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Preoperative Assessment of Mechanical Ventilation Requirement after Surgical Treatment of Esophageal Cancer

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ABSTRACT

Background: *The risk of pulmonary complications after esophagectomy is higher than after any other common operation, including major lung resection. In this study, we sought to identify risk factors associated with the development of pulmonary insufficiency requiring mechanical ventilation to identify preoperative parameters involved in the estimation of the risk of pulmonary insufficiency.*

Materials and Methods: *We performed a retrospective cohort study on consecutive patients undergoing esophagectomy for malignancy in the Thoracic Surgery Department of Modarres Hospital in Tehran from March 2002 to February 2006. Patients were assigned into two groups based on whether they required mechanical ventilation or not. Preoperative, operative, and postoperative data were compared among the two groups. To find predictive variables for requiring mechanical ventilation, backward stepwise regression analysis was carried out with risk factors as independent variables and the need for ventilatory support as the dependent variable.*

Results: *The study population included 77 males and 43 females with a mean age of 60.16±12.04 years (range 29–79 years). Twenty-seven patients (27.7%) required mechanical ventilatory support. Multivariate analysis revealed sex (Odds ratio: 4.590, CI 95%: 1.248-16.411) as a confounder and duration of operation (Odds Ratio: 1.677, CI95% : 1.102-2.533) as a risk factor for requiring mechanical ventilation.*

Conclusion: *Proper patient selection for esophagectomy is important for reducing the postoperative mortality and morbidity and benefiting from a radical resection.* ***(Tanaffos 2010; 9(1): 34-41)***

Key words: *Esophageal cancer, Esophagectomy, Mechanical ventilation, Preoperative assessment*

INTRODUCTION

Radical esophagectomy remains the most effective treatment method for patients with esophageal cancer, while it could achieve a five-year survival rate of 40% or higher (1-3).However, esophagectomy may be one of the greatest surgical operations. It is often undertaken on elderly patients and those with significant co-morbidity. Postoperative pulmonary complications (POPCs) are common after

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esophagectomy (4,5), and their risk is higher than after any other common operation, including major lung resection. The reasons posited for this high risk include surgical entry into 2 separate body cavities, disruption of bronchial innervation and lymphatic circulation, postoperative dysfunction of muscles of respiration including the diaphragm, placement of a reconstructive organ in the substernal space, cachexia, advanced age, poor airway protection resulting from recurrent laryngeal nerve injury and uncoordinated deglutition, tobacco and alcohol abuse and poor performance status (6,7). Their occurrence is associated with prolongation of postoperative hospital stay, increased cost of care, and substantial operative mortality. Despite the recognition of this fact for more than 2 decades, efforts for predicting the risk of pulmonary complications have been only moderately successful. Alterations in intraoperative and postoperative management of patients undergoing esophageal resection have failed to reduce the incidence of pulmonary complications to desirable levels (8).

Mao et al. analyzed the risk and cause of death of 114 postoperative respiratory failure patients found among 3519 patients with esophageal cancer and 1495 patients with carcinoma of the gastric cardia surgically treated between January 1992 and May 2003. They found that postoperative respiratory complications were mainly caused by severe respiratory tract infection and operative complications such as anastomotic leakage or perforation of thoracic stomach, extensive bleeding during operation and chylothorax. In contrast with lung cancer patients, most of the postoperative respiratory failures occurred in patients who had perioperative complications but almost always normal preoperative pulmonary function tests. Other causes of postoperative respiratory failure were extubation of unconscious patients at the end of general anesthesia, over-infusion during operation, pulmonary artery embolism, severe arrhythmia and etc. (9).

Because of the high incidence of pulmonary complications and associated operative mortality after esophagectomy, a thorough preoperative evaluation of the risk of pulmonary complications is appropriate in esophagectomy candidates. The evaluation should include a general assessment of age, performance and nutritional status, measurement of spirometric values, and an assessment of diffusing capacity. (10).

In this study, we sought to identify risk factors associated with the development of pulmonary insufficiency requiring mechanical ventilation to identify preoperative parameters involved in the estimation of the likelihood of pulmonary insufficiency.

