Radical Esophagectomy for Esophageal Cancer: Results in Thai Patients

Asada Methasate MD, PhD*,
Atthaphorn Trakarnsanga MD*, Thawatchai Akaraviputh MD*,
Vitoon Chinsawangwathanakol MD, PhD*, Darin Lohsiriwat MD*

** Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Radical esophagectomy was reported to have prolonged survival in patients with esophageal cancer. However, it is associated with high morbidity and mortality. Controversy still exists regarding value of radical esophagectomy.*
Material and Method: *The authors analyzed the results, including complications and survival in 68 consecutive patients with esophageal cancer who were treated with transthoracic radical esophagectomy at the Department of Surgery, Siriraj hospital, Mahidol University between June 2002 and June 2008.*
Results: *There were 57 males and eight females with a mean age of 59.28 $\pm$ 11.25 years. Regarding T staging, 81.5% of the patients were in T3 stage while 1.5% of the patients had T1 stage, 15.4% had T2 stage, and 1.5% had T4 stage. Lymph node metastasis (N1) was found in 63.1% of the patients and N0 was in 36.9%. Most of the patients were in advanced stages with 53.8% in stage III, 44.6% in stage II, and 1.5% in stage I. The 5-year survival rate of the patients with node positive was significantly lower than the patients with node negative (p = 0.018). The survival was significantly better in stage II compared to stage III (p = 0.012). Overall 5-year survival rate was 28.5%. Most common complications were from pulmonary causes (22.1%), anastomotic leakage (8.8%), and wound infection (8.8%). Mortality rate was 4.41%.*
Conclusion: *Radical esophagectomy was associated with relatively low mortality and acceptable survival. It should be considered in surgical treatment of patients with esophageal cancer.*

Keywords: *Radical esophagectomy, Esophageal cancer, Lymph node dissection*

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Esophageal cancer has a poor outcome because most of the patients are diagnosed at late stages with less than half of the patients being curative at time of diagnosis[1]. Surgery for esophageal cancer has long been an area of debates regarding the extent of dissection[2]. Japanese surgeon groups advocate radical esophagectomy with lymph node dissection because this operation yields higher survival rates[3-5]. However, this aggressive approach is associated with high morbidity and mortality[6]. Hence, the controversy to agree that radical esophagectomy is a safe operation.

In Thailand, various surgical approaches had been adopted in the treatment of esophageal cancer. The present study is the first to report the result of radical esophagectomy done in Thai patients.

Correspondence to:
Methasate A, Division of General Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.
Phone: 0-2419-8006
E-mail: teams@mahidol.ac.th

Material and Method

Sixty-eight consecutive patients with esophageal cancer who were treated with radical esophagectomy at Department of Surgery, Siriraj Hospital, Mahidol University between June 2002 and June 2008 were studied. Only cases operated with transthoracic approach were included in the present study. Data were prospectively collected and analyzed. Exclusion criteria were patients with preoperative neoadjuvant chemoradiation, or patients with distant metastasis, direct invasion of the tumor into neighboring organs, or unfit physical condition, in whom chemoradiation was implemented instead of surgery. Cases treated with transhiatal approach were excluded from the present study due to inadequacy of lymph node removal.

In all cases, esophagoscopy with biopsy was performed. Preoperative evaluations included CT scan of the chest and abdomen, cardiac evaluation, chest x-ray and pulmonary function test. Feeding jejunostomy or nasogastric tube placement was done in case of malnutrition. Surgery was performed in a well-planned manner by a single surgeon (AM) to ensure good quality control.

Details of the operative procedure:

The surgery started with the patient in left lateral decutibus position. Posterolateral thoracotomy was done at the 4th intercostal space. After entering pleural cavity, the tumor was inspected for sign of unresectability. The azygos vein was divided. Dissection of the esophagus along with locoregional lymph nodes was performed in a systematic manner from upper to lower esophagus.

