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ORIGINAL ARTICLE

Clinical features and prognostic factors for surgical treatment of esophageal squamous cell carcinoma in elderly patients

Yongli Liu, Xiaojun Chen, Yuhu Wang, Fang Wang, Yuyan Gong, Jingui Zhang

The Central Hospital of Binzhou, Binzhou, Shandong 251700, P. R. China

Summary

Purpose: *This research was designed to analyze the clinical features and prognostic factors for surgical treatment of esophageal squamous cell carcinoma (ESCC) in elderly patients aged 70 years and over.*

Methods: *The clinical data and follow-up data of 68 ESCC patients aged 70 years and over were collected. The characteristics of surgical treatment, perioperative complications, overall survival (OS), and the factors affecting survival were analyzed.*

Results: *The incidence rate of postoperative complications was 36% and the mortality rate was 0% during and 90 days after surgery. The 5-year OS was 45.0% and the 5-year disease-free survival (DFS) was 38.0%. Univariate analysis showed that gender, Charlson Comorbidity Index (CCI), pathological type, tumor differentiation, depth of invasion, postoperative complications, and lymph node metastasis were the factors associated with OS. Multivariate analysis showed that pathologic type, depth of invasion, and lymph node metastasis were the independent predictors of OS. The ideal long-term survival in elderly patients with ESCC was achieved with radical resection.*

Conclusion: *The pathological type and pathological stage were the important independent risk factors of prognosis.*

Key words: *elderly patients, esophageal squamous cell carcinoma, esophagectomy, prognostic factors, surgery, survival*

Introduction

Currently, the main treatment of esophageal squamous cell carcinoma (ESCC) is surgery and chemoradiotherapy [1-6]. The indications for radiotherapy in ESCC were less strict than surgical treatment; however, local recurrence is the main reason of failure for ESCC treated by chemoradiotherapy alone [7-10]. Studies have shown that 5-year OS of ESCC patients undergoing radiotherapy is about 10% [7-10]. Chemotherapy in ESCC is mainly used for advanced disease and distant metastasis, or used with surgery for combined therapy as auxiliary or palliative treatment. Surgical treatment has thus become the primary radical approach for ESCC nowadays [1-4]. Because the elderly patients with ESCC belong to a special population and the functions of most of their organs are decreased, they are less likely to tolerate surgery than the middle-aged patients [11-22]. However, the majority of elderly patients can still achieve a good result after surgery through full preoperative preparation, careful perioperative management, and improvements in anesthesia, surgical techniques, and general medicine treatment [11-22]. This article aimed to discuss the clinical features and prognostic factors of surgical treatment in elderly patients with ESCC.

Corresponding author: Jingui Zhang, MD. The Central Hospital of Binzhou, Binzhou, Shandong 251700, People's Republic of China.
Tel and Fax: +86 543 5322880, Email: ie27ju@163.com
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Methods

The research was approved by our local ethics committee. The requirement of informed consent from patients was waived because of the retrospective nature of the research.

From January 2010 to January 2015, 68 patients with ESCC, who were hospitalized and treated with radical dissection and had complete clinical and follow-up data, were enrolled in this study. There were 46 males and 22 females. All cases were pathologically diagnosed with ESCC. Routine blood tests, liver and kidney functions, pulmonary functions, electrocardiogram, electronic endoscopy, and chest and abdominal computed tomography (CT) were routinely performed preoperatively to exclude surgical contraindications and distant metastasis. PET-CT or bone scan was performed when necessary [23-26]. Preoperative risk assessment was performed in all elderly patients. Internal medicine diseases were actively treated before operation. Tumor staging was based on the 7th edition of TNM staging published in 2009.

Statistics

Data are presented as means and standard deviations for variables with a normal distribution. For data with a non-normal distribution, results are expressed as medians and ranges. Survival rates were analyzed using the Kaplan-Meier method. Univariate analyses were performed to identify prognostic variables related to OS. Univariate analyses were also performed to identify the prognostic variables related to conversion. Univariate variables with probability values <0.05 were selected for inclusion in the multivariate Cox proportional hazard regression model. P<0.05 was considered statistically significant. SPSS 14.0 (SPSS Inc., Chicago, IL, USA) Microsoft Windows version was used for all statistical analyses.

