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Esophagectomy complications and mortality in esophageal cancer patients, a comparison between trans-thoracic and trans-hiatal methods

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ABSTRACT

Introduction: Esophageal cancer is the sixth cause of cancer related deaths worldwide. Esophagectomy is the standard treatment for non-metastatic esophageal cancer, but is associated with high mortality and morbidity rates. We evaluated the mortality and complications following esophagectomy, and factors affecting it (including the surgical approach).

Methods: This retrospective study was performed from 2006 to 2012; the data were collected from medical files of esophageal cancer patients who underwent surgical procedures at Iran's cancer institute and analyzed.

Results: A total of 254 operated esophageal cancer patients entered this study. Patients included 105 males and 149 females, with a mean age of 65.70. Of all the operated patients, 121 (47.64%) underwent the trans-hiatal and 121 (47.64%) the transthoracic esophagectomy method, also 12 patients were operated by other surgical methods. Post-operative complications occurred in 61 patients (24.02%). Respiratory complications (20.08%) –including Adults Respiratory Distress Syndrome (9.45 %), pneumonia (6.30%) and ventilator dependency (4.33%) - were the most common complications. Other major complications were anastomosis leakage and fistula (6.30 %), atrial fibrillation (6.30 %), chylothorax (3.15%), bleeding requiring reoperation (1.97%) and pulmonary embolism (1.97 %). In-hospital mortality rate was 5.12 %. Pneumonia, ICU admission and intubation time were significantly higher in transthoracic than trans-hiatal method but mortality was not significantly different. ARDS, ventilator dependency and history of cardio-pulmonary disease were prognostic for in-hospital mortality.

Conclusion: Although esophagectomy is a complex surgery and associated with multiple complications, in case of proper patient selection and experienced surgeons, both the transthoracic and trans-hiatal esophagectomy methods have appropriate results.

Keywords: esophagectomy, complication, cancer, transthoracic, trans-hiatal

INTRODUCTION

Esophageal cancer is the sixth cause of cancer related deaths worldwide(1), with 456,000 new cases and 400000 mortalities in 2012 (2). The high risk region for esophageal cancer is known as the "esophageal cancer belt ", starting from northern Iran through the central Asian countries to north-central China. Since Iran is also located on this cancer belt, esophageal cancer has high prevalence in this country. Most (90%) of esophageal cancer cases in the regions located on this belt are squamous cell carcinomas, whereas this histological type is much less in the United States (26%) (2).

Two main histological types of esophageal cancer are: 1. squamous cell carcinoma (the most common type), usually occurring in the proximal two thirds of the esophagus, and 2. Adenocarcinoma, which mostly occurs in the lower third of the esophagus.

Treatment method of esophageal cancer depends on tumor site and stage. These methods include: esophagectomy, neo-adjuvant therapy followed by surgery, definitive chemo-radiation and palliative surgery for metastatic patients. In tumors invading muscularis properia, esophagectomy in combination with chemo-radiation therapy as neo-adjuvant, remains the optimal management for patients who are medically fit for esophageal cancer surgery.

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In 1940, Oschner and DeBakey reviewed the literature on esophageal resections, and reported about 72% mortality after esophagectomy (3). Many improvements have been made in esophageal cancer treatment since then, but post esophagectomy mortality and morbidity rates are still considerable. Esophagectomy usually involves the abdomen, thorax and neck, making it a greatly traumatic and technically complex surgery, and therefore having a high rate of complications and mortality (4).

According to multiple analyses performed to identify post-surgical complications and risk factors of esophagectomy, the most common complications include: pulmonary complications (such as Adults Respiratory Distress Syndrome (ARDS), pleural effusion, atelectasis, ventilator dependency and pneumonia), cardiac complications (cardiac arrhythmia and myocardial infarction), anastomotic leakage & fistula, thrombo-embolic events, chylothorax, intra and post-operative bleeding, wound infection and acid-base disorder (5-9). Complications may vary in different surgical techniques.

Regarding esophageal cancer being endemic in Iran, and previous studies conducted in the Cancer Institute of Iran, that showed a relatively high early mortality rate of esophagectomy (10), we decided to evaluate in-hospital complications and mortality of esophagectomy and factors affecting it, including patient's characteristics and the surgical approach.

