Original Article

Impact of pulmonary infection after radical esophagectomy on serum inflammatory markers, pulmonary function indices, and prognosis

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ABSTRACT

الأهداف: دراسة تأثير العدوى الرئوية بعد استئصال المريء الجذري على علامات الالتهاب في الدم، ووظيفة الرئة، والتشخيص.

المنهجية: اشتملت الدراسة على 278 مريض مسجل بسرطان المريء والذين خضعوا لاستئصال المريء الجذري. أجرينا تقسيم المرضى إلى مجموعات مصابة (العدد=51) وغير مصابة (العدد=227). وأجرينا مقارنة المعلمات الالتهابية، والمضاعفات، والتشخيص.

النتائج: في المجموعة المصابة، كانت قيمة إنترلوكين 16.19±2.63 نانوغرام/لتر، وعامل نخر الورم 19.64±3.07 ميكروغرام/لتر، وIL-β بلغ 22.49±5.13 نانوغرام/لتر في 7 أيام بعد العمل الجراحي؛ كان عدد خلايا الدم البيضاء 12.65±2.14 ×$L/10^9$ لتر، وكانت نسبة العدلات 67.04±10.48%، وكان عدد الصفائح الدموية 249.82±63.26 ×$L/10^9$ لتر؛ ارتفعت مستويات العوامل المذكورة أعلاه بعد العملية بشكل كبير مقارنة بالمجموعة غير المصابة (p<0.05). بالمقارنة مع المجموعة غير المصابة، كان حجم الزفير القسري في ثانية واحدة (FEV1)، والسعة الحيوية القسرية (FVC)، وسجل مستوى FEV1/FVC انخفاضًا أكبر (p<0.05)، وكانت حالات عدم انتظام ضربات القلب والوفيات خلال 60 يومًا بعد العمل الجراحي أكبر في المجموعة المصابة (p<0.05).

الخلاصة: العدوى الرئوية بعد العملية الجراحية يمكن أن تؤدي إلى تلف وظيفة الرئة، وزيادة تعبير عامل الالتهاب، وزيادة خطر الوفاة المبكرة.

Objectives: To analyze the influence of pulmonary infection after radical esophagectomy on serum inflammatory markers, pulmonary function, and prognosis.

Methods: We enrolled 278 esophageal cancer patients who underwent radical esophagectomy. Patients were split into the infected (n=51) and uninfected groups (n=227). The inflammatory parameters, complications, and prognosis were compared.

Results: In the infected group, interleukin (IL)-6 was 16.19±2.63 ng/L, tumor necrosis factor-α was 19.64±3.07 μg/L, and IL-1β was 22.49±5.13 ng/L at 7 days postoperatively; white blood cell counts was 12.65±2.14 ×10^9/L, percentage of neutrophils (NEU%) was 67.04±10.48%, and platelet (PLT) counts was 249.82±63.26 ×10^9/L; the increasing ranges of the above factors after the operation were much raised compared with the uninfected group (p<0.05). Compared with the uninfected group, forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and FEV1/FVC were greater declines in ranges (p<0.05), and the arrhythmia incidence and the mortality within 60 days postoperatively were greater in the infected group (p<0.05).

Conclusion: Postoperative pulmonary infection can lead to pulmonary function damage, proinflammatory factor overexpression, and an increased risk of early death.

Keywords: radical esophagectomy, pulmonary infection, pulmonary function, inflammatory factors, prognosis

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Esophageal cancer (EC) has high malignancy, extensive metastasis, and poor prognosis.[1] Its morbidity rank 7th and mortality rank 6th among malignant tumors worldwide.[2] China is a high-risk EC nation, particularly in Central North China, which has the highest incidence rates in the world.[3] Current treatment options include surgery, radiotherapy, and chemotherapy, all of which are widely applied in clinical practice.[4] However, the 5-year overall survival rate of EC patients is 30-40%, and for the intermediate and advanced stages, it is less than 10%.[1]

Radical esophagectomy with lymph node dissection is an important and curative approach to cases of early or locally advanced EC.[5] However, the consequent complications can worsen the quality of life due to complex procedures with surgical incisions in the neck, chest, and abdomen.[5] Pulmonary infection occurs in 13-40% of EC cases and is the most predominantly occurring nosocomial infection in patients after curative esophagectomy.[6] Patients experience various degrees of pulmonary function decline postoperatively.[7] Consequently, the pulmonary infection may be associated with increased postoperative death.[5,7] However, there is still no consensus on whether postoperative pulmonary infection adversely affects patients' prognosis.[8,9]

Therefore, in the present study, we focused on pulmonary infection-related factors, including serum factors and pulmonary function indicators. We further analyzed the impact of pulmonary infection on the patient's outcome after curative esophagectomy.

