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Original Article

Risk factors of postoperative infection after McKeown esophagogastrectomy

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Abstract: Background: Esophageal cancer is the sixth-most common cause of cancer-related death worldwide. Surgery is the gold standard treatment for resectable esophageal cancer, and McKeown esophagogastrectomy—one of the most frequently performed operations in these cases-is often associated with severe postoperative infection. Aim: To analyze the risk factors of postoperative infection in patients who have undergone McKeown esophagogastrectomy. Methods: We retrospectively investigated the clinical data of 428 patients who have undergone McKeown esophagogastrectomy, and divided them into infection and non-infection groups. Data were analyzed using SPSS 22.0 software. Results: Between the infection and non-infection groups, smoking status (66.7% vs. 49.2%; P=0.007), male gender (86.1% vs. 74.7%; P=0.037), hoarseness (23.6% vs. 12.4%; P=0.013), poor coughing ability (51.4% vs. 13.2%; P<0.001), preoperative white blood cell (WBC) count (7.64±2.86×10^9/L vs. 7.04±2.27×10^9/L; P=0.049), postoperative day 1 (POD1) WBC count (13.24±4.98×10^9/L vs. 11.53±4.15×10^9/L; P=0.03), POD1 neutrophil count (11.84±4.73×10^9/L vs. 10.24±3.87×10^9/L; P=0.02), POD1 serum albumin (ALB) level (29.46±6.41 g/L vs. 31.76±3.64 g/L; P=0.000), POD1 creatine level (CRE; 78.15±24.09 μmol/L vs. 70.74±20.92 μmol/L; P=0.008), and POD1 blood glucose levels (11.45±4.39 mmol/L vs. 9.38±3.21 mmol/L; P=0.000) were significantly different. These factors were assessed using logistic regression analysis, and factors with P≤0.05 in the univariate analysis were entered into multivariate analysis based on the forward stepwise (conditional) method. Poor coughing ability (odds ratio [OR], 6.916, 95% confidence interval [CI], 3.716-12.871), smoking status (OR, 2.434; 95% CI, 1.299-4.563), POD1 WBC count (OR, 1.113; 95% CI, 1.040-1.191), POD1 serum ALB level (OR, 0.821; 95% CI, 0.752-0.897), and POD1 blood glucose levels (OR, 1.093; 95% CI, 1.005-1.187) were determined as independent risk factors for postoperative infection. We established a scoring system based on these 5 factors, and the area under the curve for this predictive model was 0.792 (range, 0.736-0.848); the sensitivity, specificity, and cut-off score were 73.6%, 73.0%, and 2.5, respectively. Conclusion: Among patients who have undergone McKeown esophagogastrectomy, poor coughing ability, smoking habit, high WBC and blood glucose levels, and low serum ALB levels can be used to predict the occurrence of postoperative infections.

Keywords: McKeown esophagogastrectomy, postoperative infection, risk factor

Introduction

Esophageal cancer is the sixth-most frequent cause of cancer-related death worldwide, and male patients account for a larger proportion of deaths [1]. In 2009, the incidence (22.14 per 100,000 person-years) and mortality (16.77 per 100,000 person-years) of patients with esophageal cancer in China were the highest globally [2]. Surgery remains the gold standard treatment for resectable esophageal cancer. However, esophagogastrectomy is a complex procedure, with morbidity and mortality rates of 23-50% and 2-8%, respectively, in western countries [3, 4], and 9-29% and 2-4%, respectively, in China [5, 6].

Compared with those undergoing other types of esophagogastrectomy, patients receiving McKeown esophagogastrectomy are exposed to a higher risk of trauma and infection. Moreover, patients with esophageal cancer are at a greater risk of antimicrobial exposure due to their impaired immunological functions and are also at an increased risk of infection with multidrug-resistant bacteria; hence, postoperative

Table 1. Baseline characteristics and clinical disease features between the infection group and non-infection group

