Original Article
Minimally invasive esophagectomy for esophageal squamous cell carcinoma in elderly patients

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Abstract: The purpose of this retrospective study was to investigate the value of minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) for esophageal squamous cell carcinoma in elderly patients (≥70 years). From January 2009 to December 2014, 58 consecutive patients aged older than 70 years with clinical stage stage I or II esophageal squamous cell carcinoma underwent minimally invasive esophagectomy. We reviewed short- and long-term outcomes. There were 41 men and 17 women with a median age of 74 years. Postoperative 30-day complications occurred in 21 patients. There was no 30-day death. Median hospital stay was 10 days. Median follow-up was 32 months. The 5-year overall survival and disease-free rates were 55% and 38% respectively. In summary, with appropriate selection of patients and procedures, minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) can be safely used for esophageal squamous cell carcinoma in elderly patients with acceptable prognostic results.

Introduction

According to the latest statistical analysis, life expectancy in 70-year-olds was 13 years for men and women in China. The population in China is aging, and mass screening of the general population for esophageal squamous cell carcinoma is also increasing as the proportion of elderly patients with esophageal squamous cell carcinoma continues to increase [1-5]. Radical resection with sufficient lymphadenectomy remains the treatment of choice for operable esophageal squamous cell carcinoma in elderly patients (≥70 years), but surgical morbidity and mortality rates are higher among elderly patients than in young patients (<70 years) because of the increased prevalence of coexisting cardiovascular or pulmonary disease, such as hypertension, stable angina and chronic obstructive pulmonary disease [6-10]. Surgeons are often faced with the critical decision of whether to operate with elderly patients. Recently, several authors have emphasized the efficacy of minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) [11-18]. To determine whether cura-

tive resection using minimally invasive esophagectomy is feasible in elderly patients with clinical stage I-II esophageal squamous cell carcinoma, we reviewed the early morbidity, mortality, and the long-term survival outcomes of patients older than 70 years who underwent minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) in a single institution in China.

Patients and methods

This study complied with the Declaration of Helsinki. This retrospective research was approved by our local ethics committees. The need for informed consent from patients was waived because of retrospective study, not prospective research.

From January 2009 to December 2014, 358 patients underwent radical esophagectomy for primary esophageal squamous cell carcinoma at our institution, and 64 patients (17.9%) aged 70 years or older (≥70 years) underwent surgical resection with radical intent. As a rule, surgical treatment was used in primary esophageal

Table 1. Patient baseline characteristics

Age (years)	74 (70-81)
Sex	
Male	41
Female	17
ASA score	
I	20
II	35
III	3
Performance status	
0	39
1	18
2	1
Comorbidity	
Chronic obstructive pulmonary disease	8
Prior tuberculosis	3
Hypertension	15
Angina pectoris	6
Prior acute coronary syndrome	4
Diabetes mellitus	7
Clinical TNM stage (7th AJCC-UICC)	
IB	20
IIA	29
IIB	9

squamous cell carcinoma patients with clinical stage I or II disease.

Radical esophagectomy was performed in elderly patients with good performance status (Performance Status 0 to 2), when the predicted postoperative forced expiratory volume in the first second was more than 1000 ml, or when patients did not have severe preoperative cardiopulmonary disease and delirium. The preoperative workup included upper gastrointestinal endoscopy, biopsy, magnetic resonance imaging scan or computed tomographic scan of brain, computed tomographic scan chest, and ultrasonography of neck and abdominal. In selected cases, positron emission tomography-computerized tomography (PET-CT) and bone scanning were performed when tumor metastasis was suspected. The clinical stage of esophageal squamous cell carcinoma was based on the 7th edition of the TNM classification of esophageal carcinoma which was proposed by American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC) [19-21]. For those of the patients treated before 2010, their staging was

recalculated to match the 7th TNM classification by AJCC and UICC.

