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Post-operative Mortality and Survival Rate in the Patients With Esophageal Carcinoma

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Abstract

Background: Esophageal cancer is the eighth-most common cancer and the sixth-most common cause of cancer death worldwide. In Iran, its prevalence is high. Surgery is recommended for tumors in early stages.

Objectives: This study aims to determine demographic data, therapeutic approaches, postoperative mortality, and survival rate in patients with esophageal cancer who were managed in a referral hospital.

Methods: In a cohort study, the patients hospitalized during six-year period were evaluated. Demographic data, tumor characteristics, laboratory data, surgical approaches, and survival time were obtained. Statistical analysis was performed using life tables, proportional hazard Cox regression, and the Kaplan-Meier method by SPSS version 20 software. Survival curves were compared by log-rank analysis.

Results: Over six years, 92 patients were admitted of which 54 (58.7%) were male. The average age was 63.08±12.03 years. Ten patients (10.8%) were below 50 years old. Squamous cell carcinoma (SCC) was the most common type (85.8%). Fifty-three patients (57.6%) were selected for the surgery. Postoperative mortality in 30 days occurred in 7 patients (13.2%). The median survival rate was 12.8±2.92 months. The survival rate for one, three and five years were 51.94%, 24.67% and 19.48%, respectively. Two factors that had significant statistical correlation with median survival time were metastasis ($P=0.01$) and vomiting ($P=0.003$).

Conclusion: Esophageal cancer is a poor prognostic disease and esophagectomy is a morbid operation. To reduce postoperative mortality and increase the survival time, better patient selection and operations by expert surgeons must be considered.

Keywords: Esophageal Neoplasm, Adenocarcinoma, Squamous Cell Carcinoma, Esophageal Cancer, Esophagectomy

1. Background

Esophageal cancer is the eighth-most common cancer and represents 1% of all types of malignancies. It is the sixth-most common cause of cancer death worldwide.[1,2] In Iran, based on the standardized-age rate study, about seven people per 100 000 suffer from this disease, although some suggest that in Asian belt, including the Northeastern of Iran, the incidence of the cancer is more than 100 per 100 000.[2] The disease's five-year survival rate is low (about 0.8%), while this rate is 5.5% in the developed countries.[2,3] Esophageal cancer is one of the leading causes of cancer-related deaths among Iranians. There is still high mortality and low five-year survival ratio related to late-onset and diagnosis.[4]

Squamous cell carcinoma (SCC) accounts for the majority of esophageal carcinomas worldwide. Its incidence is highly variable in different countries. Adenocarcinoma of the esophagus is diagnosed with increasing frequency and accounts for more than 50% of esophageal cancer in some western countries. Sarcomas and carcinosarcomas are rare esophageal tumors.[5]

Risk factors that can be associated with esophageal carcinoma include low intake of fresh fruit, vegetables, meat, vitamins, and minerals as well as geographical issues, smoking, obesity, lifestyle, alcohol consumption, and intrinsic disorders such as Barrett's esophagus, chronic achalasia, esophageal diverticula's, lye strictures and human papillomavirus.[1-3,5]

Dysphagia is the most common symptom in patients (87%-95%), which usually more than 60% of the esophageal circumferences are usually involved. Other symptoms, such as pain in swallowing, anorexia, weight loss, and back pain, may be present.[5]

Staging is necessary to select the best therapy for every patient. It begins with the history and physical examination. Computed tomographic (CT) scanning and endoscopic ultrasound (EUS) are critical for evaluation. Positron emission tomography (PET) with CT may also be necessary.[5]

Surgery is the standard treatment, although the patient's age and physical status together with the tumor staging determine whether it should be palliative or curative surgery or nonsurgical approach.[1-3,5,6] Surgery is recommended for tumors limited in the esophagus.