Outcome	Infection group (%)	Non-infection group (%)	χ^2	*P* value
Sum	72	356	-	
Sex			4.341	0.037*
Male	62 (86.1)	266 (74.7)		
Female	10 (13.9)	90 (25.3)		
Age			1.668	0.196
≥65	27 (37.5)	106 (29.8)		
<65	45 (62.5)	250 (70.2)		
Smoking habit			7.357	0.007*
Yes	48 (66.7)	175 (49.2)		
No	24 (33.3)	181 (50.8)		
Alcohol consumption			1.385	0.239
Yes	28 (38.9)	113 (31.7)		
No	44 (61.1)	243 (68.3)		
Chemotherapy			0.304	0.708
Yes	13 (18.1)	55 (15.4)		
No	59 (81.9)	301 (84.6)		
Radiotherapy			1.773	0.183
Yes	4 (5.6)	38 (10.7)		
No	68 (94.4)	318 (89.3)		
Type of cancer			0.000	0.992
Squamous	71 (98.6)	351 (98.6)		
Others	1 (1.4)	5 (1.4)		
Other chronic disease		3.724	0.054	
Yes	38 (52.8)	144 (40.4)		
No	34 (48.2)	212 (59.6)		
Dysphagia			2.869	0.090
Yes	67 (93.1)	305 (85.7)		
No	5 (6.9)	51 (14.3)		
Substernal pain			0.473	0.491
Yes	25 (34.7)	139 (39.0)		
No	47 (65.3)	217 (61.0)		
Acid regurgitation/Vomiting			0.001	0.981
Yes	5 (6.9)	25 (7.0)		
No	67 (93.1)	331 (93.0)		
Weight loss			0.694	0.405
Yes	29 (40.3)	125 (35.1)		
No	43 (59.7)	231 (64.9)		
Other clinical features			0.578	0.447
Yes	5 (6.9)	17 (4.8)		
No	67 (93.1)	339 (95.2)		

*Statistically significant at P≤0.05.

infections in these patients present a critical problem to their health.

In the present single-center study, we assessed the risk factors for infections following McKeown esophagogastrectomy using clinical data, and developed recommendations for clinicians treating patients with these risk factors.

Methods

Data collection

We collected clinical data from 428 esophageal cancer patients (including 100 male and 328 female patients) who were admitted for McKeown esophagogastrectomy (right thoracotomy followed by laparotomy and cervical anastomosis) between July 2014 and October 2016 at Sun Yat-sen University Cancer Center (SYSUCC). The average age of the patients was 60.55±7.87 years (range, 41-82 years). Based on the occurrence of postoperative infections, we divided the patients into the infection and non-infection groups, and then retrospectively assessed the baseline characteristics, clinical disease features, perioperative features, preoperative and postoperative laboratory test results (including white blood cell [WBC], neutrophil, hemoglobin [HB], aspartate aminotransferase [AST], alanine aminotransferase [ALT], serum albumin [ALB], blood urea nitrogen [BUN], creatinine [CRE], blood glucose, C-reactive protein [CRP], and lactic acid levels) between the groups. All the postoperative day 1 (POD1) indicators were analyzed within 24 h after surgery. The authenticity of this article has been validated with the approval RDD number as RDDA2018000537, the data has been provided as Supplementary Data.

Inclusion and exclusion criteria

The inclusion criteria were as follows: patients aged >18 years with esophageal cancer who un-

Table 2. Difference in perioperative features among patients who underwent McKeon esophagogastrectomy

Outcome	Infection group (%)	Non-infection group (%)	Statistic	*P* value
Total no. of patients	72	356	-	
Hoarseness			6.204	0.013*
Yes	17 (23.6)	44 (12.4)		
No	55 (76.4)	312 (87.6)		
Poor coughing ability			55.362	<0.001*
Yes	37 (51.4)	47 (13.2)		
No	35 (48.6)	309 (86.8)		
Wound pain			0.005	0.946
Yes	14 (19.4)	68 (19.1)		
No	58 (80.6)	288 (80.9)		
Chest pain/chest distress			0.487	0.485
Yes	1 (1.4)	2 (0.6)		
No	71 (98.6)	354 (99.4)		
Heart rate			3.070	0.080
>100/min	16 (22.2)	50 (14.0)		
≤100/min	56 (77.8)	306 (86.0)		
Respiratory rate			0.774	0.379
>24/min	3 (4.2)	8 (2.2)		
≤24/min	69 (95.8)	348 (97.8)		
Atrial fibrillation			0.071	0.790
Yes	2 (2.8)	8 (2.2)		
No	70 (97.2)	348 (97.8)		
MAP	90.20±9.83	89.83±10.33	-0.281	0.779

*Statistically significant at P≤0.05. MAP: mean artery pressure.

