·Esophageal Carcinoma Column·

Efficacy of surgical resection of left and right transthoracic approaches for middle thoracic esophageal squamous cell carcinoma

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[Abstract] Background and Objective: For squamous cell carcinoma of the middle thoracic esophagus, surgical resection of left or right transthoracic approach has its advantages and disadvantages, respectively. This study was to compare the outcomes between the two approaches. **Methods:** A total of 482 consecutive patients with middle thoracic esophageal squamous cell carcinoma (ESCC) underwent transthoracic esophagectomy between January 1999 and June 2005. These patients were divided into left transthoracic approach group (n=350) and right transthoracic approach group (n=132). Surgical resection rate, postoperative complications, lymphadenectomy, recurrence pattern, disease-free survival, and overall survival of the two groups were compared retrospectively. **Results:** The surgical resection rate was 92.0% in left approach group and 92.4% in right approach group (P=0.878). The incidence of postoperative complications was higher in right approach group than in left approach group (57.6% vs. 35.4%, P<0.001). The average number of lymph nodes resected was 11.8±6.6 in left approach group and 16.3±8.0 in right approach group (P<0.001). Lymphatic recurrence rate was lower in right approach group than in left approach group (51.1% vs. 69.6%, P=0.028), especially occurring to mediastinal lymph nodes (15.6% vs. 38.4%, P=0.005). Three-year disease-free survival was higher in right approach group than in left approach group (22.92±0.74 vs. 25.09±1.22, P=0.039). **Conclusions:** Although left transthoracic resection reduced the incidence of postoperative complications, esophagectomy of right transthoracic approach was more effective in survival improvement.

Key words: esophagus neoplasm/surgical operation, postoperative complication, lymphadenectomy, outcome

The surgical operation for thoracic esophageal squamous cell carcinoma (ESCC) is performed via left or right approaches. The left transthoracic approach can adequately expose inferior mediastinum, hiatal passage, and anatomic structures of upper abdomen, and is theoretically the favorable approach for the resection of carcinomas involving middle-to-lower esophagus and the junction of esophagus and stomach. The right transthoracic approach can facilitate separating middle-to-upper esophagus under direct visualization, exposing entire mediastinum and abdominal structures via midline incision while sparing diaphragm incision. This approach is suitable for the excision of middle-to-upper esophageal tumors. A total of 482 cases of middle thoracic ESCC treated in Sun Yat-sen University Cancer Center from January 1999 to June 2005 were analyzed for resection rate, postoperative complications, status of lymph node resection, disease-free survival rate and overall survival rate to investigate the impact of surgical approaches on clinical outcome.

Data and Methods

Clinical data

Of the 482 patients with middle thoracic ESCC, 350 received operation via the right transthoracic approach and 132 via the left transthoracic approach. Clinical data of the two groups are listed in Table 1.

Surgical approaches

In the left approach group, left posterolateral incision was made through the sixth intercostals space, the esophagus was

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Table 1 Clinical data of the patients with esophageal carcinoma in left and right approach groups

Item	Left approach group	Right approach group	*P*
Gender			1.713
Male	262	91	
Female	88	41	
Age (years)	56.6±9.6	58.8±9.2	0.025
Differentiation			0.702
Well	89	31	
Moderate	168	69	
Poor	93	32	
Depth of invasion			5.415
pTis-T1	27	7	
pT2	113	32	
pT3	196	88	
pT4	14	5	
Lymph node metastasis			1.201
pN0	205	70	
pN1	145	62	
pStage (1997 UICC)			-
0	3	0	
Ⅰ	23	7	
Ⅱa	174	61	
Ⅱb	42	12	
Ⅲ	106	44	
Ⅳ	2[a]	8[b]	

[a]Hepatic metastasis (1 case), paraaortic (abdominal) lymph node metastasis (1 case); [b]cervical lymphatic metastasis (7 cases), paraaortic (abdominal) lymph node metastasis (1 case).

The cases mentioned above were diagnosed during the operations.

separated, followed by thoracic lymph node resection. Then the stomach was separated through the diaphragm, followed by abdominal lymph node resection. The stomach was lifted to the thoracic cavity to perform gastro-esophagus anastomoses above the aortic arch in 344 patients and in left neck in six patients.

In the right approach group, right posterolateral incision was made and the esophagus was separated via the fifth intercostals space, followed by thoracic lymph node resection. Another incision on upper abdominal midline was made to separate the stomach, followed by abdominal lymph node resection. Then the stomach was lifted up to the neck through right thoracic cavity and original esophageal bed (posterior mediastinum). The left cervical lymph node resection was performed. Gastro-esophagus anastomoses were performed in left neck for 125 patients and in right chest for four patients. Esophageal replacement with colon was performed for three patients.

