Peer review

The paper is scientific, innovative and readable, showing the advanced level of clinical research in gastroenterology both at home and abroad.

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