METHODS

Iran's Cancer Institute is the only hospital specialized for cancer treatment in the country, and it is one of the most important referral centers for esophageal cancer in Iran.

In our center, spirometry and echocardiography is done for all patients who need esophagectomy, and also consultation with a cardiologist and pulmonary specialist is done for patients aged over 40 years. High risk patients (according to the cardiac and pulmonary consultation), were referred for definite chemo-radiotherapy, and the rest underwent surgery. The operated patients may have a history of cardiopulmonary disease (coronary angioplasty or bypass), but have a moderate risk for surgery at present.

In this center, esophagectomy is mainly done by two methods: Three-hole Trans-Thoracic Esophagectomy (TTE) and Trans-Hiatal Esophagectomy (THE).

In the TTE method, at first a right thoracotomy is performed, the thoracic esophagus and the lymph nodes are dissected, followed by closure of chest incision; through the abdominal incision, gastric pull up or colon interposition is done in supine position and reconstruction is performed by neck anastomosis.

In the THE method, after laparotomy and gastro lysis, esophageal dissection is done from hiatus to the neck, esophagus is explored in the neck and then anastomosis is done between cervical esophagus and stomach, so there is no thoracic incision.

This retrospective study was performed during the years 2006 to 2012; all the medical files of esophageal cancer patients who underwent surgical procedures at the department of surgery of Iran's Cancer Institute were collected. Eligible patients were defined as esophageal cancer patients who underwent curative surgery. Patients with distant metastasis were excluded, except one patient who had a minor limited metastasis that was resected.

Esophageal cancer staging was done based on standardized workup, including endoscopy with biopsy, endoscopic ultrasound (EUS) and computed tomography scan of thorax, abdomen and pelvis, according to the sixth edition of AJCC guideline for staging.

The collected data included: patient's demographic data (age, gender, tumor stage and location), patient's pre-operative condition (history of cardio-pulmonary disease and general health), pathological findings (tumor site, histology, invasion of adjacent organs, and lymph node metastasis), surgical technique, intra-operative blood transfusion (at least two units of packed blood cells), hospital mortality and post-operative complications (including pneumonia, ARDS , ventilator dependency - ventilator support beyond 48 h- , pulmonary embolism, chylothorax, atrial fibrillation, anastomotic leakage and fistula formation). Complications were defined according to the "international consensus on standardization of data collection for complications associated with esophagectomy"(5) .

In the current study we evaluated:

1. the association between complications and hospital mortality, and
2. the association of complications and hospital mortality with the patient's characteristics and surgery method.

This study was approved by the ethics committee of Tehran University of Medical Sciences.

Statistical Analysis

Statistical analysis was performed using the STATA software version 11 (State Corp., College station, TX), and all considered p-values were two sided. In order to signify data distribution, we conducted the Shapiro-Wilk test and considered normal distribution based on p-value≥0.05. Using unconditional logistic regression, we estimated odds ratio (OR) and 95% confidence intervals to evaluate the association between esophageal cancer complications and potential risk factors. Fully adjusted models included any variable which showed p-value more than 0.2 in univariate analysis. In order to choose the best model, we fitted the last multivariate model based on the likelihood ratio test and estimated the area under the curve, that was between 0.70-0.80. Also, we evaluated the co-linearity between risk factors based on their variance inflation factor (VIF), and selected all variables with a variance inflation factor (VIF) less than 10. Furthermore, in order to assess the co-linearity, we tested the association between each variable based on Chi2, independent t-test, and ANOVA.

RESULTS

Demographic Data

A total of 254 operated esophageal cancer patients entered the present study. Patients included 105 males (41.34%), and 149 females (58.66%), with a mean age (±SD) of 65.70 (±12.80). Cases of SCC and adenocarcinoma were 96.06% and 3.94% respectively. Of all the operated patients, 121 (47.64%) underwent the trans-hiatal and 121 (47.64%) the transthoracic esophagectomy method, also 12 patients were operated by other surgical methods (Ivor Lewis, Left thoracotomy…etc.). The clinico-pathological characteristics of all 254 patients have been demonstrated in **Table 1**. According to this table, 44.49% of patients were categorized as stage II, and 51.97% as stage III. In 39. 76% and 49.21% of patients the middle and lower third of esophagus were involved respectively. Intra-operative blood transfusion (at least 2 units of packed cell) was required in 27(10.63%) patients.