Postoperative treatment

After radical resection, nine patients in the left approach group underwent adjunctive therapy, including seven with chemotherapy and two with radiochemotherapy; 12 in the right approach group underwent adjunctive therapy, including six with radiotherapy, four with chemotherapy and two with radiochemotherapy. Twenty-eight patients in the left approach group underwent non-radical resection, 11 of them underwent postoperative radiotherapy and three underwent chemotherapy. Ten patients in the right approach group underwent non-radical resection, four of them underwent postoperative radiotherapy, two underwent postoperative chemotherapy and one underwent radiochemotherapy. The rest 14 patients in the left approach group and three in the right approach group refused further treatment.

Follow-up and statistical analysis

The patients were followed up by mail, telephone and outpatient visit till July 1, 2008. The total follow-up rate was 97.3%. Nine (2.57%) patients in the left approach group and four (3.03%) in the right approach groups lost to follow-up (the time of death cannot be determined).

Statistical analysis was performed with SPSS13.0 software. Quantitative data were analyzed using χ^2 test, and continuous data with t-test. The 3-year disease-free survival (DFS) and overall survival (OS) were calculated with Kaplan-Meier method and analyzed with log-rank test.

Results

Intraoperative and perioperative conditions

The mean durations of operation were (188.6±47.5) min in the left approach group and (303.6 ±84.8) min in the right approach group (P<0.001). The mean blood loss volume and blood transfusion were (232.0±97.5) mL and (19.5± 86.1) mL in the left approach group, and (333.3± 155.1) mL and (92.4± 166.1) mL in the right approach group (P<0.001).

The ICU stay were (2.5±1.3) days in the left approach group and (3.0±1.6) days in the right approach group (P=0.001); the performance rates of tracheotomy were 1.4% and 2.3%, respectively (P=0.531). The hospital mortalities (occurred within 30 days after operation) were 2.0% and 0.8%, respectively (P=0.304).

Surgical resection rate

The radical resection rates were 92.0% in the left approach group and 92.4% in the right approach group (P=0.878). The marginal positive rates were 4.0% and 1.5%, respectively (P=2.145); the primary tumor residual rates were 4.3% and 4.5%, respectively (P=0.016); the metastatic lymph node residual rates were 1.7% and 1.5%, respectively (P=0.024). In the left approach group, eight patients had involvement of ipsilateral mediastinal structures (such as the thoracic aorta, left inferior pulmonary vein and left bronchus), five had involvement of contralateral mediastinal structures (such as the right lung, right bronchus, and azygos vein), one had involvement of the diaphragm, and one had involvement of the bilateral mediastinum; in the right approach group, three patients had involvement of ipsilateral mediastinal structures (such as the right bronchus and azygos vein), and three had involvement of contralateral mediastinal structures (such as the thoracic aorta, left lung and left bronchus). Six patients in the left approach group and two in the right approach group had abdominal metastatic lymph node residual; none had thoracic lymph node residual.

Resection of lymph nodes

The numbers of resected lymph nodes were 11.8±6.6 in the left approach group and 16.3±8.0 in the right approach group (P<0.001), including 7.2±4.7 and 10.8± 6.3 in the thoracic field (P<0.001) and 4.6±3.5 and 5.4±4.1 in the abdominal field (P=0.028). In the left and right approach groups, the numbers of resected lymph nodes surrounding the upper esophagus and neighboring areas (bilateral recurrent laryngeal nerves and bronchus) were 0.5±1.2 and 3.3±3.5, respectively (P<0.001); the numbers of resected lymph nodes surrounding the middle esophagus and neighboring areas (thoracic duct and aorta) were 5.8±3.9 and 6.4±4.4, respectively (P=0.200); the numbers of resected lymph nodes surrounding the lower esophagus and neighboring areas (diaphragm and inferior pulmonary ligaments) were 0.9±1.4 and 1.2±1.6, respectively (P=0.067).

The lymph node metastatic rate and degree were 41.43% (145/350) and 9.30% (383/4118) in the left approach group, and were 46.2% (61/132) and 9.46% (204/2156) in the right approach group. The following regions showed remarkable differences in lymph node metastatic rate and degree: 1) in regions around the right recurrent laryngeal nerve, the metastatic rate and degree were 0 (0/1) and 0 (0/1) in the left approach group, and were 28.79% (19/66) and 21.21% (28/132) in the right approach group; 2) in regions around the left recurrent laryngeal nerve, the metastatic rate and degree were 0 (0/34) and 0 (0/70) in the left approach group, and 15.15% (5/33) and 8.96% (6/67) in the right approach group; 3) in regions around intrathoracic bronchus, the metastatic rate and degree were 0 (0/1) and 0 (0/3) in the left approach group, and 9.76% (4/41), 4.17% (6/144) in the right approach group.