In locally advanced cases, a multimodality approach or trimodality therapy (neoadjuvant then surgery) is indicated. In disseminated cancers, treatment aims to palliate.[3,5-9] Open surgical procedures for esophageal cancer include transhiatal esophagectomy (THE), complete three-field esophagectomy (McKeown surgery), Ivor Lewis esophagectomy, and esophagectomy via thoracotomy alone.[5,6,9] Although open esophagectomy is the classic approach, laparoscopic/thoracoscopic minimally invasive esophagectomy and robotic-assisted minimally invasive esophagectomy are becoming more common.[6,9-11] After esophageal resection, postoperative mortality in 30 days and survival rate are the important variables. In a large review of 9217 patients, postoperative mortality and median survival were 3.9% and 42 months, respectively.[6]

2. Objectives

This study aims to determine demographic data, therapeutic approaches, postoperative mortality and survival rate in relation to the patients' age, stage, and pathology of esophageal cancer.

3. Methods

Patients with a primary diagnosis of esophageal cancer hospitalized over six-year period from 2001 to 2007 in a referral hospital in Tehran, the capital city of I.R. Iran were evaluated. In this analytic cohort study, the sampling was done by the census and ethical points were considered. All hospitalized patients with esophageal cancer were included. Patients with secondary esophageal involvement due to other cancers were excluded.

Demographic and background data from the patients associated with medical and surgical approaches and complications were recorded. In all patients, blood tests were performed and laboratory variables such as alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), hemoglobin, white blood cell, platelets and serum albumin were measured. Other variables included chief complaints, tumor size and site, pathology, stage, metastasis, and treatment type. Chest CT scan with intravenous contrast and abdominal CT scan with oral and intravenous contrasts were performed in all patients to check the tumor and lymph nodes conditions. Additional tests such as spirometry, ECG, and echocardiography were performed in patients who were candidates for surgery.

In this study, 53 patients underwent surgery. Forty-one patients underwent THE, eight patients underwent McKeown surgery, two patients underwent Ivor Lewis esophagectomy, and two patients underwent esophagectomy via left thoracotomy with resection of the esophageal tumor and gastric bypass and anastomosis by opening the diaphragm.

In THE, initially laparotomy was performed. After gastric release, by dilating the hiatus of the diaphragm and passing the surgeon's hand through it, the thoracic esophagus was released. Then, by incision in the left side of the neck, the upper esophagus was also released and esophagus was resected. Tubularized stomach was polled up through hiatus and posterior mediastinum and was anastomosed in the neck with the remaining of the esophagus. In McKeown's surgery, at first, right thoracotomy and esophageal release were conducted and thoracotomy was closed, then laparotomy and gastric release were carried out, finally after cervical incision and esophageal dissection and resection, the tubularized stomach was anastomosed with esophagus in the neck. In Ivor Lewis esophagectomy, laparotomy and gastric release was performed, then right thoracotomy and resection of the tumoral lower esophagus were carried out and gastric anastomosis was performed to the rest of the esophagus inside the thorax.[5]

At the follow-up period, the patients after recovery and discharge were followed via clinical visits or phone contacts to achieve their clinical course data until they died or lost contact. A questionnaire designed by the researchers was utilized for data collection.

Statistical analysis was performed using life tables and proportional hazard Cox regression by SPSS version 20 software. The Kaplan-Meier method was used to assess and compare the disease-related survival of patients with different variables. Survival curves were compared by log-rank analysis. The level of statistical significance was set at P of less than 0.05.

4. Results

In six years, 92 patients were admitted of which 54 (58.7%) were male and 38 (41.3%) were female. The average age was 63.08 ±12.03 years (minimum 30 years and maximum of 90 years old). The majority of the patients were in the 60-69 years old age group (32.6%). The other common age group was 70-79 year-old individuals (27.2%). Ten patients (10.8%) were under 50 years old. About 34 % of the patients were smokers. Seven patients (7.6%) had a history of esophageal cancer in their first degree family member (Table 1).

Ninety-one percent of the patients had dysphagia as their chief complaint. Almost all the patients had dysphagia around four months before diagnosis (minimum one month and maximum of 24 months). Other signs and symptoms were weight loss (84.8%), anorexia (47.8%), vomiting (22.8%), and epigastric pain (21.7%).

