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Prognostic Benefits of Thoracoscopic Esophagectomy for Thoracic Esophageal Squamous Cell Carcinomas

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Rezumat

Beneficiile asupra prognosticului postoperator al esofagectomiei toracoscopice în cancerul esofagian cu celule scuamoase toracic

Date generale: Esofagectomia toracoscopică a fost introdusă pentru a reduce complicațiile pulmonare postoperatorii la pacienții cu cancer de esofag cu celule scuamoase (ESCC). Totuși, beneficiile acestei intervenții în ceea ce privește supraviețuirea nu au fost analizate în profunzime. Studiul de față analizează retrospectiv rezultatele clinice ale esofagectomiei toracoscopice la pacienți cu ESCC toracic operabil.
Metode: 84 de pacienți au fost incluși în studiu. Aceștia au fost diagnosticați cu ESCC toracic rezecabil în stadiile clinice I-III și au fost supuși rezecției esofagiene toracice cu disecția ganglionilor limfatici din 3 câmpuri de diseminare, la Spitalul Universitar Tottori, în perioada ianuarie 2007 – decembrie 2013. Incidența complicațiilor postoperatorii, supraviețuirea fără semne de boală (DFS) și supraviețuirea globală (OS) au fost comparate între grupul de toracotomie deschisă și grupul supus esofagectomiei toracoscopice.
Rezultate: 51 de pacienți au fost supuși metodei toracoscopice, iar 38 metodei deschise. Morbiditatea a fost de 42,9% și mortalitatea de 2,4%. Metoda toracoscopică a demonstrat o incidență mai mică a complicațiilor pulmonare postoperatorii. Supraviețuirea fără semne de boală la 5 ani nu a diferit între cele două grupuri. Totuși, supraviețuirea globală la 5 ani a pacienților supuși metodei toracoscopice a fost superioară celei aferente grupului supus metodei deschise.
Concluzii: Esofagectomia toracoscopică pentru ESCC toracic este fezabilă din punct de vedere tehnic, iar rata scăzută a complicațiilor pulmonare postoperatorii poate prelungi supraviețuirea globală a pacienților.

Cuvinte cheie: supraviețuire fără semne de boală, carcinom cu celule scuamoase esofagian, supraviețuire globală, esofagectomie toracoscopică

Abstract

Background: Thoracoscopic esophagectomy has been introduced to reduce postsurgical pulmonary complications in patients with esophageal squamous cell carcinomas (ESCCs). However, the survival benefit of this procedure has not been well examined. In the present study, we retrospectively investigated the clinical outcomes of thoracoscopic esophagectomy in patients with operable thoracic ESCCs.
Methods: Eighty-four patients were enrolled in this study. They were diagnosed with resectable clinical stage I-III thoracic ESCCs and underwent thoracic esophageal resection with three-field lymph node dissection at Tottori University Hospital between January 2007 and December 2013. Occurrence of postoperative complications, disease-free survival (DFS) and overall survival (OS) were compared between the open thoracotomy group and the thoracoscopic esophagectomy group.
Results: Fifty-one patients underwent the thoracoscopic method, while 38 underwent the open method. Morbidity was 42.9% and mortality was 2.4%. The thoracoscopic method showed a lower occurrence of postoperative pulmonary complications. The 5-year DFSs of the two

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groups were not different. However, the 5-year OS of patients in the thoracoscopic method group was superior to that of those in the open method.
Conclusions: Thoracoscopic esophagectomy for thoracic ESCCs is technically feasible and the low rate of postoperative pulmonary complications may prolong the OS of patients.

Key words: disease-free survival, esophageal squamous cell carcinomas, overall survival, thoracoscopic esophagectomy

Introduction

In a study on Japanese patients with resectable thoracic esophageal squamous cell carcinomas (ESCCs), it was found that metastatic lymph nodes were detected in the neck, chest, and abdomen, and that subtotal esophagectomy with radical lymph node dissection remains an effective therapeutic strategy for localized thoracic ESCCs (1,2). However, because of the high operative invasiveness during thoracotomy and laparotomy, high morbidity, and high mortality occur in patients with thoracic ESCCs, and therefore, surgical treatment for thoracic ESCCs has been limited (3,4). For example, patients with T4 cancer (invasion to adjacent organs), with distant metastasis (to lung, liver, bone, or extended lymph nodes), with poor Eastern Cooperative Oncology Group Performance Status (PS), with severe dysfunction of organs, such as cardio-pulmonary, liver, and kidney, or over 80 years of age have been excluded from surgical treatments (5,6).