Postoperative complications

The occurrence rates of complications were 35.4% in the left approach group and 57.6% in the right approach group (P<0.001) (Table 2).

Table 2 Incidence of postoperative complications of patients with esophageal carcinoma in left and right approach groups

Complication	Left approach group [number(%)]	Right approach group [number(%)]	P
Anastomotic leakage	7(2.0)	25(18.9)	<0.001
Arrhythmia, severe	45(12.9)	23(17.4)	0.199
Anastomotic stricture (long-term complication)	37(10.6)	16(12.1)	0.628
Pneumonia	37(10.6)	18(13.6)	0.345
Delayed gastric emptying	2(0.6)	5(3.8)	0.015
Bleeding, reoperation	2(0.6)	4(3.0)	0.044
Incision infection	5(1.4)	4(3.0)	0.269
Chylothorax	3(0.9)	3(2.3)	0.238
ARDS	5(1.4)	1(0.8)	0.533
Heart failure	7(2.0)	0	0.034
Multiple organs failure	2(0.6)	0	1.000

ARDS, acute respiratory distress syndrome.

Follow-up

Till the end of follow-up, the recurrence rates of the left and right approach groups were 50.0% (175/350) and 42.4% (56/132), respectively (P=0.138) (Table 3). In the left approach group, two patients had local recurrence and lymphatic recurrence, six had multiple lymph node recurrence, six had lymph node recurrence with distal metastasis. In the right approach group, two patients had multiple lymph node recurrence. The location and/or time of recurrence cannot be determined in 63 patients in the left approach group and 11 patients in the right approach group. Moreover, 14 patients in the left approach group (four underwent radiotherapy, three with chemotherapy and seven with radiochemotherapy) and five in the right approach group (one underwent radiotherapy, three with chemotherapy and one with radiochemotherapy) continued to survive after recurrence.

The 1- and 3-year DFS rates were 69.5% and 44.3% in the left approach group, and were 57.0% and 72.6% in the right approach group, respectively (Fig. 1). The mean DFS durations were (22.92±0.74) and (25.09±1.22) months in the two groups (P=0.039).

The 1- and 3-year OS rates were 78.9% and 48.2% in the left approach group, and were 82.6% and 57.6% in the right approach group, respectively (Fig. 2). The mean OS durations were (25.63±0.63) and (27.42±1.01) months, respectivley (P=0.080).

Discussion

Surgical resection of middle thoracic esophageal carcinoma via right transthoracic approach is more complex than via left approach, which, however, can expose upper mediastinum and upper abdomen, ensuring adequate resection of the esophagus and thorough two-field resection. Due to different anatomic structures involved during operations via the two approaches, their injury to tissues, the completeness of tumor resection and lymph node resection are all different, causing differences in complications and survival rates.

Intra-and peri-operative conditions

The left approach requires only one incision and one position, while the right approach requires two or three incisions and two positions. The left approach has advantages over the right

Table 3 Patterns of recurrence and metastasis in left and right approach groups

Item	Left approach group [%(ratio)]	Right approach group [%(ratio)]	*P*
Locoregional	16.1(18/112)	15.6 (7/45)	0.936
Anastomotic[a]	14.3(16/112)	11.1 (5/45)	0.597
Esophageal bed	1.8 (2/112)	4.4 (2/45)	0.363
Lymph node	69.6(78/112)	51.1(23/45)	0.028
Cervioc	28.6(32/112)	37.8(17/45)	0.260
Mediastinal	38.4(43/112)	15.6 (7/45)	0.005
Abdominal	10.7(12/112)	4.4 (2/45)	0.213
Metastasis	23.2(26/112)	31.1(14/45)	0.305
Distant organ[b]	21.4(24/112)	28.9(13/45)	0.319
Dissemination[c]	1.8 (2/112)	2.2 (1/45)	1.000
Unkown location of recurrence	36.0(63/175)	19.6(11/56)	–

[a]anastomotic site; [b]including lung, liver, bone, or other organs; [c]including pleural, peritoneal, or pericardial dissemination.

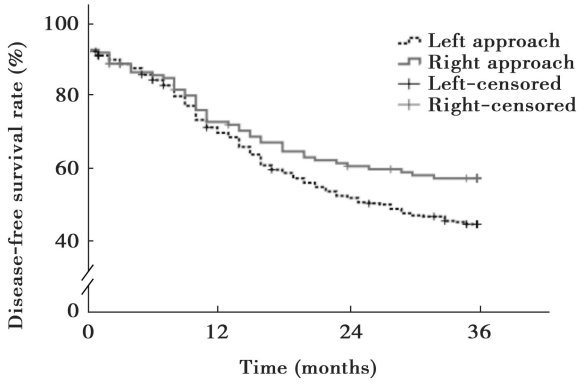

Figure 1 The disease-free survival curves of patients with esophageal carcinoma in left and right approach groups