The lymph node groups dissected in the operation are shown in Fig. 1. Care was taken to have complete clearance of the following lymph nodes:

Right and left paratracheal nodes: lymph nodes along the anterior and lateral wall of the trachea including the lower part of the trachea (tracheobronchial angle).

Right and left recurrent laryngeal nodes: lymph nodes along the right and left recurrent nerves.

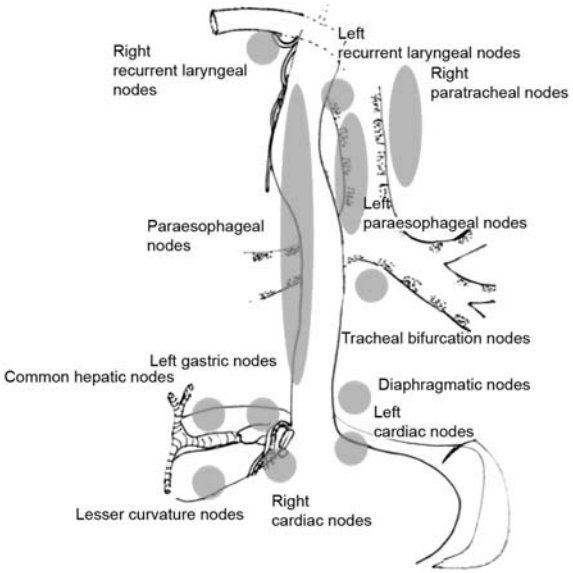

Fig. 1 Lymph nodes dissected during radical esophagectomy. Right lung and right bronchus were retracted anteriorly to expose posterior aspect of the trachea and entire esophagus

Paraesophageal nodes: lymph nodes along the esophagus from upper to lower part. In the upper part, lymph node dissection included the area around azygos vein and right bronchial artery.

Tracheal bifurcation nodes: lymph nodes located caudal to the carina.

Diaphragmatic nodes: lymph nodes located in the area surrounded by the diaphragm, pericardium and esophagus.

Abdominal lymph nodes: Cardiac node, lesser curvature nodes, left gastric nodes, and common hepatic nodes.

After complete dissection, the esophagus was then transected at upper esophagus above the tumor and secured with a plastic shield to prevent contamination. Intercostal chest drainage tube was inserted and the chest was closed in the usual manner.

The position of the patient was changed to supine position and the abdominal cavity entered via upper midline incision. Preparation of the gastric tube was done by dividing the gastrocolic ligament preserving right gastroepiploic arcade as the feeder vessel. Ligation of left gastric vessels was done along with dissection of common hepatic node (8a), left gastric node (7), and celiac node (9). Esophageal hiatus was opened and the esophagus was extracted into the abdomen. Kocherization and pyloroplasty was performed. The stomach was then divided longitudinally using staple device to form the gastric tube.

The left neck was opened with oblique incision along the anterior border of the sternocleidomastoid. Cervical fascia was opened and the esophagus was pulled out from the chest. In cases with upper and middle lesions, cervical lymph nodes were also dissected. The gastric tube was pulled up via the posterior mediastinal route into the neck region and anastomosis was done between gastric tube and upper esophagus using one layer interrupted sutures. The drain was placed behind the anastomosis. The abdomen and neck were closed in the usual manner.

The SSPS 14.0 software package was used for statistical data analysis (SSPS, Chicago, IL, USA). Descriptive statistics were used to summarize the data in terms of mean $\pm$ standard deviation (mean $\pm$ SD) and frequency with percentage. Survival times and curves were established according to the Kaplan-Meier method and compared by the log-rank test. All p-values were two-sided in tests and p-values < 0.05 were considered significant.

Results

Sixty-eight patients were enrolled in the present study. There were three deaths from pulmonary failure (mortality rate of 4.41%). Demographic data and survival rate were analyzed from 65 patients who survived the operations. Demographic data is shown in Table 1. There were 57 males and 8 females with a mean age of 59.28 ± 11.25 years. Location of the tumor was in the lower esophagus in 63.1%, middle esophagus in 35.4%, and upper esophagus in 1.5% of the patients. Mean tumor size was 5.16 ± 2.20 cm. Histologic types included squamous cell carcinoma in 72.3% and adenocarcinoma in 27.7%.

