Cancer Management and Research

ORIGINAL RESEARCH

Prognostic Nutritional Index as a Prognostic Indicator for the Occurrence of Postoperative Complications in Patients with Esophageal Squamous Cell Carcinoma Following Neoadjuvant Immunochemotherapy

Wenbin Zou[1,*], Wan Kuang[2,*], Chun Cai[1], Yan Qian[1]

[1]Department of Thoracic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, People's Republic of China; [2]Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, People's Republic of China

*These authors contributed equally to this work

Correspondence: Yan Qian, Tongji Hospital, Tongji Medical College, 1095 Jiefang Avenue, Qiaokou District, Wuhan, Hubei Province, 430000, People's Republic of China, Tel +86-27-83665211, Email qianyan@tjh.tjmu.edu.cn

Background & Aims: The objective of this study was to evaluate the prognostic nutritional index (PNI) as a predictor of short-term postoperative complications in esophageal squamous cell carcinoma patients undergoing neoadjuvant immunochemotherapy.

Methods: Clinical data were collected from 77 patients undergoing radical esophageal cancer surgery after neoadjuvant immunochemotherapy at Tongji Hospital from January 2022 to January 2023. The receiver operating characteristic curve (ROC) was utilized to establish the optimal cut-off point for the PNI. Subsequently, patients were stratified into low and high PNI groups according to this cut-off point, and comparisons were made between the two groups in terms of clinical data and postoperative complications.

Results: Out of the 77 patients included in the study, 31 were categorized in the low PNI group and 46 in the high PNI group, with a defined cutoff point of 47.38. Significant statistical variances were noted in the occurrence rates of general complications ($P < 0.001$), pulmonary infections ($P < 0.001$), and anastomotic fistula ($P = 0.034$) between the two groups. The low PNI group displayed elevated rates of these complications in comparison to the high PNI group.

Conclusion: The research findings indicate that preoperative nutritional assessment using the PNI can effectively predict short-term postoperative complications in esophageal squamous cell carcinoma patients who have undergone neoadjuvant therapy. Furthermore, the results suggest that implementing nutritional interventions for patients with moderate-to-severe malnutrition, as indicated by preoperative PNI evaluation, may help reduce the incidence of postoperative complications.

Keywords: prognostic nutritional index, neoadjuvant immunochemotherapy, postoperative complications, esophageal squamous cell carcinoma

Introduction

Esophageal squamous cell carcinoma (ESCC) is the predominant form of esophageal cancer in East Asia, with a particularly high incidence in China.[1] Over time, there have been advancements and enhancements in the treatments available for esophageal squamous carcinoma, encompassing surgical procedures, radiation therapy, chemotherapy, and the emerging field of immunotherapy.[2] In the treatment of locally advanced esophageal squamous cell carcinoma, neoadjuvant chemotherapy followed by surgical intervention has been a well-established approach. Recently, the use of neoadjuvant chemotherapy and immunotherapy has emerged as a hopeful option for individuals diagnosed with advanced esophageal squamous cell carcinoma. Preoperative neoadjuvant therapies are implemented to diminish the size and extent of the tumor, thereby facilitating the execution of surgery.[3] Subsequent to neoadjuvant therapy, surgical intervention may enhance the survival rates of certain patients in contrast to immediate surgery; however, it concurrently

Received: 23 February 2024
Accepted: 18 June 2024
Published: 21 June 2024

heightens the likelihood of short-term postoperative complications, including infection, bleeding, and cardiopulmonary complications.[4] This phenomenon could potentially be attributed to the modified nutritional and immune statuses observed in patients following neoadjuvant therapy.

The Prognostic Nutritional Index (PNI) serves as a valuable instrument for assessing patients' nutritional and immune health, determined by factors like white blood cell count, lymphocyte ratio, and total protein levels. Originally used in gastrointestinal tumors to predict patient outcomes and post-surgery issues.[5,6] The PNI has been associated with patient survival in the management of esophageal squamous cell carcinoma.[7,8] Nevertheless, there is a lack of adequate research on the use of PNI in predicting short-term postoperative complications in esophageal cancer after neoadjuvant therapy. Thus, this study aims to examine the potential utility of the PNI in predicting short-term complications necessitating reoperation following neoadjuvant therapy for esophageal cancer, thereby offering a more nuanced and targeted approach to the management of this disease.