MATERIALS AND METHODS

We performed a retrospective cohort study on consecutive patients undergoing esophagectomy for malignancy in the Thoracic Surgery Department of Modarres Hospital in Tehran (the capital of Iran) from March 2002 to February 2006. Since it was an observational study, patient grouping was not done at the first step .Preoperative, operative, and postoperative data were obtained from chart reviews. The operative procedures depended on the location of the tumor and the state of the patient and included McCon, transhiatal, left thoracotomy and transposition. Initial data including age, sex, past medical history, smoking status, opium addiction, duration of hospital stay, duration of operation, transfusion, tumor site, histopathological diagnosis, operation type (Table 1), and in-hospital mortality were collected. Patients were assigned into 2 groups based on their need for mechanical ventilation.

Deterioration of respiratory status that would necessitate mechanical ventilatory support included respiratory rate>30/min, inability to maintain arterial O_2 saturation>90% with fractional inspired O_2 (FIO_2)>0.60, and PCO_2>50 mmHg with pH<7.25. Nevertheless, physician's clinical judgment based on patient's condition clarified the need for ventilatory support.

Table 1. ASA* physical status classification

ASA I	Healthy patient
ASA II	Mild systemic disease with no functional limitation-for example, controlled hypertension
ASA III	Severe systemic disease with definite functional limitation-for example, chronic obstructive pulmonary disease
ASA IV	Severe systemic disease that is a constant threat to life-for example, unstable angina
ASA V	Moribund patient who is not expected to survive for 24 hours with or without surgery-for example, with an abdominal aortic aneurysm
Suffix E	Emergency procedure

* American Society of Anesthesiologists

Results were expressed as mean ± standard deviation (SD) for continuous variables, unless otherwise stated. Differences between groups were analyzed using Student's unpaired t-test or Mann-Whitney when appropriate. Qualitative data were compared using Chi-square or Fisher exact tests. To find predictive variables for the need for mechanical ventilation, unconditional stepwise logistic regression (forward and backward) was carried out with risk factors as independent variables and the need for ventilatory support as the dependent variable. Two-tailed significance tests were used in all statistical analyses. For all tests, significance was defined as $p<0.05$ (95% confidence interval). All statistical analyses were performed using SPSS software (version 16, SPSS Inc., Chicago, IL, USA).

RESULTS

The under study population included 120 patients, 77 males and 43 females with a mean age of 60.16±12.04 years (range: 29–79 years).The information regarding one patient requiring mechanical ventilation was missed. From 119 patients, 33 patients (27.7%) had deterioration of respiratory status necessitating mechanical ventilatory support.

Eighty-two patients (73.9%) had squamous cell carcinoma (SCC), while 29 (26.1%) had adenocarcinoma (AC). Development of pulmonary insufficiency was not associated with the type of tumor (p-value=0.09). The majority of patients (94.4%) did not have previous history of pulmonary disorders. Operations were carried out through transhiatal (n=44, 41.9%), McCon (n=41, 34.2%), left thoracotomy (n=18, 17.1%), and transposition (n=2, 1.9%) approaches. In comparison with other procedures, the majority of patients who underwent left thoracotomy did not require mechanical ventilation (17 cases, 94.4%).

A total of 14 patients (15.1%) received blood transfusion. Most patients had esophageal cancer in the third lower part of the esophagus (63.2%). Meanwhile, the vast majority of patients were on ASA grade II (n=87, 65.4%), followed by ASA grade I (n=41, 30.8%) and ASA grade III (n=5, 3.8%).

Preoperative ejection fraction was significantly lower in ventilated group (53.82±5.46 versus 57±5.20, p=0.06). The duration of operation was significantly longer in ventilated group (7.23±1.36 versus 6.57±1.36, p=0.02). Furthermore, ICU stay was longer in the ventilated group. However, this difference was not statistically significant (9.42±5.90 versus 7.18±4.54, p=0.10).

On the other hand, 17 patients (14.3) had in-hospital mortality; all of whom underwent mechanical ventilation. Table 2 compares

demographic and other characteristics of all patients. Multivariate analysis revealed male sex (Odds Ratio: 4.590, CI95%:1.248-16.411, p=0.019) as a confounder and duration of operation (Odds Ratio: 0.517, CI95%:1.102-2.553, p-value=0.016) as a risk factor for requiring mechanical ventilation (Table 3). All other covariates of the multivariate analysis did not prove to be statistically significant.