Table 1: *Characteristics of patients who underwent esophagectomy between the years 2006 to 2012 in Cancer Institute of I.R Iran, Tehran, Iran*

Variable	Number (%)
Age group	
<50	67(26.38)
50-60	88 (34.65)
60-70	67 (26.37)
>70	28 (11.02)
Missing	4 (1.57)
Gender	
Female	149 (58.66)
Male	105 (41.34)
Tumor Stage	
I	6 (2.36)
II	113 (44.49)
III	132 (51.97)
IV	1 (0.39)
Unknown	2 (0.79)
Tumor Location	
Upper third of Esophagus	8 (3.15)
Middle third of Esophagus	101 (39.76)
Lower third of Esophagus	125 (49.21)
Unknown	20 (7.87)
History of cardiopulmonary Disease	
No	198(77.95)
Yes	56 (22.05)
Intraoperative Blood Transfusion*	
No	227 (89.37)
Yes	27 (10.63)
General health**	
Inappropriate	27 (10.63)
Appropriate	227 (89.37)
Surgical approach	
Trans-hiatal esophagectomy	121 (47.64)
Trans-thoracic(Three-hole) esophagectomy	121 (47.64)
Other*** method	12 (4.72)
Neo-adjuvant treatment	
No	214 (84.25()
Yes	40 (15.75)

*at least 2 units of packed blood cells
**General condition: the patient's appearance regarding being healthy, cachexia, etc. that was evaluated based on the notes of the nurse at the time of admission to the ward
***Other means: Ivor Lewis, Left thoracotomy, etc.

Complications and Mortality Rates

The overall in-hospital mortality was 13 (5.12 %) and post-operative complications were 61 (24.02%). Some patients experienced more than one complication. However, the major post-operative complications included: ARDS 24 (9.45%), pneumonia 16 (6.30%), anastomotic leakage and fistula formation 16 (6.30%), ventilator dependency 11 (4.33%), chylothorax 8 (3.15%), pulmonary embolism 5 (1.97%) and bleeding requiring re-operation 5 (1.97%) (**Table 2**).

Table 2: *Post-operative complications and hospital mortality in patients who underwent esophagectomy between the years 2006 to 2012 in Cancer Institute of I.R Iran, Tehran, Iran*

Complication	Number (%)
No	193 (75.98)
Yes	61 (24.02)
pneumonia	
No	238 (93.70)
Yes	16 (6.30)
ARDS*	
No	230 (90.55)
Yes	24 (9.45
Pulmonary embolism	
No	249 (98.03)
Yes	5 (1.97)
ventilator dependency (ventilation support beyond 48 hours)	
No	243 (95.67)
Yes	11 (4.33)
Chylothorax	
No	246 (96.85)
Yes	8 (3.15)
Anastomotic leakage & fistula	
No	238 (93.70)
Yes	16 (6.30)
Bleeding requiring re-operation	
No	249 (98.03)
Yes	5 (1.97)
Atrial fibrillation	
No	238 (93.70)
Yes	16 (6.30)
Recurrent laryngeal nerve paralysis	
No	253 (99.61)
Yes	1 (0.39)
Hospital mortality	
No	241(94.88)
Yes	13(5.12)

*Adults Respiratory Distress Syndrome

Risk Factors

In the multi-variate logistic model, the association of complications and mortality with other parameters was evaluated (**Table 3**).

Our findings showed that in patients with history of cardio-pulmonary disease, the risk of mortality and complications are significantly higher. Also, risk of complication increases with age in the 60-70 year age group. Complications were significantly higher in patients who received intra-operative blood transfusion. There was no difference regarding complications and mortality in the group who received neo-adjuvant treatment compared to the group who didn't. Furthermore, risk of complications and mortality was not related to tumor stage and location.