Materials and Methods

Patients

We retrospectively analyzed the clinical data of patients with esophageal squamous cell carcinoma who underwent neoadjuvant immunotherapy and radical surgery for esophageal cancer at the Department of Thoracic Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, China, between January 2022 and January 2023. In order to qualify for inclusion in this research study, individuals must possess a preoperative diagnosis of esophageal squamous cell carcinoma and have undergone a minimum of two cycles of neoadjuvant immunotherapy in conjunction with chemotherapy. Additionally, patients must have full clinical information, be suitable for surgery, and have no previous cancer diagnoses. The exclusion criteria for this study encompassed several factors: (1) the presence of relevant examinations indicating tumor metastasis, (2) preoperative examinations indicating an infectious condition, (3) the coexistence of severe cardiopulmonary function or metabolic diseases of the immune system, and (4) a previous history of other malignant tumors.

Methods

The study gathered comprehensive patient data, encompassing age, gender, presence of comorbidities, neoadjuvant treatment regimen, and TNM stage prior to treatment. We applied the age-adjusted Charlson Comorbidity Index[9] to assess patients' risk of adverse events, and the 8th edition of TNM staging for esophageal cancer published by the American Joint Committee on Cancer was used to assess tumor staging.[10] Additionally, preoperative assessments were conducted, encompassing serum albumin levels, lymphocyte count, lung function test results, and lesion site, among other factors. Surgery-related information included surgical method, duration of surgery, and amount of intraoperative bleeding, and postoperative pathology including pathology type, degree of differentiation, TNM stage, number of days of hospitalization, and number of days of postoperative surgery. We analyzed all complications that occurred within 1 month of surgery. Postoperative complications related data include lung infection, anastomotic fistula, postoperative rebleeding, celiac chest, pulmonary atelectasis, incision infection, venous thrombosis and so on.

Blood samples were obtained at various time points, including pre-surgery, admission day, and the first and third days post-surgery, in order to calculate the PNI for the participants in the study. The PNI was calculated according to the formula PNI = serum albumin (g/L) + 5 × lymphocyte count (10^9/L).[7] Furthermore, ROC curves were generated for the subjects using the blood test outcomes. It was observed that the PNI calculated using the pre-surgery blood samples exhibited the largest area under the curve. The ideal threshold for this PNI was established based on the Youden index. The 77 participants were divided into two cohorts based on their PNI levels: a low PNI group (n = 30) and a high PNI group (n = 47), as defined by the ideal PNI threshold. Subsequently, a comparison was made between the two patient groups regarding general information and postoperative complication rates.

Statistical analysis was conducted using SPSS 26.0 software, with group comparisons carried out through the chi-square test. Statistical significance in the results was determined at a significance level of $P < 0.05$.

Results

The study population consisted of 77 patients with a median age of 62 years (range 41–79), consisting of 62 males and 15 females. All patients received two cycles of a chemotherapy regimen consisting of Paclitaxel (175 mg/m^2) and cisplatin (75 mg/m^2). Additionally, 70 patients underwent an immunotherapy regimen with intravenous tirilizumab 200 mg every 3 weeks, while the remaining 7 patients received an immunotherapy regimen with pembrolizumab 200 mg every 3 weeks. The clinical stage of esophageal cancer before neoadjuvant therapy was stage 3 in 52 patients and stage 4 in 25 patients. The median age-adjusted Charlson Comorbidity Index was 4 (range 2–7) in this patient cohort. A total of 65 patients underwent McKeown esophagectomy and 12 patients underwent SWEET radical esophagectomy for the treatment of esophageal cancer. Postoperative pathology findings indicated complete pathological remission in 19 patients, accounting for 24.7% of the total cohort. Overall, 68 patients, representing 80.5% of the cohort, achieved pathological remission.