In laboratory data, the mean value of hemoglobin was 13.02 g/dL, platelets number was 234900/mm^3, lymphocytes number was 2930/mm^3, and serum albumin was 3.94 mg/dL. The liver function tests were in normal ranges.

Esophageal tumors were more (46.7%) in the lower third of the esophagus. In most patients (46.7 %), the size of the tumor was between 3 and 6 cm. SCC was found in 85.8% of pathologic reports.

Twenty-one patients (22.8%) showed metastatic evidence, although in 16 patients (17.4%), metastasis could not be confirmed. The most common sites of metastasis were the liver (38.1%), stomach (19%), and lung (14.3%).

Table 1. Descriptive Characteristics in the 92 Patients With Esophageal Cancers

Variables	Measure
Age, year, mean (SD)	63.08 (12.0)
Male Gender, n (%)	54 (58.7)
Smoker, n (%)	31 (34)
Family H. of esophageal cancer, n (%)	7 (7.6)
The main complaint, n (%)	
Dysphagia	84 (91.3)
Epigastric pain	6 (6.5)
Others	2(2.2)
Hemoglobin, g/dL	13.02
Platelets, number /mm^3	234900
Serum albumin, mg/dL	3.94
Tumor location, n (%)	
Upper third	7 (7.6)
Middle third	15(16.3)
Lower third	43 (46.7)
Othe r(cardia or mixed)	27 (29.3)
Tumors size, n (%)	
<3cm	31 (33.7)
3-6 cm	43 (46.7)
>6 cm	18 (19.5)
Surgical method (in 53patients), n (%)	
Transhiatal esophagectomy	41 (77.4)
McKeown surgery	8 (15.1).
Other	4 (7.5).
Tumors Type, n (%)	
SCC	79 (85.8)
Adenocarcinoma	12 (13.1)
Sarcoma	1 (1.1)
Length of hospital stay, days (SD)	19 (13.3)
30 day Mortality, n (%)	7 (13.2)
Follow-up period, months (SD)	42.7(9.4)
Survival Time, months, mean (SD)	27.43(3.97)
Survival Time, months, median(SD)	
Overall	12.8 (2.9)
Metastatic patients	4.8 (2.6)
Non- Metastatic patients	15.5 (1.3)

The stage of the diseases, according to TNM classification was mostly II A (37.7%).

Fifty-three patients (57.6%) were selected for surgery by seven surgeons. Other patients (42.4%) received nonsurgical treatment such as chemotherapy, radiotherapy, laser ablation, endoscopic stent insertion, or a combination.

Surgical approach selection was adopted to tumor characteristics, patient condition, and surgeon judgment. The most common surgical methods were transhiatal esophagectomy in 41 cases (77.4%) and the McKeown surgery in 8 cases (15.1%).

After surgery, postoperative mortality in 30 days occurred in seven patients (13.2%). The mean length of hospital stay was 19±13.3 days.

In the follow-up period, which was 42.7±9.4 months, from 92 patients, 77 cases could be followed up thoroughly.

The mean of the patients' survival time was 27.43±3.97 months whereas the median of the survival rate was 12.8±2.92 months.

Based on analyses and Kaplan Meier curves, the survival rate for one, two, three and five years in these patients were 51.94%, 31.16%, 24.67%, and 19.48%, respectively (Figure 1).

The correlation between survival time and different variables were evaluated by Log Rank and Breslow tests. In females, the median survival time was longer than that of males (15.5 m vs. 8.9 m), but this difference was not statistically significant ($P=0.08$). The median survival time in adenocarcinoma was longer than that of SCC, although significant statistically ($P=0.23$). The type of surgery had no statistical impact on the median survival time ($P=0.141$). None of the laboratory data in this study had a significant correlation with survival time.