Table 3: *Adjusted odds ratios (OR) and corresponding 95% confidence interval (CI) for association between complications, hospital mortality and patient characteristics, among patients who underwent esophagectomy from 2006 to 2012 in Cancer Institute of I.R Iran, Tehran, Iran*

Variables	Total complication			Hospital Mortality		
	(Yes (%)/No(%))	Adjusted OR (95% CI)	P-Value	(Yes(%)/No(%))	Adjusted OR (95% CI)	P-Value
Age group						
<50	11(16.42) /56(83.58)	Reference	.....	0(0.00)/67(100.00)	.....	.....
50-60	20(22.73)/68(77.27)	2.16 (0.85, 5.50)	>0.05	6(6.82)/82(93.18)	.....	.....
60-70	22(32.84)/45(67.16)	3.84 (1.50, 9.90)	< 0.05	6 (8.96) /61(91.04)	.....	.....
>70	7(25.00)/21(75.00)	2.94 (0.90, 9.96)	>0.05	1(3.57)/27(96.43)	.....	.....
Missing	1 (25)/ 3 (75)	.....	.....	0(0.00)/4(100.00)	.....	.....
Gender						
Female	36(24.16)/113(75.84)	Reference		10(6.71)/139(93.29)	Reference	.....
Male	25(23.81)/80 (76.19)	1.03 (0.53, 2.00)	>0.05	3(2.86)/102(97.14)	0.53 (0.13, 2.20)	>0.05
Tumor stage						
I	1(16.67)/5 (83.33)	0.64 (0.06, 6.60)	>0.05	0 (0.00)/ 6 (100.00)	.....	.....
II	25 (22.12) / 88 (77.88)	Reference	.....	7 (6.19)/ 106 (93.81)	Reference	.....
III	35 (26.52) / 97 (73.48)	1.70 (0.90, 3.25)	>0.05	6 (4.55) / 126 (95.45)	0.90 (0.25, 3.03)	>0.05
IV	0 (0.00)/ 1 (10.00)	.....	.....	0 (0.00)/ 1 (100.00)	.....	.....
Unknown	0 (0.00)/ 2 (100.00)	.....	.....	0 (0.00)/ 2 (100.00)	.....	.....
Tumor location						
Upper third of esophagus	3(37.50) /5(62.50)	2.96 (0.60, 15.07)	>0.05	0 (0.00)/ 8 (100.00)	.....	.....
Middle third of esophagus	27(26.73)/ 74(73.27)	Reference	.....	5 (4.95)/ 96 (95.05))	Reference	.....
Lower third of esophagus	24 (19.20)/ 101 (80.80)	0.70 (0.33, 8.50)	>0.05	7 (5.60)/ 118 (94.40)	1.26 (0.34, 4.70)	>0.05
Unknown	7 (35.00)/ 13 (65.00)	2.62 (0.82, 8.45)	>0.05	1 (5.00)/ 19 (95.00)	1.50 (0.12, 16.82)	>0.05
History of cardio-pulmonary disease						
No	41(20.71) /157(79.29)	Reference	.....	5 (2.53)/ 193 (97.47)	Reference	.....
Yes	20(35.71) /36(64.29)	2.45 (1.17, 5.12)	<0.05	8 (14.29)/ 48 (85.71)	5.02 (1.44, 17.53)	<0.05
Intra-operative blood transfusion						
No	50(22.03) /177(77.97)	Reference	.....	10 (4.41)/ 217 (95.59)	Reference	.....
Yes	11(40.74) /16(59.26)	3.32 (1.24, 8.88)	<0.05	3 (11.11)/24 (88.89)	2.40 (0.50, 11.40)	>0.05
General health						
Appropriate	55(90.16) /172(89.12)	Reference	.....	12 (5.29)/ 215 (94.71)	Reference	.....
Inappropriate	6(9.84) /21(10.88)	1.00 (0.35, 2.84)	>0.05	1 (3.70)/ 26 (96.30)	0.62 (0.07, 5.63)	>0.05
Surgical approach						
Trans-hiatal	21(17.36) /100(82.64)	Reference	.....	5 (4.13)/ 116 (95.87)	Reference	.....
Transthoracic	37(30.58) /84(69.42)	1.84 (0.92, 3.70)	>0.05	7 (5.79)/ 114 (94.21)	1.40 (0.40, 5.23)	>0.05
Other	3(25.00) /9(75.00)	0.72 (0.13, 4.00)	>0.05	1 (8.33)/ 11 (91.66)	1.23 (0.08, 18.90)	>0.05
Neo-adjuvant treatment						
No	50(23.36) /164(76.64)	Reference	.....	9 (4.21)/ 205 (95.79)	Reference	.....
Yes	11(27.50) /29(72.50)	1.06 (0.43, 2.60)	>0.05	4 (10.00)/ 36 (90.00)	1.71 (0.40, 7.20)	>0.05