Table 2. Characteristics of patients undergoing esophagectomy

Characteristics		Overall	Mechanically ventilated subjects (n=33)	Non-ventilated subjects (n=86)	P-value
Age		60.16±12.04	61.33±12.65	59.72±11.91	0.51
Sex					0.04
	Male	77(64.2%)	26(78.8%)	50(58.1%)	
	Female	43(35.8%)	7(21.2%)	36(41.9%)	
Hx of pulmonary disorders		6 (5.6%)	3 (11.5%)	3 (3.8%)	0.16*
Hx of cardiovascular disorders		19 (17.4%)	7 (25%)	12 (15%)	0.255*
Prior or current cigarette use		49 (41.2%)	14 (42.2%)	34 (40%)	0.81
Prior or current opium use		15 (12.9%)	7 (21.2%)	7 (8.5%)	0.11*
Hemoglobin		12.76±1.76	12.56±1.77	12.85±1.77	0.47
Platelet		212627.27±71837	191482±54492.9	216912±70425.9	0.08
Blood transfusion		14 (15.1%)	6 (22.2%)	8 (12.1%)	0.22*
Tumor type					0.09
	SCC **	82 (73.9%)	20 (62.5%)	61 (78.2%)	
	AC ***	29 (26.1%)	12 (37.5%)	17 (21.8%)	
Tumor place					0.16*
	Lower	43 (63.2%)	14 (77.8%)	28 (57.1%)	
	Middle	19 (27.9%)	2 (11.1%)	17 (34.4%)	
	Higher	6 (8.8%)	2 (11.1%)	4 (8.2%)	
ASA grade					0.69
	I	41 (30.8%)	9 (24.3%)	32 (33.3%)	
	II	87 (65.4%)	28 (75.7%)	59 (61.5%)	
	III	5 (3.8%)	0	5 (5.2%)	
Operation type					0.009
	McCon	41(39%)	16(50%)	24(33.3%)	
	Transhiatal	44(41.9%)	13(40.6%)	31(43.1%)	
	Left Thoracotomy	18(17.1%)	1(3.1%)	17(23.6%)	
	Transposition	2(1.9%)	2(6.2%)	0(0%)	
Outcome					< 0.0001*
	Discharge	102 (85.7%)	16 (48.5%)	85 (100%)	
	Mortality	17 (14.3%)	17 (51.5%)	0(0%)	
Postoperative extubation		98 (85.2%)	21 (63.6%)	76 (93.8%)	<0.0001*
Preoperative ejection fraction		55.71±5.47	53.82±5.46	57±5.20	0.06
Preoperative hospital stay		6.86±3.7	7.70±4.58	6.56±3.31	0.15
Operation duration		6.75±1.4	7.23±1.38	6.57±1.36	0.02
ICU stay		8.08±6.16	9.42±5.90	7.18±4.54	0.10

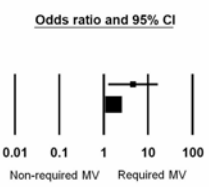
* Fisher exact test

** Squamous Cell Carcinoma

*** Adenocarcinoma

Table 3. Multivariate Logistic Regression

	Odds ratio	Lower limit	Upper limit	p-Value
Sex = Male	4.590	1.284	16.410	0.019
Operation duration	1.677	1.102	2.553	0.016



DISCUSSION

Postoperative pulmonary complications occur in 25 to 50% of patients after esophagectomy (11-13). These complications arise from a number of factors, including the type of incision, the extent of mediastinal dissection, recurrent laryngeal nerve injury that may impair coughing efficiency postoperatively, and the presence of an intrathoracic reconstructive organ or pleural effusion that may directly impair ventilation in the early postoperative period. The risk of pulmonary complications after esophagectomy is predicted on the basis of a number of preoperative factors, including patient's age, spirometric values, diffusing capacity, performance status, nutritional status, and a diagnosis of COPD (11-13). Intraoperative factors also strongly predict the likelihood of pulmonary complications. An increase in complications is associated with an increased volume of blood loss, use of the substernal rather than the posterior mediastinal route for esophageal reconstruction, and routine use of ventilatory support rather than early extubation postoperatively (11,12,14).

In this study, we studied risk factors associated with the development of pulmonary insufficiency requiring mechanical ventilation. We found that male sex, operation type, necessity of re-intubation, preoperative low ejection fraction and duration of operation are associated with the development of respiratory insufficiency.