Methods. In this study, we recruited 278 EC patients who underwent radical resection at the Department of Cardiothoracic Surgery of The Affiliated Hospital of Putian University, Putian, China, between January 2016 and June 2020. Among them, 51 patients with postoperative pulmonary infection were assigned to the infected group, and the remaining cases were assigned to the uninfected group. Each patient provided written informed consent to participate in the trial. The ethics committee of the Affiliated Hospital of Putian University, Putian, China, approved the study plan (no.: 202305). All procedures were carried out based on the Helsinki declaration.

The inclusion criteria were as follows: I) according to the Chinese guidelines for diagnosis and treatment of esophageal carcinoma 2018, patients should undergo contrast-enhanced computed tomography (CT) of the neck, chest, and upper abdomen, abdomen ultrasound, gastroscopy, and pathological biopsy; II) tumor staging met the criteria for the International Union Against Cancer and the American Joint Committee on Cancer tumor, node, and metastasis (TNM) staging (8th edition); III) all patients were newly diagnosed and underwent radical resection at the same hospital; and IV) the case records were complete.[10,11] The exclusion criteria were as follows: I) cases of coagulation defects, cardiopulmonary dysfunction, hepatorenal insufficiency, immune system disorders, and other primary malignancies; II) patients complicated with serious end-stage diseases that may affect the prognosis; III) patients having received anti-tumor therapy preoperatively; IV) patients with postoperative infections at other sites besides the lung; V) patients for whom pulmonary function tests could not be carried out postoperatively; and VI) pregnant or lactating patients. Diagnostic criteria for postoperative pulmonary infection: significant symptoms included coughing and sputum 48 hours after the operation based on the diagnostic criteria of Hospital Acquired Bronchial-Pulmonary Infection.[12] Other criteria (specific pathogens and new inflammatory lesions) should rely on imaging and laboratory examinations, such as blood culture, pathogen isolation, sputum washing and quantitative culture, and chest CT.

The study group established the quality control system and prepared the quality control protocol. The terms to be searched in the hospital information system database were carried out uniform by the study protocol. The 2 independent groups entered the data into the Statistical Package for the Social Sciences (SPSS), version 23.0 software after extracting medical data. Then the group director reviewed the data. If there were discrepancies in the data, the group director convened the 2 study teams to discuss and decide the final results. In addition, the previous related research in this manuscript was all obtained from the PubMed database.

Data on several basic characteristics, including age, gender, smoking history, underlying disease, TNM stage, surgical method, operation time, blood loss, and preoperative plasma albumin (Alb), were extracted in this investigation. Tumor necrosis factor (TNF)-α, interleukin (IL)-6, IL-1β, peripheral white blood cell (WBC), percentage of neutrophils (NEU%), and platelet (PLT) counts were examined one day preoperatively and 7 days postoperatively. Forced expiratory volume in one second (FEV1) and forced vital capacity (FVC) were simultaneously measured to calculate FEV1/FVC.

Statistical analysis. The Statistical Package for the Social Sciences, version 23.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis. Measurement data were shown as mean ± standard deviation (SD). Count variables were presented as numbers or percentages. Factors consistent with independence, normal distribution, or homogeneity of variance were assessed using the t-test between the groups. Sample rates were assessed with the Chi-square or Fisher exact probability test. A p-value of <0.05 was considered significant.

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Results. Table 1 revealed that 2 groups had comparable TNM stages (stages I, II, and III) and surgical methods (open and minimally invasive) (both $p>0.05$). The infected patients had higher proportions of smoking history and diabetes mellitus than the uninfected counterparts (both $p<0.05$). However, the 2 groups had a similar rate of hypertension disease ($p>0.05$). The infected group had longer operation time and lower preoperative Alb levels than the uninfected group ($p<0.05$).

Compared with the indices one day before the operation, 7 days after radical resection, the blood indicators (IL-6, TNF-α, IL-1β, WBC, NEU%, and PLT counts) of the 2 groups significantly increased and the pulmonary function parameters (FEV1, FVC, and FEV1/FVC) significantly decreased (Table 2, $p<0.05$). The pre-and postoperative indicators showed significant differences between the 2 groups ($p<0.05$). However, the 2 groups had similar inflammatory factor levels and pulmonary function indices one day before the operation ($p>0.05$). Conversely, the above indicators before and after the operation showed higher change ranges in the infected groups ($p<0.05$).