ROC Curves of PNI

The preoperative PNI values demonstrated the highest predictive capacity. Figure 1 illustrates the calculation of corresponding PNI values based on blood check results obtained on the day of admission, the day before surgery, the first and third days after surgery. Complete data on 77 patients were available for each group. ROC curves were created, revealing the highest area under the curve for the PNI values the day prior to surgery at 0.754 (95% CI, 0.632–0.876; P<0.001). The optimal threshold was identified as 47.38, with a sensitivity of 81.3% and specificity of 72.4%.

Clinical Characteristics

The study encompassed a cohort of 77 patients, with a mean age of 60.14 ± 7.83 years, ranging from 41 to 79 years. Patients were divided into two categories depending on their PNI levels: a high PNI category (PNI ≥ 47.38, including patients with adequate nutrition or slight malnutrition, n = 47) and a low PNI category (PNI < 47.38, including patients with moderately severe malnutrition, n = 30). Table 1 presents a comparison of fundamental patient data between the low PNI group and the high PNI group. In the high PNI group, 14 patients (29.79%) were aged over 65 years, a proportion that did not significantly

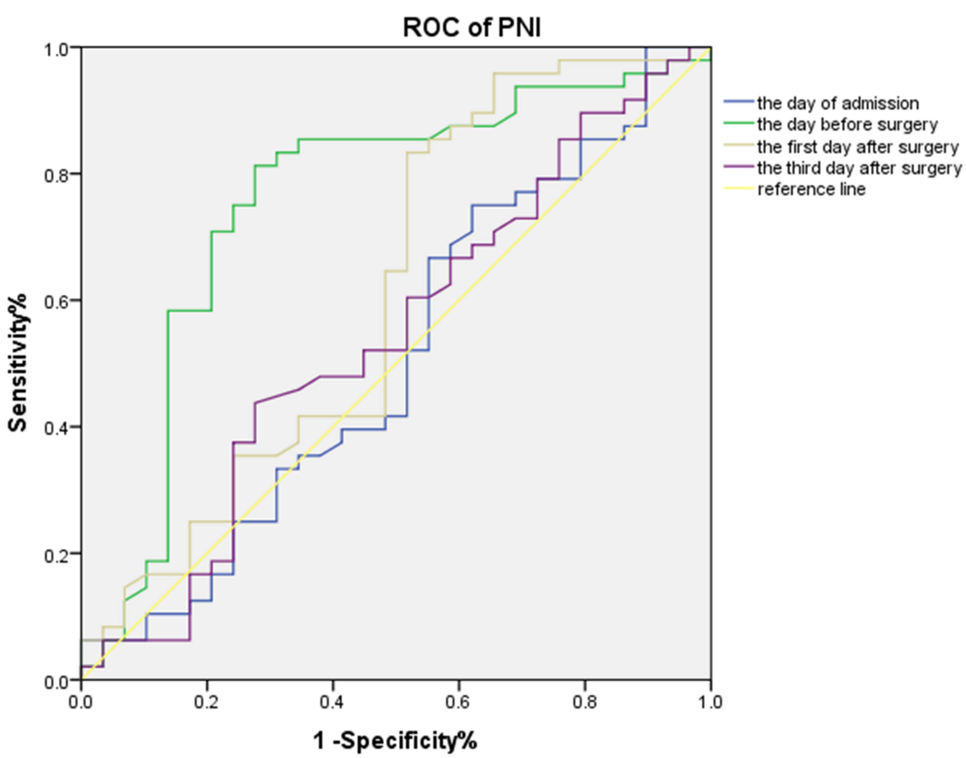

Figure 1 The ROC curves of PNI: The ROC curve based of PNI on the day before surgery has the maximum area under the curve, with a value of 0.754 (95% confidence interval: 0.632~0.876, *P*<0.001).