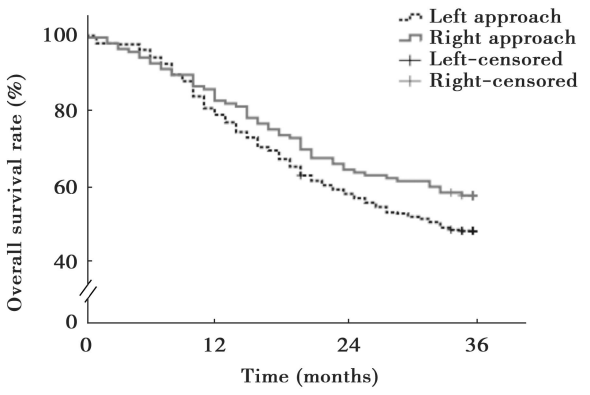

Figure 2 The overall survival curves of patients with esophageal carcinoma in left and right approach groups

approach in terms of operation time, blood loss, and blood transfusion. Meanwhile, the left approach causes less injury, shorter ICU stay, less occurrence of tracheotomy and lower hospital mortality as compared with the right approach.

Postoperative complications

Because the left approach stimulates the heart and aorta more frequently than the right approach, it has more impact on venous return and cardiac output, thereby increases the incidence of postoperative heart failure. The right approach causes more complications than the left approach, especially anastomotic leakage. It was reported that the incidence of anastomotic leakage after extended or total mediastinal lymph node resection was 10%-20%.[1] The reasons are as follows: 1) upper mediastinal resection and cervical anastomosis greatly compromise the blood supply of the esophagus; 2) the re-established gastric blood supply is influenced by the local mechanical compression of the chest bone or original esophageal bed; 3) the tension of gastro-esophagus anastomosis is great. The local compression and anastomotic tension may result in impaired postoperative gastric emptying. Moreover, the operation is extensive and the incidence of secondary operation caused by postoperative hemorrhage is high. Particularly, those lifting the stomach through the thoracic cavity without direct visualization are likely to increase the risk of hemorrhage.

Radical surgical resection and survival benefit

Radical resection is an independent prognostic factor of esophageal carcinoma. The relationship between surgical margin and prognosis has drawn wide attentions. Univariate and multivariate analyses show that positive margin is an independent factor for poor prognosis.[2-4] Therefore, adequate resection is mandatory to completely resect the mass. However, the present study showed that surgical margin was not influenced by different approaches. Moreover, the right and left approaches have pros and cons in exposing anatomic structures and regional lymph nodes surrounding the esophagus, and have no impact on the radical resection of middle thoracic esophageal carcinoma.

Thoroughness of lymph node resection is another factor that affects the efficacy of surgical treatment. Once the submucosa is involved, the lymph node metastatic rate markedly rises to 54.1%, and the metastasis is prone to involve extensive regions from the neck to the abdomen.[5] Due to the interruption by the aortic arch and related branches via the left approach, the lymph nodes around the esophagus and recurrent laryngeal nerve cannot be resected completely. In contrast, the right transthoracic

approach plus an incision on abdominal midline can sufficiently expose mediastinal and abdominal fields, facilitating the lymphadenectomy. The lymphadenectomy via the right approach is more favorable than that via the left approach, especially for the lymph nodes neighboring the esophagus and recurrent laryngeal nerve, which, as demonstrated by some studies, are important regions for lymph node metastasis of thoracic esophageal carcinoma.[6] Nagatani *et al*.[7] even proposed to perform intraoperative biopsy of lymph nodes surrounding the esophagus to determine whether cervical lymph node dissection should be performed. Thus, the surgical approach has great impact on the thoroughness of lymph node resection.

About half of the patients in the present study showed recurrence in three years, which is consistent with other reports.[8,9] Both the left and right approach groups were predominated with lymph node recurrence. However, this study showed that thorough lymph node resection via the right transthoracic approach could significantly reduce the recurrence rate. The patients in the right approach group had significant benefit in tumor-free survival despite their older ages than those in the left approach group. Altorki *et al*. [10] reported that extended lymph node dissection had survival benefit, especially for those with lymph node metastasis. Thus, most investigators think that radical lymphadenectomy can not only obtain accurate pathological stages but also decrease recurrence rate and improve survival.[1] In addition, Udagawa *et al*.[11] reported that three-field resection via the right transthoracic approach would get a 3- and 5-year survival rates of 60% and 53.8%, respectively. Thus, the right approach appears to be better than the left approach.

In conclusion, accurate staging, including exact positioning of tumor mass, involved extent and lymph node metastasis, will facilitate making surgical plans to excise the mass completely and choosing appropriate approach. From the present study, the right approach seems more desirable.

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