The complications and prognosis were compared and examined within 60 days postoperatively. There were no cases of loss to follow-up in either group. As shown in Table 3, the infected patients had significantly increased arrhythmia incidences during 60 days after surgery ($p<0.05$). In contrast, the 2 groups did not statistically significantly differ in terms of other postoperative complications, including heart failure, atelectasis, and pulmonary embolism ($p>0.05$). There were 5 (9.8%) deaths during the study period in the infected group and one (0.44%) death in the uninfected group ($p<0.05$).

Discussion. In this research, we evaluated the influence of pulmonary infection after curative EC resection on serum inflammatory markers, pulmonary function indices, and patient prognosis. Consistent with previous studies, we found the overall incidence rate of pulmonary infection to be 18%.[13] Several studies reported high multidrug-resistant bacteria detection rates and found that *Escherichia coli* and *Staphylococcus aureus* were the most prevalent pathogens with severe antibiotic resistance.[14,15] Therefore, preventing and treating pulmonary infection is of great clinical significance. For effective control of respiratory complications after radical esophagectomy, it is of critical importance to select effective antibiotics with evidence from bacterial culture and drug sensitivity tests. Our results further showed that the probability of developing a pulmonary infection postoperatively was associated with underlying diseases and preoperative Alb level. The situation was much worse for the elder individuals with relatively poor cardiopulmonary function and nutrition reserves.[16] Considering that EC patients present with long-term difficulties with eating and the consequent malnutrition after undergoing radical surgery, they should receive standardized adjustments

Table 1 - Clinical characteristics of the 2 groups.

Characteristics	Infected group (n=51)	Uninfected group (n=227)	χ^2/t	*P*-values
Age (years)	58.36±3.82	58.09±3.95	0.444	0.558
Gender				
Male	33 (65.0)	139 (61.0)	0.213	0.645
Female	18 (35.0)	88 (39.0)		
Smoking history	31 (61.0)	76 (33.0)	13.113	<0.001
Diabetes mellitus	26 (51.0)	55 (24.0)	14.434	<0.001
Hypertension	18 (45.0)	71 (31.0)	0.309	0.578
TNM stage				
I	8 (15.0)	41 (18.0)	1.415	0.493
II	33 (65.0)	156 (69.0)		
III	10 (20.0)	30 (13.0)		
Surgical method				
Minimal invasive	41 (80.0)	198 (87.0)	1.612	0.204
Open	10 (20.0)	29 (13.0)		
Operation time (h)	5.68±0.76	4.72±0.64	9.339	<0.001
Blood loss (mL)	192.34±23.68	188.36±24.71	1.047	0.103
Alb (g/L)	36.18±5.05	42.64±6.17	-6.968	<0.001

Values are presented as numbers and precentages (%) or mean ± standard deviation (SD).
TNM: tumour, node, and metastasis, Alb: albumin, h: hour

Table 2 - Comparisons of serum inflammatory markers and pulmonary function indices before and after the operation between the 2 groups.

Indexes	Infected group (n=51)				Uninfected group (n=227)				*P*-values†	
	Before the operation (one day)[a]	After the operation (7 days)	D-value[c]	*P*-values*	Before the operation (one day) [b]	After the operation (7 days)	D-value[d]	*P*-values*	a vs. b	c vs. d
IL-6 (ng/L)	1.24±0.26	16.19±2.63	13.84±2.07	<0.001	1.26±0.28	8.95±1.71	7.03±0.96	<0.001	0.862	<0.001
TNF-α (ng/mL)	1.18±0.33	19.64±3.07	17.56±2.18	<0.001	1.15±0.36	9.48±2.62	7.11±1.14	<0.001	0.619	<0.001
IL-1β (ng/L)	7.23±2.68	22.49±5.13	14.77±2.45	<0.001	7.41±2.82	15.03±4.29	6.98±1.92	<0.001	0.724	<0.001
WBC ($\times10^9$/L)	6.75±1.96	12.65±2.14	5.83±0.67	<0.001	6.81±2.02	9.04±1.81	2.21±0.56	<0.001	0.707	<0.001
NEU%	56.14±7.19	67.04±10.48	10.39±1.21	<0.001	55.73±8.71	61.03±9.35	4.04±0.52	<0.001	0.597	<0.001
PLT ($\times10^9$/L)	223.64±67.48	249.82±63.26	24.20±4.39	<0.001	225.78±69.32	236.13±67.51	10.32±2.21	<0.001	0.621	<0.001
FEV_1 (L)	2.86±0.18	0.95±0.09	-1.93±0.08	<0.001	2.81±0.12	1.48±0.10	-1.21±0.07	<0.001	0.806	<0.001
FVC (L)	3.28±0.52	1.91±0.47	-1.35±0.22	<0.001	3.31±0.56	2.59±0.66	0.68±0.12	<0.001	0.753	<0.001
FEV1/FVC (%)	87.24±3.19	48.82±3.05	-38.34±2.72	<0.001	87.78±3.07	59.31±3.05	26.48±2.09	<0.001	0.776	<0.001