Table 1 Relationship Between Clinical Characteristics and Prognostic Nutritional Index n (%)

Characteristic	PNI-High (n=47)	PNI-Low (n=30)	χ^2	*P*-value
Age(yr)			0.912	0.34
≥65	14(29.79%)	6(20%)		
<65	33(70.2%)	24(80%)		
Gender			0.465	0.495
Male	39(82.98%)	23(76.67%)		
Female	8(17.02%)	7(23.33%)		
Tumor location			1.757	0.415
Upper 1/3	5(10.64%)	1(3.33%)		
Middle 1/3	20(42.55%)	16(53.33%)		
Lower 1/3	22(46.81%)	13(43.33%)		
T stage			14.814	0.001
cT2	7(14.89%)	2(6.67%)		
cT3	34(72.34%)	12(40%)		
cT4	6(12.77%)	16(53.337%)		
N stage			12.943	0.002
cN1	23(48.94%)	5(16.67%)		
cN2	17(36.17%)	14(46.67%)		
cN3	4(8.51%)	11(36.67%)		
TNM stage				0.000
3	41(87.23%)	11(36.67%)	21.355	
4	6(12.77%)	19(63.33%)		
COPD	5(10.64%)	1(3.33%)	1.36	0.244
Hypertension	16(34.04%)	12(40%)	0.281	0.596
Diabetes	7(14.89%)	7(23.33%)	0.877	0,349
Coronary Heart Disease	7(14.89%)	9(30%)	2.539	0.111
Hyperlipidemia	3(6.38%)	2(6.67%)	0.002	0.961
Age-adjusted Charlson Comorbidity Index			4.090	0.043
≥4	29(61.70%)	25(83.33%)		
<4	18(38.30%)	5(16.67%)		
Surgical Methods			1.165	0.28
McKeown Esophagectomy	38(80.85%)	27(90%)		
SWEET	9(19.15%)	3(10%)		
Thoracoscopic Surgery	23(48.94%)	16(53.33%)	0.142	0.707
Complete Pathological Remission	13(27.66%)	6(20%)	0.578	0.447
Body Mass Index			4.591	0.1
<18.5	3(6.38%)	6(20%)		
18.5–24	30(63.83%)	18(60%)		
>24	15(0.32%)	5(0.17%)		

differ from the 6 patients (20%) in the low PNI group. The high PNI group consisted of 39 male patients (82.98%), while the low PNI group had 23 male patients (76.67%), with no statistically significant difference between the two groups. Additionally, the tumour T-stage, N-stage, and TNM-stage were found to be more advanced in the low PNI group compared to the high PNI group, with a statistically significant difference (P<0.01). There were no statistically significant differences observed in the incidence of COPD, hypertension, diabetes, coronary artery disease, and hyperlipidemia between the two groups. However, a higher proportion of individuals in the low PNI group (83.33%) had an age-corrected Charlson's co-morbidity index greater than 4 compared to the high-PNI group (61.70%), with a statistically significant difference noted between the two groups (P=0.042). There was no significant difference in surgical approach and BMI between the two groups. Postoperative pathology indicated complete pathological remission in 20% of patients in the low PNI group and 27.66% in the high PNI group, with no statistically significant variance between the groups.

Short-Term Postoperative Complications

The study displays the postoperative complications observed in Table 2. The comprehensive complication rate was approximately 37.66%, with a notably higher prevalence of pulmonary infection (33.77%) and anastomotic fistula (10.39%). The results depicted in Figure 2 indicate that short-term postoperative complications were markedly more prevalent in the low PNI group as opposed to the high PNI group, with occurrence rates of 70% and 17.02% respectively (P < 0.01). Furthermore, a notable discrepancy was observed in the prevalence of lung infections between the low PNI group (70%) and the high PNI group (10.64%). Additionally, anastomotic fistula was detected in 20% of patients in the low PNI group, a significantly higher incidence compared to the 4.26% observed in the high PNI group, indicating statistical significance. There was a lack of statistically significant variation observed in the occurrence of postoperative bleeding, suboptimal incision healing, and thrombosis.