Table 3. Difference in laboratory test results between the infection and non-infection group before McKeown esophagogastrectomy

	Infection group	Non-infection group	T value	*P* value
WBC (×10^9/L)	7.65±2.86	7.04±2.27	-1.974	0.049*
Neutrophils (×10^9/L)	4.84±2.66	4.36±1.70	-1.483	0.142
HB (g/L)	137.58±15.93	137.51±14.31	-0.035	0.972
Serum ALB (g/L)	42.29±3.62	42.85±2.96	1.228	0.223
ALT (IU/L)	19.61±12.26	21.93±35.58	0.545	0.586
AST (IU/L)	21.81±11.46	22.66±33.39	0.763	0.829
BUN (mmol/L)	5.05±1.55	5.16±1.41	0.586	0.558
CRE (μmol/L)	77.99±15.26	74.76±14.93	-1.667	0.096
Glucose (mmol/L)	5.42±0.99	5.60±1.32	1.092	0.275
CRP (mg/L)	7.38±14.33	5.67±13.91	-0.782	0.435
Lactic acid (mmol/L)	1.59±0.89	1.57±0.83	-0.197	0.844

*Statistically significant at P≤0.05. WBC, white blood cell; HB, hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALB, serum albumin; BUN, blood urea nitrogen; CRE, creatinine; CRP, C-reactive protein.

derwent McKeown esophagogastrectomy and developed an infection during hospitalization. Patients aged <18 years, those with esophageal cancer who did not undergo McKeown esophagogastrectomy, and those with infection prior to hospital admission were excluded from the study.

Statistical analysis

Student's t-test was used to examine continuous variables, and the Chi-squared test or Fisher's exact test was used to assess categorical variables. Multi-variate analysis was performed to determine the predictors of nosocomial infection, and the forward stepwise (conditional) method was used to identify factors to enter into the multivariate regression model. Receiver operating characteristic (ROC) curves were constructed to estimate the sensitivity, specificity, and the area under the curve (AUC) for various cutoff points of the relevant indicators. Statistical significance was set at P≤0.05, and all statistical analyses were computed using SPSS Version 22.0.

Results

Differences in the baseline characteristics

Table 1 describes the characteristics of the 72 patients (16.8%) with postoperative infection, from among the 428 patients who had undergone McKeown esophagogastrectomy in the present study. We compared the baseline patient characteristics and clinical disease features between the infection and non-infection groups, and identified significant differences in smoking habits and gender between the 2 groups. The

Table 4. Difference in laboratory test results between the infection and non-infection group, within 24 h after McKeown esophagogastrectomy

	Infection	Non-infection	T value	*P* value
WBC count ($\times10^9$/L)	13.24±4.98	11.56±4.15	-3.026	0.003*
Neutrophil count ($\times10^9$/L)	11.84±4.73	10.24±3.87	-3.067	0.002*
HB level (g/L)	126.03±19.92	122.86±18.56	-1.308	0.192
Serum ALB level (g/L)	29.46±3.87	31.76±3.64	4.826	<0.001*
ALT level (IU/L)	38.79±28.57	37.39±47.64	-0.241	0.810
AST level (IU/L)	51.53±30.27	47.60±49.98	-0.643	0.520
BUN level (mmol/L)	7.12±2.17	7.00±2.56	-0.348	0.728
CRE level (μmol/L)	78.15±24.09	70.74±20.92	-2.673	0.008*
Glucose level (mmol/L)	11.45±4.03	9.38±3.21	-4.103	<0.001*
CRP level (mg/L)	84.35±39.09	87.18±32.33	0.653	0.514
Lactic acid level (mmol/L)	1.92±1.02	1.74±0.95	-1.459	0.145

*Statistically significant at P≤0.05. WBC, white blood cell; HB, hemoglobin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALB, serum albumin; BUN, blood urea nitrogen; CRE, creatinine; CRP, C-reactive protein.

Table 5. Multivariate logistic regression analysis of the risk factors for infections after McKeown esophagogastrectomy

	B	Wald	P	OR	95% CI
Poor coughing ability	1.934	37.234	<0.001*	6.916	3.716-12.871
Smoking habit	0.890	7.706	0.006*	2.434	1.299-4.563
WBC count (POD1)	0.107	9.555	0.002*	1.113	1.040-1.191
Serum ALB level (POD1)	-0.197	19.234	<0.001*	0.821	0.752-0.897
Blood glucose level (POD1)	0.089	4.348	0.037*	1.093	1.005-1.187

*Statistically significant at P≤0.05. WBC (POD1): WBC count within 24 h after surgery. Serum ALB (POD1): serum ALB level within 24 h after surgery. Blood glucose (POD1): blood glucose level within 24 h after surgery. Factors were entered into multivariate regression using the forward stepwise (conditional) approach (P≤0.05).

smoking habit frequency (66.7% vs. 49.2%; P=0.007) and proportion of males (86.1% vs. 74.7%; P=0.037) were greater in the infection group than in the non-infection group.

Differences in the perioperative clinical features

In the present study, the factors of hoarseness (23.6% vs. 12.4%; P=0.013) and poor coughing ability (51.4% vs. 13.2%; P<0.001) were found to be significantly different between the groups; both were more frequent in the infection group. However, other perioperative clinical features, including wound pain, increased heart rate and respiratory rate, chest pain/chest distress, and atrial fibrillation, did not exhibit a significant difference (**Table 2**).