For some variables, also there was no correlation between survival time and age ($P=0.454$), smoking ($P=0.52$), tumor location ($P=0.16$), tumor size ($P=0.22$), stage ($P=0.129$), and weight loss ($P=0.72$).

The median survival time was 4.8±2.54 months in patients with metastasis, whereas it was 15.5±1.34 months in no metastatic patients. This difference was statistically significant ($P=0.0145$) (Figure 2). Meanwhile, epigastric pain ($P=0.022$) and vomiting ($P=0.004$) had a significant statistical correlation with median survival time.

After more evaluation using cox regression analysis, two factors that had a significant statistical correlation with median survival time were metastasis ($P=0.01$) and vomiting ($P=0.003$) (Table 2).

Table 2. Hazard Ratios Based on Cox Regression

Variable	Hazard Ratio	*P* Value
Metastasis	2.33	**0.01**
Vomiting	2.91	**0.003**
Tumor stage	1.89	0.92
Tumor size	139	0.33
Smoking	0.001	0.23
Dysphagia	1.08	0.93
Epigastric pain	0.53	0.59
White blood cell	1.29	0.53
Lymphocyte	1.02	0.37
Hemoglobin	1.11	0.55
Platelet	1.00	0.96
Aspartate transaminase	1.04	0.24
Alanine transaminase	0.94	0.26
Alkaline phosphate	0.99	0.78
FEV_1	0.573	0.18
Albumin	0.340	0.99

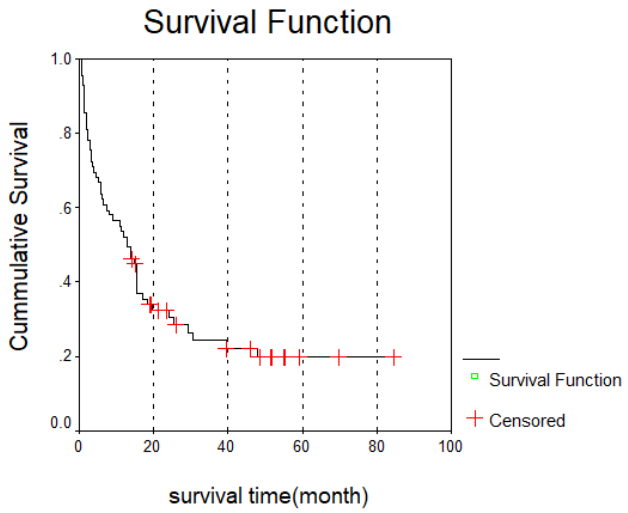

Figure 1. Kaplan–Meier Survival Curve for Total Patients With Esophageal Cancer.

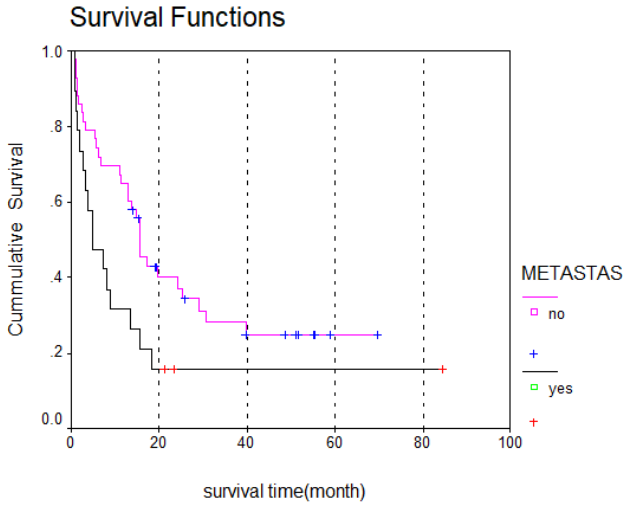

Figure 2. Kaplan–Meier Curve for Role of Metastasis in Survival in Total Patients With Esophageal Cancer

5. Discussion

Esophageal cancer is a health problem and is one of the leading causes of cancer-related deaths.[1,2]

Different studies have reported esophageal cancer to be more prevalent in men.[2,3,5,9,10] Our study confirms a similar pattern. Patients are more involved in their seventies (32.6%); however, some studies state that those between 50 and 59 years of age are the ones mostly involved.[5] Some studies also maintain that esophageal cancer has an incidence among a younger population less than 50 years old.[2,5] About 11% of the patients in our study were found to be in this age group.