Preoperative examinations showed that 58 patients had clinical stage I or II esophageal squamous cell carcinoma without lymph nodes metastais. These 58 patients underwent minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) with radical intent. All the surgeries were performed by two experienced surgeons (Yong Li and Gongning Shi) with proven expertise in esophageal carcinoma. The resection was performed with curative intention in all patients. The procedures of the MIE were as follows: thoracoscopic esophageal mobilization and mediastinal lymphadenectomy, laparoscopic gastric mobilization, gastric tube formation, abdominal lymphadenectomy and cervical anastomosis [13].

A retrospective review of patient clinical variables included age, sex, pulmonary function, comorbidity, American Society of Anesthesiology (ASA) class, clinical TNM stage, as well as perioperative data, such as operation time, blood loss, duration of chest drainage, postoperative hospital stay, pathologic TNM stage, results of lymphadenectomy, operative morbidity, and mortality.

Morbidity was defined as postoperative complications occurring within 30 postoperative days. Mortality was defined as death of any cause occurring within 30 postoperative days. Postoperative complication severity was stratified according to the modified Clavien classification. The definition of Clavien-Dindo system was as follows: Grade 1: oral medication or bedside medical care required; Grade 2: intravenous medical therapy required; Grade 3: radiologic, endoscopic, or operative intervention required; Grade 4: chronic deficit or disability associated with the event; and Grade 5: death related to surgical complication. Major complications were defined as grades 3, 4 and 5. Minor complications were classified as 1 and 2. The detail of Clavien-Dindo classification has been reported [22, 23].

All the patients were followed with a standard oncologic protocol of surveillance that included abdominal and chest computed tomography scan and ultrasonography of neck every 6 months after esophagectomy. Upper gastroin-

Table 2. Surgical and pathological data

Operative time (min)	230 (180-370)
Blood loss (ml)	280 (190-490)
Blood transfusion *n*	3
Chest drainage (day)	4 (3-12)
Postoperative hospital stay (day)	10 (8-36)
Retrieved lymph nodes	16 (9-25)
Pathological TNM stage (7th AJCC-UICC)	
IB	6
IIA	20
IIB	17
IIIA	5
IIIB	6
IIIC	4
Surgical margin (R0/R1/R2)	58/0/0

Table 3. Postoperative 30-day complications and outcome

Pulmonary complications	
Pneumonia	11
Pulmonary dysfunction	3
ARDS	2
Pulmonary embolism	1
Cardiacvascular complications	
Atrial fibrillation	5
Heart failure	3
Acute coronary syndrome	1
Gastrointestinal complications	
Anastomotic leak	4
Delayed gastric emptying	3
Others	
Recurrent laryngeal nerve injury	2
Chylothorax	1
Total (events/patients)	36/21
Morbidity	21
Major complications	6
Minor complications	30
Mortality	0

ARDS: acute respiratory distress syndrome.

testinal endoscopy is suggested every once a year after esophagectomy. The last follow up was June 2015. Tumor recurrence was diagnosed by history, physical examination, endoscopic evaluation, radiologic investigations, or pathology when available. Recurrence was classified as locoregional recurrence, distant metastasis and mixed. Locoregional disease was defined as recurrence within the esopha-

gus bed, the regional lymph nodes, or the anastomosis. Distant disease included metastasis at distant organ sites (brain, lung, liver, bone, adrenal, distant lymph nodes or other organs). The overall survival was assessed from the date of esophagectomy until the last follow up or death of any cause. The disease-free survival was calculated from the date of esophagectomy until the date of cancer recurrence or death from any cause.

Data were presented as mean and standard deviations for variables following normal distribution. For data following non-normal distribution, results were expressed as median and range. Survival rates were analyzed using the Kaplan-Meier method. $P<0.05$ was considered statistically significant. SPSS (Solutions Statistical Package for the Social Sciences) 15.0 for Windows version (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results

The characteristics of 58 patients are listed in **Table 1**. Their median age was 74 years (range 70 to 81 years), and 41 were men and 17 were women. The preoperative Performance Status of the 58 patients was 0 to 2. Thirty of 58 patients (51.7%) had comorbidity. Pulmonary comorbidities included chronic obstructive pulmonary disease in 8 patients, of which 6 were receiving oral bronchodilators or inhaled medication; others were prior tuberculosis in 3 patients. The most common cardiacvascular comorbidity was hypertension in 15 patients, 6 had a history of angina pectoris and 4 had a prior acute coronary syndrome. Seven patients had diabetes mellitus which were treated by insulin or hypoglycemic drugs.