Values are presented as mean ± standard deviation (SD). *Indicates paired t-test. †Indicates independent samples t-test. TNF: tumor necrosis factor, IL: interleukin, WBC: white blood cell, NEU%: percentage of neutrophils, PLT: platelet, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, vs: versus

Table 3 - Comparisons of postoperative complications and short-term prognosis between the 2 groups.

Indexes	Infected group (n=51)	Uninfected group (n=227)	χ^2	*P*-values
Arrhythmia	8 (15.69)	3 (1.32)	-	<0.001
Heart failure	2 (3.92)	1 (0.44)	-	0.088
Atelectasis	2 (3.92)	1 (0.44)	-	0.088
Pulmonary embolism	1 (1.96)	2 (0.88)	-	0.457
Death	5 (9.80)	1 (0.44)	-	0.001

Values are presented as numbers and precentages (%). Fisher exact probability with no χ^2 value.

to cardiopulmonary function and get ample nutritional support before the operation.[17] We also discovered that intraoperative bleeding was attributed to pneumonia, possibly due to the suppression of the immune system during the procedure. Similarly, Fuchita et al[18] revealed that blood loss was related to pulmonary morbidities and hospital death after EC surgery.

The present study found significantly reduced lung function and inflammatory response in infected cases than in uninfected cases. Nevertheless, it is noteworthy that patients without pulmonary infection have reportedly shown reduced pulmonary function after the operation.[19] Therefore, the deterioration of postoperative pulmonary function could not be entirely attributed to the pulmonary infection. The pulmonary function status of patients was decided by multiple factors. First, minimally invasive esophagectomy with a shorter operative time and lesser surgical trauma could better preserve pulmonary function than traditional open esophagectomy; this finding could be attributed to the suppressed level of inflammatory stress and the reduced degree of immune damage after surgery.[20] Second, resection of the pulmonary vagal branch had little effect on lung function during the surgical procedure, particularly in patients with airway hyperresponsiveness, which may facilitate improvement and recovery of postoperative pulmonary function.[21,22] Third, the drug used for intraoperative anesthesia could have affected the pulmonary function. The anesthetic regimen of propofol + dexmedetomidine showed less damage than sevoflurane.[23] Fourth, preoperative pulmonary function was correlated with the risk of postoperative infection and pulmonary function indicators.[24] Furthermore, the postoperative decline in patients' pulmonary infection can also be attributed to the invasion of pathogenic microorganisms like bacteria and viruses; this change can result in the chemotaxis of phagocytes and immune cells to lung tissues. The inflammatory mediators released by the immune cells induce vascular endothelial cell damage, inflammatory reactions, hemorrhage, and edema in the lung tissue, thus further compromising postoperative lung function.[25]

The findings confirmed that patients with postoperative pulmonary infection had a poor clinical prognosis. Our follow-up was primarily aimed at the short-term outcome at 60 days postoperatively. The main factor contributing to patient mortality within this period was postoperative complication; this might

be related to organ dysfunction without including long-term prognostic factors like recurrence and distant metastasis. The reasons may comprise the following aspects. First, the pulmonary infection can result in a postoperative hyperinflammatory reaction. Elevated systemic inflammation can cause multiple organ damage and poor prognosis.26 Second, the pulmonary infection can slow down the process of pulmonary rehabilitation and negatively impact postoperative pulmonary function. The postoperative lung function impairment can reportedly exacerbate tissue oxygen supply disorders, increase multiple organ dysfunction risks, and ultimately affect the patient's prognosis.[8] Third, pathogenic microorganism invasion and proliferation can intensify the body's stress response and impair immune function.[27] Finally, the decreased immune function can exacerbate the immunosuppressive state during postoperative chemoradiotherapy, thus leading to treatment-related adverse effects, such as superinfection.[28]

Study limitations. First, we did not investigate the medium- and long-term outcomes for postoperative patients because long-term follow-up of discharged cases is relatively complex in clinical practice. Second, the relatively small samples in this study were obtained from a single center, thus affecting the generalizability of our findings. Finally, we could not incorporate other potential risk factors into this research, such as education level, chronic obstructive pulmonary disease, and anesthesia method.[29,30] Further studies are required to explore the factors associated with pulmonary infection after curative resection for EC.