The operation was performed using transthoracic approach in all cases. Mean operating time was 386.00 ± 74.79 minutes. Average blood loss was 785.00 ± 355.07 ml. Average length of hospital stay was 19.65 ± 6.34 days.

Most of the tumors were in T3 stage (81.5%) while 1.5% of the patients had T1 stage, 15.4% had T2, and 1.5% had T4. Lymph node metastasis (N1) was found in 63.1% of the patients and N0 was in 36.9%. Most of the patients were in advanced stages, with stage III in 53.8%, stage II in 44.6%, and stage I in 1.5%. Harvested lymph nodes were 14.37 ± 9.32 nodes. Proximal margin was not free in 13.8% of the patients while circumferential margin was not free in 33.8%. Angiolymphatic invasion was found in 52.3% of the patients.

5-year survival of the patients with positive node was significantly lower than patients with negative node ($p = 0.018$) (Fig. 2). The survival was significantly better in stage II compared to stage III ($p = 0.012$) (Fig. 3). Overall 5-year survival rate was 28.5%.

Complications are shown in Table 2. Over all morbidity rate was 52.9%. Most common complications were from pulmonary causes (22.1%), anastomotic leakage (8.8%), and wound infection (8.8%). Recurrent nerve paresis was found in 7.4%. Rare complications included postoperative bleeding, tracheal injury, graft necrosis, and chylothorax. Mortality rate was 4.41% and all cases were the results of pulmonary complications that had developed to adult respiratory distress syndrome (ARDS).

Discussion

Radical esophagectomy with en-bloc dissection of lymph nodes is the standard surgery for esophageal cancer in Japan[7]. This procedure has benefits regarding extensive removal of the lymph

Table 1. Demographic data of the patients with radical esophagectomy

Characteristics	n = 65 (%)
Age (years): mean ± SD	59.28 ± 11.25
Male/female	57/8
Location	
Upper	1 (1.5)
Middle	23 (35.4)
Lower	41 (63.1)
Tumor size (cm)	5.16 ± 2.20
Histology	
Squamous cell carcinoma	47 (72.3)
Adenocarcinoma	18 (27.7)
Surgical margin	
Free	56 (86.2%)
Not free	9 (13.8%)
Circumferential margin	
Free	43 (66.2%)
Not free	22 (33.8%)
T category	
T1	1 (1.5%)
T2	10 (15.4%)
T3	53 (81.5%)
T4	1 (1.5%)
N category	
N0	24 (36.9%)
N1	41 (63.1%)
Staging	
I	1 (1.5)
II	29 (44.6)
III	35 (53.8)
Angiolymphatic invasion	
Presence	34 (52.3)
Absence	31 (47.7)
Harvested lymph nodes (nodes)	14.37 ± 9.32
Operation time (minutes)	386.00 ± 74.79
Blood loss (ml)	785.00 ± 355.07
Length of hospital stay (days)	19.65 ± 6.34

Table 2. Complications and mortality

	n = 68 (%)
Pulmonary complications	15 (22.1)
Chylothorax	1 (1.5)
Anastomotic leakage	6 (8.8)
Postoperative bleeding	1 (1.5)
Tracheal injury	1 (1.5)
Wound infection	6 (8.8)
Graft necrosis	1 (1.5)
Recurrent laryngeal nerve paresis	5 (7.4)
Over all morbidity	36 (52.9)
Mortality	3/68 (4.4)