Table 1. Baseline characteristics of the patients (n=68)

Characteristics	*n (%)*
Age, years, median (range)	73 (70-76)
Sex	
Male	46 (67.6)
Female	22 (32.4)
ASA score	
I	19 (27.9)
II	21 (30.9)
III	28 (41.2)
Tumor location	
Upper	16 (23.5)
Middle	28 (41.2)
Lower	24 (35.3)
Charlson Comorbidity Index > 2	21 (30.9)
Clinical TNM stage (7th AJCC-UICC)	
I	20 (29.4)
II	27 (39.7)
III	21 (30.9)

Results

The general information of the patients is shown in Table 1. CCI was>2 in about 30% of the patients and about 40% of the patients were ASA Grade III. The tumor was located in the upper chest in 16 cases, in the middle chest in 28 cases, and in the lower chest in 24 cases.

The short-term outcomes of the patients are shown in Tables 2 and 3. All patients successfully completed the operation and none of them died during surgery. The 90-day complication rate was 36%. The incidence rates of complications with decreasing frequency were pulmonary infection (11.8%), anastomotic fistula (8.8%), and incision infection (7.4%).

The 5-year OS was 45.0%. Among them, 39 patients died of tumor recurrence, and 3 patients died of non-cancer causes. Among them, 2 died of ischemic stroke and 1 died of myocardial infarction. During follow-up, 45 patients had tumor recurrence. The 5-year DFS was 38.0% (Table 4).

Table 2. Postoperative 90-day complications (n=68)

Complications	*n*
Morbidity within 90 postoperative days	25
Pneumonia	8
Anastomotic leak	6
Incision infection	5
Pulmonary embolism	1
Atrial fibrillation	1
Heart failure	1
Delayed gastric emptying	1
Acute coronary syndrome	1
Chylothorax	1
Mortality within 90 days	0

Table 3. Surgical and pathological data (n=68)

Data	*n (range)*
Operation duration (min)	210 (160-300)
Blood loss (ml)	290 (150-450)
Blood transfusion (n)	10
Chest drainage (days)	5 (4-8)
Postoperative hospital stay (days)	12 (7-30)
Retrieved lymph nodes, n	17 (15-28)
Pathological TNM stage (7th AJCC-UICC)	
IB	13
II	24
IIIA	31
Surgical margin (R0/R1/R2)	68/0/0

Table 4. Recurrence data (n=68)

Data	*n (%)*
Recurrences	39 (57.4)
Locoregional	23 (33.8)
Cervical lymph node	8 (11.8)
Anastomosis	6 (8.8)
Mediastinal lymph nodes	9 (13.2)
Distant	9 (13.2)
Brain	3 (4.4)
Liver	3 (4.4)
Lung	2 (2.9)
Kidney	1 (1.5)
Mixed	7 (10.3)

Univariate analysis showed that gender, CCI, pathological type, tumor differentiation, depth of invasion, postoperative complications, and lymph node metastasis were the factors affecting the OS. Multivariate analysis showed that pathologic type, depth of invasion, and lymph node metastasis were the independent predictors of OS.

Discussion

Studies have shown that about 40% of elderly cancer patients give up treatment because of underlying diseases, whereas this rate is only 10% in younger patients [27-30]. With the development and improvement of esophageal surgery and technology, anesthesia technology, perioperative management and related disciplines and equipment, surgical treatment for ESCC, and the surgical safety factor have been greatly improved [11-22]. Studies have shown that age is not a risk factor for the prognosis of ESCC [11-22]. Thus, most authors believe that ESCC can be completely dissected. As long as the patient can tolerate, surgery should be the preferred treatment option and age should not be a limiting factor for surgical treatment in ESCC. The short- and long-term outcomes of this study were similar to those reported in previous studies [11-22].