Since administration of minimally invasive approaches to esophageal resection including laparoscopic mobilization of the stomach and thoracoscopic mobilization of the esophagus, surgical management for ESCCs has been dramatically changed (6,7). However, prognosis of patients with ESCCs developed in the thoracic esophagus is still poor. Thus, in the present study, we analyzed survival benefits of minimally invasive esophagectomy in thoracic ESCCs.

Materials and Methods

Patients

Esophagogastroscopy, computed tomography (CT) scanning, endoscopic ultrasound and positron emission topography were all routinely used in staging the tumors of patients diagnosed with ESCCs. Fitness for surgery was assessed through clinical examination, pulmonary function tests, electrocardiography, echocardiography, and exercise tolerance testing. Following physical examination, and hematological and biochemical investigations, patients with potentially resectable disease, who were deemed physiologically fit for surgery, were analyzed in this study. Between January 2007 and December 2013, 84 patients with clinical stage I-III thoracic ESCCs underwent thoracic esophageal resection and three-field lymph node dissection at Tottori University Hospital. Patients who underwent transhiatal esophagectomy without thoracotomy, left side thoracotomy with laparotomy plus two-field lymph node dissection, or a salvage operation were excluded from this study. Average age of patients was 65.7 years old (range: 49-78 years). Seventy-three were males and 11 were females. Informed consent was obtained from all patients. All investigations reported in this study were conducted in conformity with recommendations from the Declaration of Helsinki. All patients were followed at Tottori University Hospital until September 2015. The median follow-up period was 35.5 months (range: 1–102 months).

Operation

Between January 2007 and August 2009, traditional right anterolateral thoracotomy with laparotomy (open method) was routinely performed. Since September 2009, thoracoscopic thoracic esophagectomy under the prone position was introduced (thoracoscopic method) to reduce postoperative pulmonary complications. In this procedure, the patient is placed in the prone position and the esophagus is approached through the right chest (thoracoscopic method). The right lung is kept ventilated but is collapsed due to the action of gravity and an 8-mm Hg CO2 pneumothorax (8). However, right anterolateral thoracotomy is indicated in cases with strong adhesion between the lungs and the pleura. The open method was performed on 33 patients and the thoracoscopic method, on 51 patients.

The narrow gastric tube was used as a substitute esophagus in 74 patients, but in 10 patients with double cancers (esophageal and gastric) or in gastrectomized cases, jejunum was elongated to the cervical esophagus or pharynx through the ante-sternum root. Anastomoses between the cervical esophagus or pharynx and gastric tube or jejunum were performed using the Gambee method.

Chemotherapy

S-1 adjuvant chemotherapy had been introduced for patients with stage II or III ESCCs prior to 2010 in our institute. Neoadjuvant chemotherapy with cisplatin plus 5-fluorouracil has been offered to patients who were diagnosed with clinical stage II and III ESCCs since 2010, according to information from the Japan Clinical Oncology Group (JCOG) study (9). Thus, chemotherapy was used to treat 45 patients (adjuvant: 7, neoadjuvant: 27, and both: 11).

Pathological analysis

The UICC TNM classification for esophageal cancer was used for tumor staging (10). An R0 resection was defined as complete tumor excision with all margins histologically free of tumor. According to the UICC TNM classification, there were 29 patients with stage I, 22 with stage II, and 33 with stage III ESCCs.

Statistical analysis

The Mann–Whitney U test, chi-squared test and Fisher's exact probability test were used to compare the clinicopathological characteristics of the two groups. Spearman's rank correlation coefficient was used to assess the correlation between the two numerical parameters. Long-term survival was calculated using the Kaplan–Meier method and the prognostic difference between the two groups was compared using the log-rank test. Multivariate Cox regression analysis was used for all parameters that were found to be significant using univariate analysis. A P-value <0.05 was considered statistically significant.