Discussion

Despite the current lack of comprehensive data pertaining to the optimal strategy for treating esophageal cancer, the existing findings indicate that the integration of neoadjuvant immunotherapy with chemotherapy holds significant promise.[11] The literature reports an average pathological complete response rate (PCR) of 28.3% for the combined use of neoadjuvant immunotherapy and chemotherapy. Notably, certain studies[12–17] have reported PCR rates exceeding 30%. Furthermore, the pairing of neoadjuvant immunotherapy and chemotherapy demonstrated an impressive major pathological response (MPR) rate, averaging 50.3%.[18] Among the 77 patients included in our research, 19 patients (24.7%) achieved complete pathological remission after surgery. This remission rate aligns closely with the findings reported in existing literature. Additionally, 62 patients (80.5%) attained pathological remission, surpassing the rates documented in previous studies. This discrepancy can likely be attributed to our exclusion of patients who experienced disease progression after neoadjuvant therapy, as well as those who did not undergo surgery. These results offer promising evidence supporting the efficacy of combining neoadjuvant immunotherapy with chemotherapy.

Regarding surgical safety, the literature has documented the occurrence of surgical complications in neoadjuvant immunotherapy combined with chemotherapy at rates of 47.1%,[15] 26.3%,[19] and 51.0%.[20] Our research revealed a postoperative complication rate of 37.7%, which closely matches the rates documented in previous studies. Despite the existence of multiple studies demonstrating the manageable nature of postoperative complications following the administration of neoadjuvant immunotherapy in conjunction with chemotherapy, and the absence of any reported deaths during the perioperative period,[19,21] it is undeniable that the incidence of complications remains higher compared to patients solely undergoing surgery. This disparity may be attributed to the occurrence of leukopenia and lung injury subsequent to treatment.[16,19] At present, there is a dearth of literature concerning the prediction of postoperative complications following neoadjuvant therapy. Given the elevated rate of complications associated with this treatment, there is an immediate requirement for a dependable predictive index that can effectively evaluate the likelihood of postoperative complications in patients prior to surgery subsequent to neoadjuvant therapy. Such an index would aid in mitigating the occurrence of postoperative complications through timely intervention.

Table 2 Relationship Between Short-Term Postoperative Complications and Prognostic Nutritional Index n (%)

Complications	PNI-High (n=47)	PNI-Low (n=30)	χ^2	*P* value
Total	8(17.02%)	21(70%)	21.891	0.000
Pulmonary Infection	5(10.64%)	21(70%)	28.852	0.000
Anastomotic Fistula	2(4.26%)	6(20%)	4.876	0.027
Poor Wound Healing	1(2.13%)	0(0%)	0.647	0.421
Bleeding	0(0%)	1(3.33%)	1.587	0.207
Thrombosis	1(2.13%)	1(3.33%)	0.105	0.746

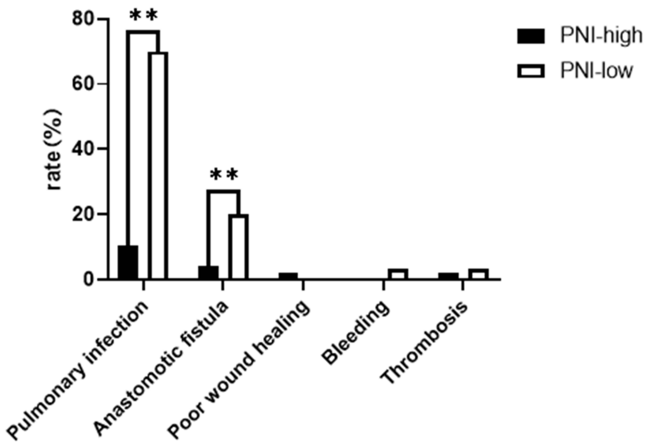

Figure 2 Short-term postoperative complications in patients: Patients in the PNI-low group exhibited significantly higher rates of pulmonary infection and anastomotic fistula compared to those in the PNI-high group. ***P*<0.01.