In conclusion, the present study identified smoking history, diabetes mellitus, and preoperative Alb level as predictors of the risk of postoperative pulmonary infection. The pulmonary infection could result in pulmonary function decline, inflammatory factor overexpression, and increased short-term mortality. Clinicians should adopt targeted interventions preoperatively to reduce the incidence of postoperative infection. Future evaluations should be carried out with large samples and multi-center institutions.

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References

1. He F, Wang J, Liu L, Qin X, Wan Z, Li W, et al. Esophageal cancer: trends in incidence and mortality in China from 2005-2015. *Cancer Med* 2021; 10: 1839-1847.
2. Uhlenhopp DJ, Then EO, Sunkara T, Gaduputi V. Epidemiology of esophageal cancer: update in global trends, etiology and risk factors. *Clin J Gastroenterol* 2020; 13: 1010-1021.
3. Zhu H, Ma X, Ye T, Wang H, Wang Z, Liu Q, et al. Esophageal cancer in China: practice and research in the new era. *Int J Cancer* 2023; 152: 1741-1751.
4. Watanabe M, Otake R, Kozuki R, Toihata T, Takahashi K, Okamura A, et al. Recent progress in multidisciplinary treatment for patients with esophageal cancer. *Surg Today* 2020; 50: 12-20.
5. Matsui K, Kawakubo H, Matsuda S, Hirata Y, Irino T, Fukuda K, et al. Clinical predictors of early postoperative recurrence after radical esophagectomy for thoracic esophageal cancer. *Esophagus* 2023; 20: 679-690.
6. Yuan P, Hu W, Liu Z, Wu N, Lin H, Li S, et al. Left-primary and right-auxiliary operation mode in mediastinoscope-assisted radical esophagectomy. *Surg Endosc* 2023; 37: 7884-7892.
7. Li S, Su J, Sui Q, Wang G. A nomogram for predicting postoperative pulmonary infection in esophageal cancer patients. *BMC Pulm Med* 2021; 21: 283.
8. Yu Z, Li S, Liu D, Liu L, He J, Huang Y, et al. Society for Translational Medicine Expert Consensus on the prevention and treatment of postoperative pulmonary infection in esophageal cancer patients. *J Thorac Dis* 2018; 10: 1050-1057.
9. Raftery NB, Murphy CF, Donohoe CL, O'Connell B, King S, Ravi N, et al. The complexity of defining postoperative pneumonia after esophageal cancer surgery: a spectrum of lung injury rather than a simple infective complication? *Ann Surg* 2022; 276: e400-e406.
10. National Health Commission Of The People's Republic Of China. Chinese guidelines for diagnosis and treatment of esophageal carcinoma 2018 (English version). *Chin J Cancer Res* 2019; 31: 223-258.
11. Inada M, Nishimura Y, Ishikawa K, Nakamatsu K, Wada Y, Uehara T, et al. Comparing the 7th and 8th editions of the American Joint Committee on Cancer/Union for International Cancer Control TNM staging system for esophageal squamous cell carcinoma treated by definitive radiotherapy. *Esophagus* 2019; 16: 371-376.
12. Manchal N, Mohamed MRS, Ting M, Luetchford H, Francis F, Carrucan J, et al. Hospital acquired viral respiratory tract infections: an underrecognized nosocomial infection. *Infect Dis Health* 2020; 25: 175-180.
13. Uchihara T, Yoshida N, Baba Y, Yagi T, Toihata T, Oda E, et al. Risk factors for pulmonary morbidities after minimally invasive esophagectomy for esophageal cancer. *Surg Endosc* 2018; 32: 2852-2858.
14. Liu G, Peng L, Liu B, Wang K, Han Y. Analysis of risk factors for pulmonary infection in patients with minimally invasive esophagectomy. *Oncol Lett* 2019; 17: 3283-3288.
15. Bassel LL, Co C, Macdonald A, Sly L, McCandless EE, Hewson J, et al. Pulmonary and systemic responses to aerosolized lysate of *Staphylococcus aureus* and *Escherichia coli* in calves. *BMC Vet Res* 2020; 16: 168.
16. Takahashi N, Umezawa R, Kishida K, Yamamoto T, Ishikawa Y, Takeda K, et al. Clinical outcomes and prognostic factors for esophageal cancer in patients aged 80 years or older who were treated with definitive radiotherapy and chemoradiotherapy. *Esophagus* 2022; 19: 129-136.
17. Mantoan S, Cavallin F, Pinto E, Saadeh LM, Alfieri R, Cagol M, et al. Long-term quality of life after esophagectomy with gastric pull-up. *J Surg Oncol* 2018; 117: 970-976.