Median operation time was 230 minutes (range, 180 to 370 minutes) (**Table 2**). Blood loss was 280 ml (range, 190 to 490 ml). No patient converted to open resection in our series. Three patients were given blood transfusion perioperatively. The chest drainage tube was removed when air leak stopped. Median duration of chest drainage was 4 days (range, 3 to 12 days). The median length of postoperative hospitalization was 10 days (range, 8 to 36 days).

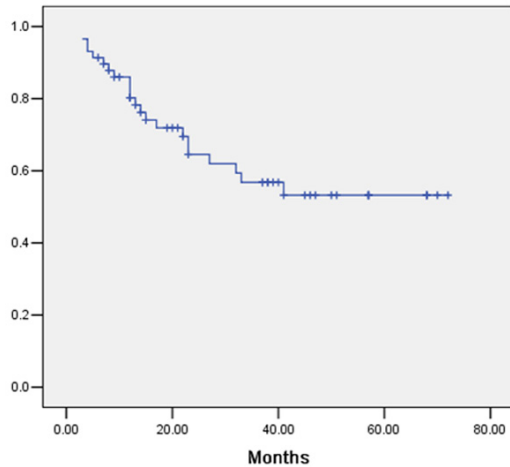The pathologic stage of esophageal squamous cell carcinoma was classified as I in 6 patients,

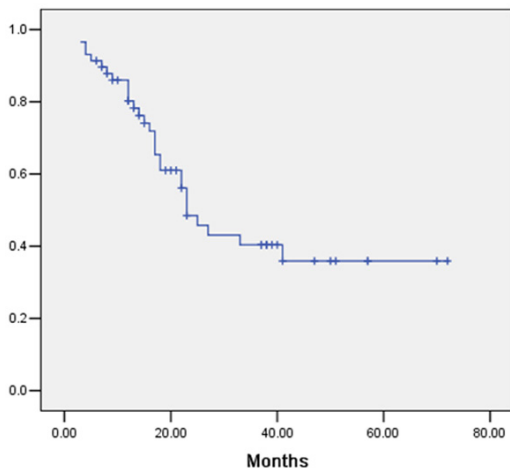Figure 1. Overall survival curve with Kaplan-Meier method.

Figure 2. Disease-free survival curve with Kaplan-Meier method.

II in 37, and III in 15 (**Table 2**). Eleven patients received postoperative cisplatin-based adjuvant chemotherapy.

Table 3 outlines the postoperative 30-day complications and outcome. One or more postoperative 30-day complications occurred in 21 patients and 37 patients had no postoperative 30-day complications. The most common postoperative complication was pneumonia in 11 patients. Other pulmonary complications were pulmonary embolism in 1 patient, respiratory failure in 3 patients, and acute respiratory distress syndrome (ARDS) in 2 patients. Most of the pulmonary complications were manageable by drugs. Cardiacvascular complications were

atrial fibrillation in 5 patients, heart failure that need medication in 3 patients, acute coronary syndrome that need emergency coronary intervention and stenting in 1 patient. There was no 30-day mortality in our series.

Median follow-up was 32 months. The 5-year overall survival and disease-free rates of the 58 patients were 55% and 38% respectively (**Figures 1** and **2**). At the time of analysis, 20 patients had died of the disease, 2 had died of other causes, and 36 patients were alive with or without evidence of cancer recurrence. The distribution of recurrence was local recurrence in 11 patients, and distant metastasis in 13 patients. Two patients had both local and distant metastases (**Table 4**). For patients with pathologic stage I esophageal squamous cell carcinoma, the 5-year overall survival was 76%, for stage II was 69%, and for stage III was 25%.

Discussion

The population in China is aging; life expectancy in 70-year-olds exceeds 10 years. The average life expectancy of patients with untreated or palliated esophageal squamous cell carcinoma is no more than 3 years; therefore, radical resection with sufficient lymphadenectomy for esophageal squamous cell carcinoma in this age group should be strongly considered if it can be performed with acceptable short-term and long-term outcomes [24].