The PNI is determined through the assessment of serum albumin levels and peripheral blood lymphocyte concentrations, integrating data on albumin and absolute lymphocyte counts to provide insight into the patient's nutritional and inflammatory status. Li[22] conducted a meta-analysis comprising nine articles to examine the prognostic implications of esophageal squamous cell carcinoma. The results showed a strong connection between decreased PNI before treatment and both overall survival (OS) and recurrence-free survival (RFS). Consequently, PNI emerges as a dependable prognostic indicator for esophageal carcinoma, with a higher prevalence of low PNI observed in advanced stages of the disease. Our research findings indicate a significant association between low PNI levels and advanced tumor T-stage, N-stage, and clinical stage in individuals with esophageal cancer, underscoring the prognostic value of PNI in this context. However, the utility of PNI in predicting surgical complications remains a subject of debate. A meta-analysis of multiple studies[23] concluded that there is insufficient evidence to support the notion that a low PNI poses a risk for postoperative complications in patients diagnosed with esophageal cancer. Nevertheless, Qi[24] identified a significantly greater occurrence of postoperative complications in the low-PNI group as opposed to the high-PNI group (29.69% vs 13.26%, $P < 0.001$). At present, there is a lack of scholarly investigation into the significance of the Prognostic Nutritional Index in predicting surgical complications among patients with esophageal cancer who have undergone neoadjuvant immunotherapy in combination with chemotherapy. Our research shows that using preoperative PNI is very helpful in evaluating postoperative complications after neoadjuvant treatment. Using the ROC curve, we found a PNI threshold of 47.38, consistent with most previous studies.[24] Subsequent analysis based on this threshold revealed a significant difference in the rates of lung infection and anastomotic fistula between the low and high PNI groups. The difference may be due to the reverse relationship between PNI and levels of leukocytes and albumin in patients, suggesting weakened immunity and nutritional status. Furthermore, our study ascertained that PNI serves as an actionable indicator. Due to the retrospective nature of this analysis, our interventions for patients with low PNI after admission were limited to generalized nutritional support and symptomatic treatment. Nonetheless, our findings indicate that preoperative PNI, adjusted for treatment, exhibited a stronger predictive value for postoperative complications compared to PNI upon admission. This suggests the potential for implementing more targeted nutritional support in hospitals, specifically for patients with low PNI, to enhance their preoperative PNI levels and mitigate complications. This assertion, however, necessitates additional clinical trials to validate.

The PNI functions as a dual indicator for nutrition and immunity, influenced by levels of ALB and lymphocyte counts, offering information on the patient's inflammatory and nutritional condition. Notably, neoadjuvant immunotherapy combined with chemotherapy commonly leads to complications such as leukopenia, granulocytopenia, and hypoproteinemia.[19] Therefore, it is logical to conclude that PNI is a useful indicator of the patient's nutritional and immune health after treatment, underscoring the importance of assessing and intervening in nutrition before surgery to reduce complications after surgery. Patients with a low PNI necessitate the involvement of dietitians and collaboration with nurses or physicians for clinical management. The initial approach to addressing cancer-related nutritional issues involves nutritional counseling by healthcare professionals, which is regarded as the primary form of nutritional therapy after the identification and categorization of such problems.

Several nutritional and inflammatory markers, such as the mGPS, CONUT score, and GNRI, have been associated with outcomes in esophageal cancer.[25,26] However, additional research is required to explore their utility, as well as their strengths and limitations in comparison to the PNI, in neoadjuvant immunization and chemotherapy patients with esophageal cancer.

This study possesses various limitations, including its retrospective nature and its confinement to a solitary institute, which may introduce selection bias. The limited sample size in this study serves as a constraint, and we anticipate the incorporation of data from additional research centers to bolster our argument. Furthermore, our analysis solely focuses on the correlation between variables, while the underlying mechanism remains indeterminate. In order to validate our results in individuals with esophageal carcinoma, it is crucial to conduct carefully designed prospective studies involving various institutions.