18. Fuchita M, Khan SH, Perkins AJ, Gao S, Wang S, Kesler KA, et al. Perioperative risk factors for postoperative delirium in patients undergoing esophagectomy. ***Ann Thorac Surg*** 2019; 108: 190-195.
19. Booka E, Kikuchi H, Hiramatsu Y, Takeuchi H. The impact of infectious complications after esophagectomy for esophageal cancer on cancer prognosis and treatment strategy. ***J Clin Med*** 2021; 10: 4614.
20. Wang WP, Ma J, Lu Q, Han Y, Li XF, Jiang T, et al. Larynx-preserving limited resection with total thoracic esophagectomy and gastric pull-up reconstruction: a promising treatment for selected cervical esophageal squamous cell carcinoma. ***Turk J Gastroenterol*** 2020; 31: 948-954.
21. Patel K, Abbassi O, Tang CB, Lorenzi B, Charalabopoulos A, Kadirkamanathan S, et al. Completely minimally invasive esophagectomy versus hybrid esophagectomy for esophageal and gastroesophageal junctional cancer: clinical and short-term oncological outcomes. ***Ann Surg Oncol*** 2021; 28: 702-711.
22. Ding Q, Zhou W, Xue Y, Han X, Yin D, Xue L, et al. Comparison of postoperative complications between different operation methods for esophageal cancer. ***Thorac Cancer*** 2019; 10: 1669-1672.
23. Hochreiter M, Uhling M, Sisic L, Bruckner T, Heininger A, Hohn A, et al. Prolonged antibiotic prophylaxis after thoracoabdominal esophagectomy does not reduce the risk of pneumonia in the first 30 days: a retrospective before-and-after analysis. ***Infection*** 2018; 46: 617-624.
24. Tukanova KH, Chidambaram S, Guidozzi N, Hanna GB, McGregor AH, Markar SR. Physiotherapy regimens in esophagectomy and gastrectomy: a systematic review and meta-analysis. ***Ann Surg Oncol*** 2022; 29: 3148-3167.
25. Tan L, Cheng D, Wen J, Huang K, Zhang Q. Identification of prognostic hypoxia-related genes signature on the tumor microenvironment in esophageal cancer. ***Math Biosci Eng*** 2021; 18: 7743-7758.
26. Xue M, Zeng Y, Qu HQ, Zhang T, Li N, Huang H, et al. Heparin-binding protein levels correlate with aggravation and multiorgan damage in severe COVID-19. ***ERJ Open Res*** 2021; 7: 00741-02020.
27. Qiao L, Zeng SQ, Zhang N. Effects of cooperative nursing and patient education on postoperative infection and self-efficacy in gastrointestinal tumors. ***World J Clin Cases*** 2021; 9: 1610-1618.
28. Buzquurz F, Bojesen RD, Grube C, Madsen MT, Gögenur I. Impact of oral preoperative and perioperative immunonutrition on postoperative infection and mortality in patients undergoing cancer surgery: systematic review and meta-analysis with trial sequential analysis. ***BJS Open*** 2020; 4: 764-775.
29. Okamura A, Watanabe M, Kitazono S, Manoshiro H, Kasama E, Takahashi K, et al. The design of and rationale for the effect of perioperative inhaled tiotropium for patients with chronic obstructive pulmonary disease in esophageal cancer surgery (EPITOPE): an open-label, randomized, parallel-group study. ***Eur Surg Res*** 2020; 61: 123-129.
30. Sun L, Xu F, Xu X, Liu C. The correlation between common postoperative complications and quality of life, serum tumor markers, and prognosis in patients with esophageal cancer. ***Transl Cancer Res*** 2022; 11: 217-226.