The most common part of involvement in our patients was the lower third of the esophagus, although the middle part of the esophagus is the most common location for this kind of tumor.[5] However, the lower part of the esophagus has also been mentioned in other studies.[2,3,9] SCC was the most prevalent type (85.8%) in this study, which was also reported previously,[5] especially in a major study in Asia,[2] however adenocarcinoma was also reported.[6] Most of our patients underwent transhiatal esophagectomy (77.4%). Due to more tumors in the lower part of the esophagus and less morbidity, it seems that utilizing this method was logical,[5] although in some reviews, its proportion was lower.[9,10]

In our patients, the postoperative mortality in 30 days was 13.2%. In another report published in Iran in 2014, in a sample of 409 patients, it was 27.8 %.[3] Some previous reports had suggested a mortality rate greater than our results, especially when few surgeons operated in low-volume hospitals.[13] In another report in1998, the mortality rate in 30 days was 13 %.[12] Modern studies have significantly lower mortality, with most series reporting mortality below 3% [6,9,14,15] or about 3.3%, 3.8%, and 4.2%.[6,8,10]

The mean length of hospital stay was 19 ±13.3 days. In other studies, this was from 10 to 12.3 days for open surgery and from 7 to 9 days for minimally invasive surgery,[8,10] although in a review published in 1010 patients, it was about 21 days.[14] In a recent report from Japan in about 9000 patients, the mean length of hospital stay was 26 days for open surgery and 23 days for minimally invasive surgery.[15]

Our patients had a median survival time of 12.8 months. In other studies, it ranged from 8.5 to 9.2, 36, 41, and 55 months, due to multiple factors.[3,6-8] Better results in both short- and long-term are achieved in high-volume centers in general and by high-volume surgeons in particular.[1] In our patients, three and five years survival rates were 24.6% and 19.48%, respectively. Only two factors had a significant correlation with the patients' survival, metastasis and vomiting. Almost all the patients with a poorer prognosis had a metastasis. In other studies, metastatic lesions were associated with a significant fall in patients' survival.[1,2,5,7] Vomiting was another variable with statistical significance for survival time in the current study while there was no relation between vomiting and patients' survival in other investigations.

Our study did not show any significant relationship between survival time and sex, age, smoking, tumor location and type, stage, laboratory data, and operations type. However, other studies reported a significant correlation between age, male sex, smoking, tumor type, stage, and surgeons' experience with patients' survival.[2,3,5-8]

Research Highlights

What Is Already Known?

Esophageal cancer is a poorly prognostic disease. Adenocarcinoma is more common cell type. Postoperative mortality is low.

What Does This Study Add?

Esophageal cancer is a poorly prognostic disease especially in metastatic situation. In our center, SCC is more common cell type and postoperative mortality is nearly high. To reduce postoperative mortality and increase the survival time, better patient selection and operations by expert surgeons must be considered.

6. Conclusion

Esophageal cancer is a poorly prognostic disease especially in metastatic situation and esophagectomy is associated with morbidity. The median survival is nearly acceptable in our center, although the postoperative mortality was nearly high. To reduce the postoperative mortality and increase survival time, better patient selection and operations by expert surgeons must be considered.

Authors' Contributions

HAM, SH and HRM developed the study concept and design. HRM performed data collection. HAM, HRM and MP involved in analysis and text. All authors Contributed and approved the final version of the manuscript.

Conflict of Interest Disclosures

The authors declared that they have no conflict of interest.

Ethical Approval

The study was designed as a thesis for a medical student approved in the faculty of medicine in Baqiyatallah University of Medical Sciences with the code of IR.BMSU.93.266.

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