Surgical Approach

In comparison of the TTE and THE methods, it was observed that risk of pneumonia was significantly higher in the TTE method. Although there was no significant difference between the two groups regarding mortality, ARDS, ventilator dependency, and anastomosis leakage (**Table 4**).

Table 4: *Comparison of complications in Trans hiatal and Transthoracic surgical methods among esophageal cancer patients in Cancer Institute of I.R Iran during the years 2006 to 2012, Tehran, Iran*

Variable	Surgical approach			
	Trans-hiatal N (%)	Trans-thoracic N (%)	Adjusted OR (95% CI)	P-Value
Total complication				
No	100 (51.81)	84 (43.52)	Reference	.....
Yes	21 (34.43)	37 (60.66)	0.60 (0.11, 3.03)	>0.05
Pneumonia				
No	118 (49.79)	109 (45.99)	Reference	.....
Yes	3 (18.75)	12 (75.00)	7.62 (1.10,52.64)	<0.05
ARDS*				
No	114 (49.78)	105 (45.85)	Reference	.....
Yes	7 (29.17)	16 (66.67)	3.70 (0.70,19.03)	>0.05
Pulmonary embolism				
No	119 (47.98)	118 (47.58)	Reference	.....
Yes	2 (40.00)	3 (60.00)	0.64(0.06,7.06)	>0.05
Ventilator dependency				
No	117 (48.35))	115 (47.52)	Reference	.....
Yes	4 (36.36)	6 (54.55)	0.28 (0.03, 2.32)	>0.05
Chylothorax				
No	119 (48.57)	116 (47.35)	Reference	.....
Yes	2 (25.00)	5 (62.50)	4.80 (0.45,51.24)	>0.05
Anastomosis leakage & Fistula				
No	116 (50.88)	112 (49.12)	Reference	.....
Yes	5 (35.71)	9 (64.29)	1.70 (0.30,9.40)	>0.05
Atrial fibrillation				
No	114 (48.10)	112 (47.26)	Reference	.....
Yes	7 (43.75)	9 (56.25)	0.90 (0.24,3.26)	>0.05
Bleeding requiring second surgery				
No	119 (50.00)	119 (50.00)	Reference	.....
Yes	2 (50.00)	2 (50.00)	0.90 (0.07,10.90)	>0.05
Hospital mortality				
No	116 (48.33)	114 (47.50)	Reference	.....
Yes	5 (38.46)	7 (53.85)	1.51 (0.30, 7.54)	>0.05

*Adults Respiratory Distress Syndrome

The average days of ICU admission and intubation period were 4.70 ± 8.41 and 3.08 ±9.50 in the TTE and 3.50 ±4.54 and 1.76+_4.30 in THE methods respectively, which shows they were both significantly higher in the TTE Method(P-Value=0.0001).

Association between Complications and Mortality

Table 5 shows that risk of mortality is directly related to ARDS, ventilator dependency and post-operative bleeding that requires re-operation. Risk of pneumonia, anastomosis leakage & fistula and chylothorax were not associated with mortality.

Table 5: *Adjusted odds ratios (OR) and corresponding 95% confidence interval (CI) for association between hospital mortality and different complications among patients who underwent esophagectomy during the years 2006 to 2012 in Cancer Institute of I.R Iran, Tehran, Iran*