However, elderly patients with esophageal squamous cell carcinoma have more medical comorbidity than younger counterparts, increasing the risks associated with radical esophagectomy with sufficient lymphadenectomy. The mortality rate of patients aged 70 years and older who underwent surgical resection with radical intent for esophageal carcinoma was 10% to 20% in studies performed before 1990 [24]. In recent studies, however, operative mortality was 0% to 7% in elderly patients (≥70 years) undergoing radical esophagectomy with sufficient lymphadenectomy [25-28].

Although Ivory-Lewis esophagectomy (right thoracic-abdominal esophagectomy) is more technically challenging than left thoracic esophagectomy or transhiatal esophagectomy, it has been shown to have a two to three times lower incidence of cancer recurrence than left tho-

Table 4. Tumor recurrence data

Recurrence	
Negative	32
Positive	26
Locoregional	11
Cervical lymph node	3
Anastomosis	3
Mediastinal lymph nodes	5
Distant	13
Brain	3
Liver	4
Lung	2
Kidney	2
Mixed	2

racic esophagectomy or transhiatal esophagectomy [24]; therefore, Ivory-Lewis esophagectomy is an ideal procedure for esophageal squamous cell carcinoma in elderly patients (≥70 years). However, Ivory-Lewis esophagectomy is an invasive procedure for elderly patients with concomitant cardiopulmonary diseases. Minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) is believed to substantially reduce surgical related morbidity and mortality in elderly patients (≥70 years) [16, 29].

Two studies have looked at minimally invasive esophagectomy (combined thoracoscopic-laparoscopic esophagectomy) in the elderly [16, 29]. Li J and his hospital associates [16] have reported that operative mortality among 89 patients who underwent minimally invasive esophagectomy was 3.4% and that analyses of postoperative conditions suggest the superiority of minimally invasive esophagectomy in terms of the length of hospital stay and short stay in the ICU (intensive care unit). Patients who undergo minimally invasive esophagectomy for esophageal squamous cell carcinoma have a low incidence of postoperative complications compared with those who underwent open esophagectomy. Puntambekar S and his hospital associates [29] reported in their study that minimally invasive esophagectomy was performed on 68 elderly patients (≥70 years) with esophageal carcinoma and their mortality rate was 4.4%. However, the long-term outcome was not described.

Some previous studies have revealed that the length of postoperative hospital stay in elderly patients (≥70 years) with esophageal carcinoma is associated with the occurrence of postoperative pulmonary complications [30, 31]. Therefore, minimally invasive esophagectomy is recommended for curative resection in elderly patients (≥70 years).

Although esophagectomy with radical mediastinal and abdominal lymphadenectomy is ideal in younger patients from the viewpoint of surgical oncology, in elderly patients, this radical resection may be a risk factor for postoperative complications that can lead to severe morbidity or death. Some thoracic surgeons have doubted the efficacy of radical mediastinal and abdominal lymphadenectomy. The risk of postoperative morbidity may increase, and there may be no impact on prolonging survival [24]. However, since 2008, because minimally invasive mediastinal and abdominal lymphadenectomy had become established, radical lymphadenectomy was performed in low-risk elderly patients with esophageal carcinoma. In this study, there were no postoperative complications directly to lymphadenectomy in elderly patients and our long-term survival was acceptable compared with previous literatures.

Although the size of the sample and period of follow-up was insufficient to properly determine the effectiveness of minimally invasive esophagectomy in elderly patients, surgical treatment with minimally invasive esophagectomy was an acceptable procedure with acceptable short-term and favorable long-term outcomes. However, these patients also need careful follow-up after radical resection because of the possibility of cancer recurrence in the longer follow-up period.

In conclusion, minimally invasive esophagectomy minimally invasive esophagectomy in elderly patients (≥70 years) is a satisfactory alternative treatment. Although advanced age is not a contraindication for curative resection, we should decide on the proper selection of patients and radical resection.

Discourse of conflict of interest

None.

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