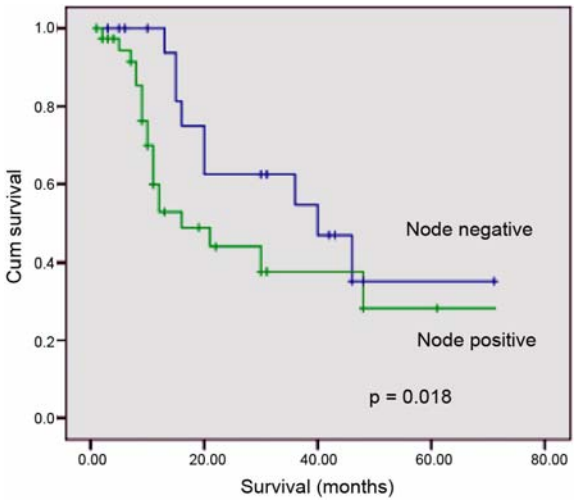

Fig. 2 The 5-year survival of the patients with positive node was significantly lower than patients with negative node (p = 0.018)

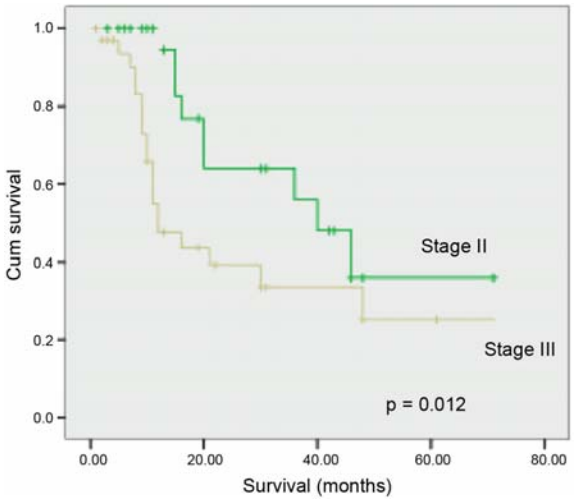

Fig. 3 The survival was significantly better in stage II compared to stage III (p = 0.012)

nodes in the upper mediastinum, especially along the recurrent nerve[8], lymph nodes along the esophagus, and at the lesser curvature of stomach. Improved survival has been reported in patients treated with aggressive lymph node dissection[9]. However, it has also been related with significant morbidity[10]. Therefore, some surgeons do not use this approach.

This is the first study to report the result of radical esophagectomy with aggressive lymph node dissection in Thailand. The authors' strategy was to use the same method as employed in Japan. Right thoracotomy approach was used to ensure adequate exposure to perform subtotal esophagectomy and meticulous dissection of lymph node in the mediastinum. After completion of the dissection, the patient was turned to supine position and the abdominal lymph node dissected with anastomosis done at the neck. Although, morbidity was seen in 52.94% of the patients, mortality rate was only 4.41% and only related with severe pulmonary complications.

In the present study, the authors had middle esophageal tumor in 35.4%, with only 1.5% in upper esophagus and 63.1% was in lower esophagus. The present finding suggests that the the middle and upper esophagus tumor is aggressive because not much of the tumor in this area could be resected. The high percentage of the tumor in the lower esophagus were more likely to be resectable compared to middle and upper esophagus. Therefore, this might be the reason for the relatively good survival rate, Moreover, 33.8% of the specimens resected were not free regarding circumferential margin. In the authors' opinion, adjuvant therapy in the form of chemoradiation is needed in the treatment of the cancer in this region.

Harvested lymph nodes in the present study were 14.37 nodes. The authors did not use transhiatal approach in the present study due to the inadequacy of lymph node dissection. This was in accordance with many studies[11-14] including randomized controlled trials comparing transhiatal approach and transthoracic approach with the result favoring transthoracic approach[15].

Survival of patients in stage III was significantly lower than those in stage II, suggesting the influence of lymph node metastasis on the survival of the patients. This finding was also supported by the poorer survival of the patients with node positive. The result was similar to the study from Omloo[16], reporting the better survival achieved by performing transthoracic esophagectomy in patients with limited lymph node metastasis.

The presented 5-year survival rate was 28.5%, which was lower than the reported 40-50% survival rate from Japan and other Western countries employing an aggressive approach[4,11,12]. This was partly due to the advanced stage of the disease presented in the present series, as can be seen from the fact that T3 stage was presented in 81.5% of the patients and 53.8% of the patients were in stage III. Attempt to detect earlier stage of the disease is required if higher survival is to be expected.