Results

A total of 84 patients underwent esophagectomy, 51 of whom underwent the thoracoscopic method and 33 the open method. *Table 1* indicates clinical differences between open and thoracoscopic methods. The thoracoscopic method had a longer operation time, less intraoperative blood loss, a more extended number of dissected lymph nodes, a lower occurrence of postoperative complications, and a shorter postoperative hospital stay than traditional esophagectomy with thoracotomy. Surgical complications were detected in 36 patients (morbidity was 42.9%). Anastomotic leakage was detected in 23 patients, pneumonia in 6, chylothorax in 4, and necrosis of the substituted esophagus in 3. Two patients (chylothorax: 1 and necrosis of substituted esophagus: 1) died because of operative complications and mortality was 2.4%. The occurrence of postoperative complications was compared between groups (*Table 2*). Thoracoscopy could reduce the occurrence of postoperative pneumonia compared with the open method. Conversely, the occurrence of postoperative chylothorax was detected only in the thoracoscopic method group.

The 5-year disease-free survival (DFS) and 5-year overall survival (OS) rates for all patients were 52.2% and 50.8%, respectively. The 84 patients were divided into the following sub-groups of two: with postoperative complications versus without postoperative complications, with pre- and/or postoperative chemotherapy versus without pre- and/or postoperative chemotherapy, open method versus thoracoscopic method, and stage I and II versus stage III. The long-term outcomes were compared between each of the two groups (*Table 3*). The mean postoperative hospital stay of 36 patients with postoperative complications (81.3 days) was significantly longer than that of 48 patients without postoperative complications (27.1 days, $P<0.001$), but postoperative complications did not affect patient survival (*Table 3*). Additionally, the 5-year DFS of the 51 patients treated using the thoracoscopic method was not different from that of the 33 patients treated using the open method. However, the 5-year OS of patients treated using the thoracoscopic method was significantly superior to that of patients treated using the open method (*Fig. 1*).

Table 1. *Intra and postoperative differences between the open method group and thoracoscopic method group*

	Open method	Thoracoscopic method	*P*
N	33	51	
Age (Mean±SD, years)	64.2±7	66.7±6.6	0.162
Gender (Male/Female)	30/3	43/8	0.382
Operation time (Mean ±SD, minutes)	590.9±101.7	686.6±116.7	<0.001
Intraoperative blood loss (Mean ±SD, mL)	805.8±603.5	261.4±368.3	<0.001
Number of dissected lymph nodes (Mean ±SD)	44.6±20.7	54.5±17.2	0.007
Histological stages of tumors (Stage I/II/III)	12/7/14	17/15/19	0.703
Postoperative complications (Yes/No)	18/15	18/33	0.082
Postoperative hospital stay (Mean ±SD, days)	69.2±89.9	38.1±27.8	0.031

SD: standard deviation

Table 2. *Postoperative complications*

	Open method	Thoracoscopic method
N	33	51
No complications	15	33
Anastomotic leakage	12 (36.4%)	11 (21.6%)
Pneumonia	5 (15.2%)	1 (2%)
Chylothorax	0	4 (7.8%)
Necrosis of substituted esophagus	1 (3%)	2 (3.9%)

Table 3. *Long-term outcomes were compared between the two sub-groups*

	N	5-year DFS	5-year OS
Postoperative complications			
No	48	53.6%	55.5%
Yes	36	50.3%	44.4%
P		0.834	0.13
Chemotherapy (pre + postoperative)			
No	40	60.9%	61%
Yes	44	43.5%	40.5%
P		0.128	0.167
Operative procedure			
Open method	33	46.2%	39.4%
Thoracoscopic method	51	55.8%	60.4%
P		0.217	0.033
Histological stages of tumors			
Stage I and II	52	74.6%	68.2%
Stage III	32	16.9%	18.5%
P		< 0.001	< 0.001