Previous studies indicated that various factors predispose patients to develop pulmonary complications (4,11,15-19), including advanced age, history of smoking, cirrhosis and diabetes, abnormal chest radiograph or lung disease, blood loss and low serum albumin, preoperative concurrent chemoradiotherapy, general performance status, inadequate postoperative analgesia and stage of disease.

General preoperative risk classifications such as the American Society of Anesthesiologists (ASA) reveal conflicting results in the literature and have not yet proved to be useful for this necessary selection of patients with esophageal carcinoma (20,21). This is mainly due to a particular risk configuration observed in patients with esophageal cancer. We also did not find any association between ASA grade and necessity of mechanical ventilation.

In our study, there was no difference between Squamous Cell Carcinoma (SCC) and Adenocarcinoma (AC) in developing respiratory insufficiency. Authors suggested that patients with AC are more likely to have an impaired cardiovascular function. On the other hand, patients with SCC predominantly suffer from an impaired pulmonary and hepatic dysfunction due to a markedly increased nicotine and alcohol consumption (22).

The type of incision used to perform the resection is also a predictor of the likelihood of postoperative pulmonary complications. We found that patients who underwent transhiatal incision were more likely to require mechanical ventilation. In other studies, an isolated left thoracotomy was associated with fewer complications when compared with Ivor Lewis approach that is a combination of a right thoracotomy and laparotomy. Nevertheless, Ivor Lewis approach is associated with fewer complications when compared with transhiatal approach, in which laparotomy and cervical incision are performed without thoracotomy (12,23).

In this study, in-hospital mortality was significantly higher in ventilated patients. The development of pulmonary complications is associated with a sevenfold increase in the risk of operative mortality, and pulmonary complications account for 40 to 60% of operative mortality (11-13,24). Due to the high morbidity and mortality rates after esophagectomy, it has been advocated to treat patients with esophageal cancer in high volume centers (25,26). Mortality rate of our patients was 14.3%, while in a prospective analysis, highly specialized centers have reported mortality rates of approximately 5% depending on the number of esophagectomies performed (27,28). Despite this reduced mortality rates, the overall morbidity remains high even in centers with expertise in the field of esophageal surgery. Indeed, main causes of postoperative morbidity are pulmonary and cardiovascular dysfunctions as well as anastomotic leakage (29). All these postoperative complications may result in sepsis with multiple organ failure if not appropriately diagnosed and treated and may cause a prolonged hospital stay with extensive ICU therapy.

We identified 5 factors that were associated with an increased risk of pulmonary complications: male sex, operation type, necessity of re-intubation, preoperative low ejection fraction and duration of operation. Others have demonstrated that advanced age and preoperative respiratory dysfunction are associated with postoperative pulmonary complications (30-33). Age and spirometry are objective measurements, and performance status is based on a method of clinical observation that has been validated during 2 decades of use (34-35). Only a brief patient interview and a single test, which can be performed in the physician's office, are necessary to enable the clinician to compile the required information. However, the risk of postoperative pulmonary complications can be reduced in patients undergoing esophagectomy by means of improving respiratory muscle strength and performance status has yet to be investigated. Although many surgeons obtain preoperative pulmonary function tests routinely for patients undergoing esophagectomy, there is no standard clinical practice in this regard. Thus, it would be helpful for the clinician to know which patients should be sent for pulmonary function testing (36).

Multivariate analysis calculated and confirmed adenocarcinoma and duration of hospital stay as independent risk factors of needing mechanical ventilation. While Mao et al. indicated that severe perioperative complications, more postoperative complications, poor preoperative pulmonary function, radical preoperative radiotherapy, intubation and/or tracheotomy after the second postoperative day and long period of mechanical ventilation were the major risk factors leading to death once the postoperative respiratory failure developed (9). The identification of single risk factors raises the question whether it is necessary to perform a complete preoperative risk analysis or just to rely on these risk factors which can be easily assessed preoperatively. However, the advantage of a complete and detailed assessment of all organ functions is that it helps to manage surgical and non-surgical complications postoperatively in ICU. The knowledge about preoperative organ dysfunctions facilitates postoperative ICU care in case of a complicated or prolonged course. Finally, this adequate and consequent ICU management has been demonstrated to be the main key to reduce postoperative mortality (37). Based on this data, an appropriate selection of patients for esophagectomy is required to reduce postoperative mortality and morbidity and to benefit from a radical resection. Knowledge about the planned approach for resection and the route to be used for reconstruction will also provide useful information regarding the risk of postoperative pulmonary complications.

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