Differences in preoperative laboratory test results

The results of laboratory tests conducted before the surgery were compared between the groups. The WBC count was greater in the infection group than in the non-infection group (7.65±2.86×10^9/L vs. 7.04±2.27×10^9/L; P=0.049). None of the other pre-operative laboratory test results showed significant differences (**Table 3**).

Differences in postoperative laboratory test results

The POD1 laboratory test results were compared between the 2 groups. The analyses showed that the WBC count (13.24±4.98×10^9/L vs. 11.56±4.15×10^9/L; P=0.003), neutrophil count (11.84±4.73×10^9/L vs. 10.24±3.87×10^9/L; P=0.002), serum ALB level (29.46±3.87 g/L vs. 31.76±3.64 g/L; P=0.000), CRE level (78.15±24.09 μmol/L vs. 70.74±20.92 μmol/L; P=0.008), and blood glucose level (11.45±4.03 mmol/L vs. 9.38±3.21 mmol/L; P=0.000) were significantly different between the groups. However, none of the other postoperative laboratory test results showed significant differences (**Table 4**).

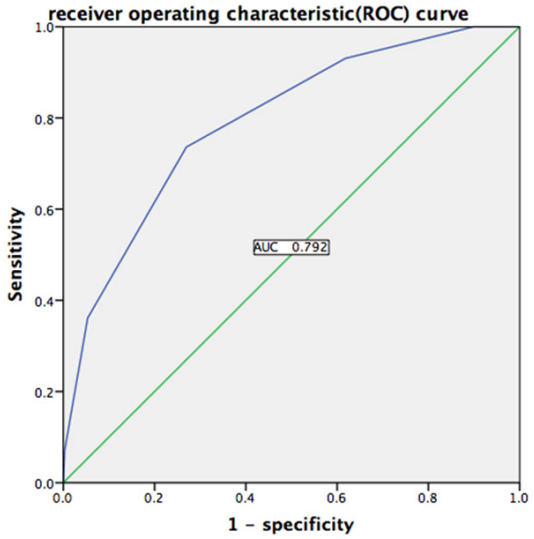

Figure 1. Receiver operating characteristic (ROC) curve of the scoring system.

Multivariate analysis

Factors that were significant in the univariate analysis (P<0.05) were included in the multivariate analysis. Accordingly, we assessed 5 factors, including poor coughing ability (odds ratio [OR], 6.916; 95% confidence interval [CI], 3.716-12.871), smoking status (OR, 2.434; 95% CI, 1.299-4.563), POD1 WBC count (OR, 1.113; 95% CI, 1.040-1.191), POD1 serum ALB level (OR, 0.821; 95% CI, 0.752-0.897), and POD1 blood glucose level (OR, 1.093; 95% CI, 1.005-1.187), using multivariate regression; male gender and the other laboratory test results were not included (**Table 5**).

Development of a scoring system to predict postoperative infections

The AUC and cut-off point were 0.600 (range, 0.526-0.673) and 11.37×10^9/L for the POD1 WBC count, 0.660 (range, 0.589-0.731) and 31.45 mmol/L for the POD1 serum ALB level, and 0.666 (range, 0.597-0.734) and 10.07 mmol/L for the POD1 blood glucose level, respectively.

Patients with were assigned a score of 1 for each of the following factors: poor coughing ability, smoking habit, POD1 WBC count and POD1 blood glucose levels greater than the cut-off values, and POD1 ALB level lower than the cut-off value; patients who did not meet these requirements were assigned a score of 0 each. The AUC of this predictive model was 0.792 (range, 0.736-0.848); the sensitivity, specificity, and cut-off score were 73.6%, 73.0%, and 2.5, respectively (**Figure 1** and **Table 6**)

Discussion

McKeown esophagogastrectomy is one of the most commonly used surgical procedures for the treatment of upper esophageal cancer; however, due to the long duration of the operation and the resulting severe trauma, it is often associated with complications and nosocomial infections. Comparisons of the infection and non-infection groups in the present study indicated that poor coughing ability (OR, 6.916; 95% CI, 3.716-12.871), smoking status (OR, 2.434; 95% CI, 1.299-4.563), POD1 WBC count (OR, 1.113; 95% CI, 1.040-1.191), POD1 serum ALB level (OR, 0.821; 95% CI, 0.752-0.897), and POD1 blood glucose level (OR, 1.093; 95% CI, 1.005-1.187) were independent risk factors for predicting postoperative infection.