	Hospital Mortality (Yes(%)/No(%))	Adjusted OR (95% CI)	P-Value
Pneumonia			
No	8(3.36)/230 (96.64)	Reference	.....
Yes	5 (31.25)/11 (68.75)	2.30 (0.20, 25.71)	>0.05
ARDS			
No	6 (2.61)/224(97.39)	Reference	.....
Yes	7(29.17)/17(70.83)	15.38 (2.203, 107.30)	<0.05
Pulmonary embolism			
No	11(4.42)/238 (95.58)	Reference	.....
Yes	2 (40.00)/3 (60.00)	5.91 (0.24, 143.71)	>0.05
Ventilator dependency (more than 48h)			
No	8 (3.29)/235 (96.71)	Reference	.....
Yes	5 (45.45)/6 (54.55)	42.60 (3.24, 558.52)	<0.05
Chylothorax			
No	11(4.47)/235(95.53)	Reference	.....
Yes	2(25.00)/6 (75.00)	1.63 (0.02, 164.90)	>0.05
Anastomosis leakage & fistula			
No	11(4.62)/ 227 (95.38)	Reference	.....
Yes	2 (12.50)/14 (87.50)	2.10 (0.16, 26.48)	>0.05
Bleeding requiring second surgery			
No	12 (4.82)/237(95.18)	Reference	.....
Yes	1(20.00)/4(80.00)	24.12 (1.05, 549.40)	<0.05
Atrial fibrillation			
No	9(3.78)/229 (96.22)	Reference	.....
Yes	4 (25.00)/12 (75.00)	2.82 (0.30, 30.31)	>0.05
Arterial PH disorder *			
No	5 (3.57)/135 (96.43)	Reference	.....
Yes	8(7.02)/106 (92.98)	0.32 (0.05, 2.00)	>0.05

* two or more abnormal Arterial Blood Gas after surgery

DISCUSSION

Esophagectomy is the standard treatment for non-metastatic esophageal cancer. Despite improvements in surgery methods, appropriate patient selection and pre/post-operative management, esophagectomy is still associated with considerable risk of morbidity and mortality (4), since it is one of the most complex and major procedures of general surgery. This complexity is considered to be due to surgery in three fields (neck, abdomen, and thoracic cavity), mediastinal dissection and presence of a reconstructive organ in the mediastinum which causes dysfunction of respiratory muscles and respiratory problems (9, 11).

Multiple factors such as surgical method, patient age and medical comorbidity, may influence post-operative complications(9, 11) .

Post-esophagectomy complications are divided into medical and surgical complication. Our findings showed that 24.02% (61/ 254) of patients experienced complications following esophagectomy.

Medical Complications

Many reports have indicated that pulmonary complications are the most common complication after esophagectomy and are one of the main causes of mortality (4, 7, 9, 11-14). Similarly, respiratory complications (including ARDS 9.45 %, pneumonia 6.30% and ventilator dependency 4. 33%)were the most prevalent complication (20.08%) in our study. Furthermore, in our study respiratory complications are significantly associated with increased mortality, except for pneumonia.

In a study by Avendano et al. (11) between 1994 and 2000, significant pulmonary complications were seen in 36.1% of patients. The most common pulmonary complication was pneumonia, occurring in 32.8% of patients, 19.7% needed ventilation support for more than 48 h, ARDS developed in 9.8% of cases, chylothorax was 8.2% and hospital mortality

8.6%. All the cases of in-hospital mortality had developed pneumonia. The mean ICU admission period was 6.1 ± 11.1 days and mean ventilation time 91.8 ± 226.2 h (11) .

Mortality, complications, duration of ventilator support and admission period in the ICU were higher in this study compared to ours, which may be due to difference in the date of the two studies. Mortality of esophagectomy has decreased since the past decades(4) which may be due to increased experience of surgeons, improvements in patient selection, ICU care, and diagnostic and therapeutic facilities. In the study mentioned above, most cases of mortality were related to pneumonia, but in our study there was no significant association between pneumonia and mortality, this indicates that in case of early diagnosis and treatment with appropriate antibiotics, and proper ICU care, patient mortality can be decreased.

Also a recent study in Japan between 2005 and 2012 showed that overall respiratory complications were 17.7 %. Pneumonia (8.7 %) and ventilator support more than 48h (5.4 %) were the main complications [12]. The results of this study, which was done at approximately the same period of our study, was relatively close to our findings.