DFS: disease-free survival, OS: overall survival

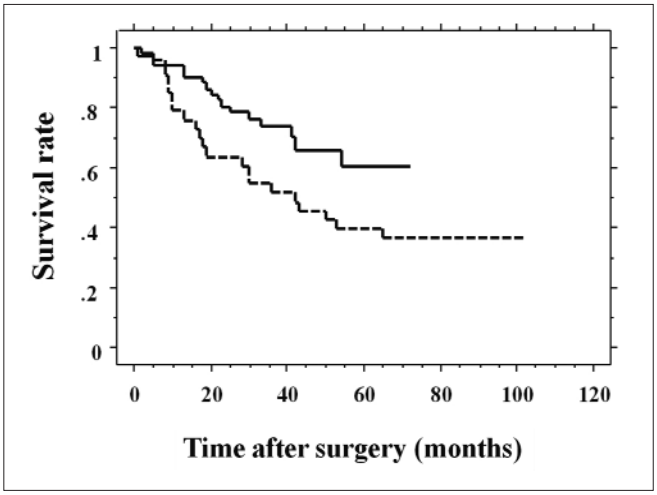

Figure 1. *The overall survival curve of 51 patients treated using the thoracoscopic method (solid line) was significantly superior to that of 33 patients treated using the open method (dotted line, P=0.033)*

Discussion

Minimally invasive surgery such as thoracoscopic esophagectomy with patients in the prone position for thoracic ESCCs has been introduced to reduce the occurrence of postoperative complications. Bailey et al. (7) reported that even though the operative time for the thoracoscopic method was longer than that for the open method, this phenomenon did not affect postoperative patient conditions. Furthermore, they reported that thoracoscopic esophagectomy was associated with a lower overall complication rate when compared with open surgery. In our cohort, we found that thoracoscopic esophagectomy could reduce the occurrence of postoperative complications and the overall length of postoperative patient hospital stays. More importantly, we found that thoracoscopic esophagectomy could reduce the occurrence of anastomotic leakage and pulmonary complications, however, this method increased the risk of chylothorax. Kubo et al. (11) and Iwahashi et al. (12) reported similar results. From these facts, it is indicated that the thoracic duct may be difficult to detect during thoracoscopic surgery or the thoracic duct is easy to catch the heat damage with an electric scalpels or the supersonic wave incision solidification devices and causes lymph fluid leakage easily. Thus, we need to pay more attention to finding the thoracic duct during thoracoscopic surgery to reduce the occurrence of postoperative chylothorax. Additionaly, Turaga et al. (13) reported that the incidence of cardiac arrhythmias was reduced in patients undergoing thoracoscopic esophagectomy because of the absence of pericardial retractors used in open surgery.

Oncological advantages of thoracoscopic esophagectomy for ESCCs have been discussed. Bailey et al. (7) reported that minimally invasive surgery for thoracic ESCCs showed comparable oncological and long-term survival outcomes when compared with open surgery. Also, Hsu et al. (14) showed that the total number of harvested lymph nodes in thoracoscopic esophagectomy was similar to that of open surgery, but that the 3-year DFS and OS were superior in the thoracoscopic group compared with those in the open surgery group. From our results, we found that the mean number of dissected lymph nodes in the thoracoscopic esophagectomy group was much greater than that in the open surgery group. Even though, no significant difference in the 5-year DFS between groups was detected, we found that the 5-year OS of patients with thoracoscopic esophagectomy was significantly better than that of patients with open surgery. From these data, we postulated that the oncological prognostic benefit of thoracoscopic esophagectomy would be equal to open surgery in thoracic ESCCs. Moreover, thoracoscopic surgery could control the occurrence of postoperative pulmonary complications. Thus, thoracoscopic surgery could be advantageous for patient postoperative recovery, and might favor for patient long-term survival.

We acknowledge that there are some weaknesses in this study. We accept that our cohort size was relatively small compared with previous studies. In addition, this study was a retrospective study and the lack of selection bias may have added considerable weight to our findings. To prove the survival benefits of thoracoscopic surgery compared with open surgery, a randomized control trial should be considered. However, if patients don't undergo thoracoscopic surgery, they will not have the same quality of life postoperatively. So, a randomized-controlled trial (thoracoscopic surgery versus open surgery) will not be feasible in the future.

Conclusion

In conclusion, this study demonstrates that performing thoracoscopic esophagectomy for thoracic ESCCs is technically feasible and has a lower postoperative complication rate when compared with open surgery with comparable 5-year DFS but better 5-year OS outcomes.

Conflicts of interest and source of funding: None

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