As mentioned above, we found that smoking is one of the independent risk factors for predicting postoperative infection. Kinugasa et al. previously showed that smoking habit and preoperative pulmonary function insufficiency were risk factors for postoperative pulmonary complications (36.84% vs. 16.25% and 52.63% vs. 31.25, respectively; P<0.05) [7]. Moreover, Ferguson et al. confirmed that smoking was an independent risk factor for pulmonary complications (OR, 1.941; 95% CI, 1.266-2.974) [8].

In patients with poor coughing ability, the occurrence of postoperative infection could be attributed to the development of sputum thrombus. A long history of smoking could lead to impairment of the respiratory epithelium cilia structure, damage to goblet cells, and weakened cilia movement, which could all increase airway resistance, resulting in numerous postoperative sputum thrombi and consequently to the risk of pulmonary infection. most patients tend not to cough or spit, as it is painful for them to do so, especially male patients with a history of smoking before the operation.

In the present study, we found that the POD1 WBC count was an independent risk factor of postoperative infection. Similar to our findings, Sugita et al. found that the preoperative WBC count did not differ between infected and non-

Table 6. Receiver operating characteristics of the independent risk factors and the scoring system

Factors	AUC (95% CI)	*P* value	Cut-off	Sensitivity (%)	Specificity (%)
WBC count (POD1)	0.600 (0.526-0.673)	0.008*	11.37	65.3	47.2
Serum ALB level (POD1)	0.660 (0.589-0.731)	<0.001*	31.45	70.8	55.3
Blood glucose level (POD1)	0.666 (0.597-0.734)	<0.001*	10.07	58.3	69.7
Scoring system	0.792 (0.736-0.848)	<0.001*	2.5	73.6%	73.0%

*Statistically significant at P≤0.05. WBC (POD1): WBC count within 24 h after surgery. Serum ALB (POD1): serum ALB level within 24 h after surgery. Blood glucose (POD1): blood glucose level within 24 h after surgery. With regard to the scoring system, patients were assigned a score of 1 for each of the following factors: poor coughing ability, smoking habit, POD1 WBC count and POD1 blood glucose levels greater than the cut-off values, and POD1 ALB level lower than the cut-off value, whereas patients who did not meet these requirements were assigned a score of 0 each.

infected patients [9], although the WBC counts on POD1 and POD7 were significantly higher in infected patients (8.8 vs. 10.0, P=0.04; 6.1 vs. 8.8, P=0.002) than in non-infected patients. This finding was also reported by Gomez et al. who showed that the median WBC count was significantly greater in patients with infection than in those without infection during the first 10 postoperative days [10].

Furthermore, we found that the POD1 serum ALB level was an independent risk factor for nosocomial infection in patients who underwent McKeown esophagogastrectomy. Zhao et al. showed that plasma albumin level <35 g/L (OR, 2.21) was an independent risk factor for postoperative infectious complications in hepatocellular carcinoma patients [11]. Yuwen et al. demonstrated that an albumin level of <35 g/L was associated with an almost 2.5-fold increased risk of surgical site infections (SSI) in orthopedic operations [12].

Finally, our study showed that the POD1 blood glucose level was an independent risk factor for predicting postoperative infection. A previous study indicated that the POD1 blood glucose level in esophageal cancer patients after esophageal cancer surgery was only associated with the length of hospitalization [13]. Moreover, Ng et al. showed that the change in the target glucose control in diabetic patients was independently associated with an increase in SSI (OR, 2.280; 95% CI, 1.250-4.162) [14]. Another study showed that elevated blood glucose levels on admission during acute illness was associated with poor outcomes among patients undergoing surgery [15]. Ambiru et al. demonstrated that the SSI rates were directly correlated with the degree of hyperglycemia observed following surgery [16].

Patients are exposed to high risks of predicting postoperative infection after McKeown esophagogastrectomy, although poor coughing ability, smoking habit, POD1 WBC count, POD1 serum ALB level, and POD1 blood glucose level may serve as independent risk factors for postoperative infections in these patients. Finally, we used a scoring system comprising these 5 factors, and observed that the AUC of this predictive model was 0.792 (range, 0.736-0.848), whereas the sensitivity, specificity, and cut-off score were 73.6%, 73.0% and 2.5, respectively.

However, improving hand hygiene compliance and enhancing clinician education are crucial preventive strategies and well-established measures to prevent avoidable postoperative infections [17, 18]. In particular, setting high compliance standards is a widely used strategy for improving hand hygiene. Thus, through effective prevention and treatment, we could significantly reduce the risk of postoperative infection after McKeown esophagogastrectomy.

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Disclosure of conflict of interest

None.

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