Conclusions

Calculating the PNI is simple and easy, making it a useful tool for predicting short-term postoperative complications in esophageal cancer patients after neoadjuvant therapy. Moreover, implementing nutritional interventions in individuals with moderate-to-severe malnutrition, as indicated by their preoperative evaluation, may potentially help to mitigate the occurrence of postoperative complications.

Institutional Review Board Statement

Ethical review and approval were waived for this study due to this study is a retrospective analysis.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the corresponding author on request.

Ethics Approval

This study was conducted at the Department of Thoracic surgery, Tongji Hospital of Huazhong University of Science & Technology. This study was conducted according to the Declaration of Helsinki and approved by the ethic committee of Tongji Medical College of Huazhong University of Science & Technology (approval number, TJ-IRB20210624). Informed consent from the patients was waived by the IRB because the nature of this retrospective study was reanalyzing of existing data, which does not involve any potential risks and benefits to the patients.

Informed Consent Statement

Written informed consent has been obtained from the patients to publish this paper.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research received no external funding.

Disclosure

Wenbin Zou and Wan Kuang are co-first authors for this study. The authors declare that they have no conflicts of interest in this work.

References

1. Zhang Y. Epidemiology of esophageal cancer. *World J Gastroenterol*. 2013;19(34):5598. doi:10.3748/wjg.v19.i34.5598
2. Pennathur A, Gibson MK, Jobe BA, Luketich JD. Oesophageal carcinoma. *Lancet*. 2013;381(9864):400–412.