Elderly patients often have cardiovascular, respiratory, and nervous system diseases, hence having more postoperative complications including surgical-related and nonsurgical-related complications, increasing the risk of perioperative death [11-22]. Surgical-related complications include anastomotic fistula, hemorrhage, chylothorax, recurrent laryngeal nerve injury, and incision infection [11-22]. Nonsurgical-related complications include pulmonary infection, respiratory failure, acute respiratory distress syndrome, pulmonary embolism, arrhythmia, myocardial infarction, heart failure, liver and kidney dysfunction, and cerebral infarction. Studies have shown that there is no statistically significant difference between elderly and non-elderly patients in terms of surgical-related complications [11-22]. However, nonsurgical-related complications are significantly higher in the elderly patients [11-22]. In this study, the postoperative 90-day complication rate was 36% and the 90-day mortality rate was 0%, similar to the results reported in other studies [11-22]. Preoperative comorbidities have an association with postoperative complications. Therefore, it is very necessary to strictly perform a preoperative risk assessment and actively treat underlying diseases before surgery for elderly patients with ESCC.

Univariate analysis showed that CCI and postoperative complications were associated with poor prognosis. In this study, the incidence of anastomotic fistula was 9%, while other large-sample studies reported 3% to 10% [11-22]. Therefore, the incidence of postoperative anastomotic fistula in elderly patients is not higher than that of non-elderly patients. Most studies have reported that age is not a risk factor for the long-term survival of ESCC patients and there is no difference in age distribution of surgical-related complications [11-22].

Esophageal mucosa and submucosal layer are rich in longitudinal lymphatic networks, which constitute the unique lymphatic metastasis pathway, and can cause lymph node metastasis in the neck, mediastinum and abdomen [31-36]. Extensive lymph node metastasis may occur in early ESCC and seriously affects the prognosis of patients. Our study showed that lymph node metastasis was an important factor in the prognosis of ESCC. It is very necessary to perform a complete and systematic lymphadenectomy when treating thoracic ESCC. Japanese authors have reported that the 5-year survival rate reached up to 34% for ESCC patients treated with three-field radical dissection, while it was 26% for patients treated with two-field radical dissection [11-15]. However, both the incidence of perioperative complications and mortality were higher for three-field radical dissection than those for two-field radical dissection.

Some authors treated elderly ESCC patients with three-field radical surgery and found that 5-year OS was 45%, suggesting that three-field radical surgery is safe and effective [37-39]. In this study, all patients were treated with two-field radical surgery and 5-year OS still reached up to 45.0%. Therefore, it is still under debate whether three-field radical dissection is necessary for elderly patients with ESCC. Univariate analysis showed that the grade of differentiation of tumor cells was

prognostic factor and the survival rate of well-differentiated group was significantly higher than that of middle- and low- differentiated group. In the 7th edition of TNM staging for esophageal cancer published in 2009, depth of tumor invasion, lymph node staging, pathological grade, and tumor site constitute the standard of staging of ESCC [37-39].

The limitations of this study are as follows: it was a retrospective single-center study and therefore had a lower level of evidence, the sample size was small (less than 100 cases) and the follow-up time was relatively short.

We concluded that the strict preoperative function assessments of heart, lung, and other organs, standardized surgical treatment, and careful management of perioperative patients, effectively reduced postoperative complications and achieved the desired long-term survival rates. In recent years, minimally invasive surgery such as thoracoscopy and laparoscopic surgery has greatly reduced the incidence of postoperative complications and perioperative mortality for ESCC patients. It is therefore especially beneficial for elderly patients and may show the direction of surgical development for elderly ESCC.

Authors' contributions

YL drafted this manuscript. YL and XC were mainly devoted on collecting and interpreting the data. YW and FW revised it critically for important intellectual content. YG and JZ were responsible for the conception and design of the study. All authors read and approved the final manuscript.

Conflict of interests

The authors declare no conflict of interests.

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