Medical Complications

Anastomosis leakage and fistula formation

Anastomosis leakage is considered as one of the most important and serious surgical complications, that can result in mediastinal infection and sepsis. In our study, the rate of anastomosis leakage and fistula was 6.30%, and it ranged between 3%-21.3% in other investigations (4, 7, 15, 16). We found no significant association between anastomosis leakage and mortality, that may be due to anastomosis being located in the neck in most surgeries, which has a lower risk of mediastinitis.

Re-operation due to bleeding

Re-operation due to bleeding was 1.97% in our study, in other studies it was reported ranging from 0.4%-7% (7, 17, 18). According to our findings, post-operative bleeding was significantly associated with mortality. Also, multiple studies have indicated peri-operative bleeding as a risk factor of mortality (4, 7, 8).

Risk factors

Multiple investigations have been performed to determine the important risk factors that affect esophagectomy complications.

Age

In the present study, older age was associated with post-operative complications, this finding correlates with other studies (6, 14). However some authors reported that, patient's age at the time of surgery, had no impact on post-operative morbidity and mortality (7, 19). Furthermore, some investigations suggest that old age is not associated with bad outcomes, if the other comorbidities of patients are properly controlled (20, 21).

History of cardio-pulmonary disease

In the current study, history of cardio-pulmonary diseases significantly increased post-operative complications and mortality. Other studies reported similar findings (7, 8, 10, 22) .

Intra-operative blood transfusion

In our study, intra-operative blood transfusion was associated with post-operative complications. Similarly, multiple investigations showed that intra-operative blood transfusion increased post-operative complications (12, 14-16, 23). Various publications have shown that blood transfusion is a factor that increases mortality (7, 8, 14, 24), whereas our findings indicated that blood transfusion increases complications, but not mortality. Also, Nozoe T et al reported that intra-operative blood transfusion was not indicative of the patient's prognosis (25).

Surgical approach

In the present study, pneumonia was significantly higher in the TTE method compared to the THE method, which is similar to other studies (8, 26) .

There was no significant difference between the two groups regarding total complications, in-hospital mortality, ARDS, anastomosis leakage and fistula formation. These findings are consistent with the results of other studies (10, 27-29).

Multiple studies (8, 26, 30-32) have shown that the TTE method is associated with more complications, and some (10, 27-29) have shown no significant difference between the two methods, which is similar to our study. Although, in a single study (33) the THE method was associated with more complications. This may be due to various factors, such as experience of the surgeons, the center in which the surgery is done, and bias in patient selection.

Therefore, for an accurate comparison between these two methods, a randomized clinical trial study is required.

Neo-adjuvant therapy

In the current study, there was no difference in total complications and mortality between the group who received neo-adjuvant treatment and the group who didn't. In a study in Norway, high dose chemo-radiation didn't affect pulmonary complications (34). Also, in a recent study, pre-operative radiotherapy didn't increase anastomotic complications in the post-operative period (35). Although, in a study in Japan, pre-operative definite chemo-radiotherapy was associated with increased respiratory complications (12).

Mortality

We found that the prevalence of in-hospital mortality was 5.12 %, which is consistent with K Ovrebo's findings (5.7%)(29). In other publications, post-esophagectomy mortality rates varied between (2.7-11%) (8, 10, 36-39) .

In a comparison between the present study and a previous study (10) also done in Iran's cancer institute (1997–2006), in-hospital mortality had decreased in our study compared to the 11% reported before. It seems that gaining more experience by the surgeons, and improvements in ICU and peri-operative care, are effective in reducing mortality rate.

Our study revealed that History of cardio-pulmonary disease, ARDS, ventilator dependency and post-surgery bleeding were risk factors for in-hospital mortality**.**

The limitation of our research was the type of study, which was retrospective and so randomization of the data was not possible. For future investigations, a prospective randomized trial is recommended.

CONCLUSION

It is concluded that post esophagectomy complications are relatively common and are divided to surgical and medical. Surgical complications (such as bleeding, anastomosis leakage and fistula, chylothorax, ...) can be reduced by increasing the experience and skill of the surgical team. The most common medical complications are respiratory complications. Medical complications can be managed by proper patient selection, respiratory care before and after surgery, improving ICU care, and early diagnosis and treatment of complications. Although, in this study, no significant difference was observed between the two methods (TTE and THE) in terms of mortality, but in patients with associated respiratory disease, the THE method may be preferable.

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