3. Wu C, Li M, Meng H, et al. Analysis of status and countermeasures of cancer incidence and mortality in China. *Sci China Life Sci*. 2019;62 (5):640–647. doi:10.1007/s11427-018-9461-5
4. Lordick F, Mariette C, Haustermans K, Obermannová R, Arnold D. Oesophageal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2016;27:v50–v7. doi:10.1093/annonc/mdw329
5. Onodera T, Goseki N, Kosaki G. Prognostic nutritional index in gastrointestinal surgery of malnourished cancer patients. *Nihon geka gakkai zasshi*. 1984;85(9):1001–1005.
6. Buzby GP, Mullen JL, Matthews DC, Hobbs CL, Rosato EF. Prognostic nutritional index in gastrointestinal surgery. *Am J Surg*. 1980;139 (1):160–167. doi:10.1016/0002-9610(80)90246-9
7. Hirahara N, Tajima Y, Fujii Y, et al. Preoperative prognostic nutritional index predicts long-term surgical outcomes in patients with esophageal squamous cell carcinoma. *World J Surg*. 2018;42(7):2199–2208. doi:10.1007/s00268-017-4437-1
8. Feng J-F, Chen Q-X. Significance of the prognostic nutritional index in patients with esophageal squamous cell carcinoma. *Therap Clin Risk Manage*. 2013;1–7. doi:10.2147/TCRM.S56159
9. Koppie TM, Serio AM, Vickers AJ, et al. Age-adjusted Charlson comorbidity score is associated with treatment decisions and clinical outcomes for patients undergoing radical cystectomy for bladder cancer. *Cancer*. 2008;112(11):2384–2392. doi:10.1002/cncr.23462
10. Rice TW, Ishwaran H, Ferguson MK, Blackstone EH, Goldstraw P. Cancer of the esophagus and esophagogastric junction: an eighth edition staging primer. *J Thorac Oncol*. 2017;12(1):36–42.
11. Liu Y, Bao Y, Yang X, et al. Efficacy and safety of neoadjuvant immunotherapy combined with chemoradiotherapy or chemotherapy in esophageal cancer: a systematic review and meta-analysis. *Front Immunol*. 2023;14:1117448. doi:10.3389/fimmu.2023.1117448
12. Shen D, Chen Q, Wu J, Li J, Tao K, Jiang Y. The safety and efficacy of neoadjuvant PD-1 inhibitor with chemotherapy for locally advanced esophageal squamous cell carcinoma. *J Gastrointest Oncol*. 2021;12(1):1. doi:10.21037/jgo-20-599
13. Yang P, Zhou X, Yang X, et al. Neoadjuvant camrelizumab plus chemotherapy in treating locally advanced esophageal squamous cell carcinoma patients: a pilot study. *World J Surg Oncol*. 2021;19(1):1–8. doi:10.1186/s12957-021-02446-5
14. Duan H, Shao C, Pan M, et al. Neoadjuvant pembrolizumab and chemotherapy in resectable esophageal cancer: an open-label, single-arm study (PEN-ICE). *Front Immunol*. 2022;13:849984. doi:10.3389/fimmu.2022.849984
15. Liu J, Li J, Lin W, et al. Neoadjuvant camrelizumab plus chemotherapy for resectable, locally advanced esophageal squamous cell carcinoma (NIC-ESCC2019): a multicenter, Phase 2 study. *Int J Cancer*. 2022;151(1):128–137. doi:10.1002/ijc.33976
16. Liu J, Yang Y, Liu Z, et al. Multicenter, single-arm, Phase II trial of camrelizumab and chemotherapy as neoadjuvant treatment for locally advanced esophageal squamous cell carcinoma. *Journal for Immunotherapy of Cancer*. 2022;10(3):e004291. doi:10.1136/jitc-2021-004291
17. Lv H, Tian Y, Li Z, Huang C, Xu Y, Tian Z. 557 neoadjuvant camrelizumab in combination with albumin paclitaxel and cisplatin for patients with locally advanced esophageal squamous cell carcinoma (ESCC). *BMJ Spec J*. 2021;3:1.
18. Wang J, Zhang K, Liu T, et al. Efficacy and safety of neoadjuvant immunotherapy combined with chemotherapy in locally advanced esophageal cancer: a meta-analysis. *Front Oncol*. 2022;12:974684. doi:10.3389/fonc.2022.974684
19. Wu Z, Zheng Q, Chen H, et al. Efficacy and safety of neoadjuvant chemotherapy and immunotherapy in locally resectable advanced esophageal squamous cell carcinoma. *J Thoracic Dis*. 2021;13(6):3518. doi:10.21037/jtd-21-340
20. Lv H, Tian Y, Li J, et al. Neoadjuvant sintilimab plus chemotherapy in resectable locally advanced esophageal squamous cell carcinoma. *Front Oncol*. 2022;12:864533.
21. Xu W, Jiang Y, Wang C, et al. The efficacy and safety of neoadjuvant camrelizumab and chemotherapy for locally advanced thoracic esophageal squamous cell carcinoma. *Am Soc Clin Oncol*. 2022;5:1.
22. Li P, Wang X, Lai Y, Zhou K, Tang Y, Che G. The prognostic value of pre-treatment prognostic nutritional index in esophageal squamous cell carcinoma: a meta-analysis. *Medicine*. 2019;98:22.
23. Hao J, Chen C, Wan F, et al. Prognostic value of pre-treatment prognostic nutritional index in esophageal cancer: a systematic review and meta-analysis. *Front Oncol*. 2020;3:10.
24. Qi Q, Song Q, Cheng Y, Wang N. Prognostic significance of preoperative prognostic nutritional index for overall survival and postoperative complications in esophageal cancer patients. *Cancer Manage Res*. 2021;13:8585–8597. doi:10.2147/CMAR.S333190
25. Wang Y, Wang L, Fang M, et al. Prognostic value of the geriatric nutritional risk index in patients exceeding 70 years old with esophageal squamous cell carcinoma. *Nutr Cancer*. 2020;72(4):620–626. doi:10.1080/01635581.2019.1650189
26. Toyokawa T, Kubo N, Tamura T, et al. The pretreatment Controlling Nutritional Status (CONUT) score is an independent prognostic factor in patients with resectable thoracic esophageal squamous cell carcinoma: results from a retrospective study. *BMC Cancer*. 2016;16(1):1–11. doi:10.1186/s12885-016-2696-0