The authors concluded that radical esophagectomy was associated with relatively low morbidity and mortality with acceptable survival. It should be considered in the surgical treatment of the patients with esophageal cancer. This is especially true for patients who had difficulty gaining access to chemoradiation such as Thai patients. Earlier study emphasized the importance of having sufficient cases of esophagectomy to achieve good results[17]. Therefore, due to its complexity, the authors think that radical esophagectomy should be done by experts who are familiar and have adequate volume of this kind of surgery.

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ผลการรักษามะเร็งหลอดอาหารในผู้ป่วยไทยด้วยการผ่าตัดหลอดอาหารร่วมกับการเลาะต่อมน้ำเหลือง

อัษฎา เมธเศรษฐ, อัฐพร ตระการสง่า, ธวัชชัย อัครวิพุธ, วิทูร ชินสว่างวัฒนกุล, ดรินทร์ โล่ห์สิริวัฒน์

ในการผ่าตัดมะเร็งหลอดอาหาร การผ่าตัดหลอดอาหารร่วมกับการเลาะต่อมน้ำเหลืองถือเป็นการรักษาที่มีรายงานว่ามีอัตราการอยู่รอดสูงที่สุด อย่างไรก็ตามการผ่าตัดชนิดนี้มีผลแทรกซ้อนและอัตราตายมาก ทำให้ในปัจจุบันยังไม่มีข้อสรุปแน่ชัดว่าควรใช้การผ่าตัดนี้หรือไม่

การศึกษานี้ทำการวิเคราะห์ผลการผ่าตัด ภาวะแทรกซ้อน และอัตราการอยู่รอดในผู้ป่วยมะเร็งหลอดอาหารที่ได้รับการผ่าตัดหลอดอาหารโดยวิธีเข้าทรวงอก และทำการเลาะต่อมน้ำเหลือง จำนวน 68 ราย ซึ่งได้รับการผ่าตัดที่หน่วยศัลยศาสตร์ทั่วไป ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ระหว่างเดือนมิถุนายน พ.ศ. 2545 ถึง เดือนมิถุนายน พ.ศ. 2551

การศึกษานี้พบว่ามีผู้ป่วย 57 ราย เป็นเพศชายและ 8 ราย เป็นเพศหญิง โดยมีอายุเฉลี่ย 59.28 $\pm$ 11.25 ปี จากการวิเคราะห์ T staging พบว่า 81.5% อยู่ใน stage T3, 15.4% อยู่ใน stage T2, 1.5% อยู่ใน stage T4 และ 1.5% อยู่ใน stage T1 มีการกระจายไปต่อมน้ำเหลืองใน 63.1% ของผู้ป่วย จากการประเมิน staging พบว่า 53.8% อยู่ใน stage III และ 44.6% อยู่ใน stage II ภาวะแทรกซ้อนที่พบได้มากที่สุด ได้แก่ ภาวะแทรกซ้อนจากปอด (22.1%) นอกจากนี้พบว่ามีการรั่วที่รอยต่อ 8.8% และแผลติดเชื้อ 8.8% โดยรวมพบอัตราตาย 4.4% ผู้ป่วยที่ไม่มีการกระจายไปยังต่อมน้ำเหลืองมีอัตราการอยู่รอดที่ 5 ปี สูงกว่าผู้ป่วยที่มีการกระจายไปต่อมน้ำเหลืองอย่างมีนัยสำคัญ ($p = 0.012$) ผู้ป่วย stage II มีอัตราการอยู่รอดสูงกว่าผู้ป่วย stage III ($p = 0.012$) อัตราการอยู่รอดที่ 5 ปี 28.5%

การศึกษานี้พบว่าการผ่าตัดหลอดอาหารพร้อมกับการเลาะต่อมน้ำเหลืองมีความปลอดภัย เนื่องจากมีอัตราตายต่ำเหมาะสมที่จะนำมาใช้ในผู้ป่วยมะเร็งหลอดอาหาร