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ORIGINAL RESEARCH

The CALLY Index as a Predictive Tool for Postoperative Pneumonia in Esophageal Squamous Cell Carcinoma: A Retrospective Cohort Study

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Background: Esophageal Squamous Cell Carcinoma poses a significant global health challenge, with postoperative pneumonia being a critical complication affecting recovery and prognosis. Traditional predictive models have proven to be insufficient. This study investigates the CALLY Index as a novel tool for predicting postoperative pneumonia in resectable ESCC patients.

Methods: A retrospective cohort study was conducted involving 209 patients undergoing thoraco-laparoscopic McKeown procedure for resectable ESCC from January 2019 to December 2022. Patients with chronic pulmonary diseases or previous malignancies were excluded. Clinical data, including age, gender, tumor stage, preoperative albumin, lymphocyte counts, and CRP levels, were analyzed to calculate the CALLY Index. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of postoperative pneumonia, and receiver operating characteristic curves were used to evaluate the CALLY Index's predictive validity.

Results: Among the cohort, 63.8% of patients with low CALLY Index scores developed postoperative pneumonia compared to 12.1% with high scores ($p < 0.001$). The optimal cutoff for the CALLY Index was determined to be 3.47, achieved sensitivity of 0.721 and specificity of 0.865. In multivariate analyses, the CALLY Index remained a strong predictor of pneumonia (adj. OR: 0.64, 95% CI: 0.51–0.77, $p < 0.001$). Notably, higher tumor stage and prolonged hospital stays were also associated with an increased risk of pneumonia.

Conclusion: The CALLY Index is an effective predictor of postoperative pneumonia in patients with esophageal squamous cell carcinoma, especially when evaluated in conjunction with tumor stage and length of hospital stay. This approach can aid clinicians in conducting early risk assessments and customizing therapeutic strategies, ultimately enhancing patient management and outcomes.

Keywords: esophageal squamous cell carcinoma, postoperative pneumonia, CALLY Index, predictive tool, surgical outcomes

Introduction

Esophageal cancer remains a prominent global health concern, with notable variations in incidence and mortality across different geographical regions.[1,2] Among its subtypes, esophageal squamous cell carcinoma (ESCC) accounts for a substantial proportion of cases, particularly in Eastern Asia and parts of Africa, where its prevalence is influenced by specific environmental and lifestyle factors.[3–5] In China, the regional patterns of ESCC incidence are striking, particularly within the so-called "esophageal cancer belt", underscoring the necessity for localized data and tailored intervention strategies.[6,7] For patients with resectable ESCC, surgical resection remains the cornerstone of treatment, occasionally supplemented by neoadjuvant therapies, depending on the cancer stage and the patient's general condition.[8–10] However, postoperative complications—such as arrhythmias, anastomotic leaks, and notably, pulmonary infections—can significantly hinder recovery and adversely affect long-term prognoses.[11]

Recent studies have emphasized the detrimental impact of postoperative pulmonary infections on the prognosis of ESCC patients; these infections are associated with prolonged hospital stays and elevated healthcare costs.[12,13] Furthermore, they have been linked to poorer disease-free survival (DFS) and overall survival (OS) outcomes.[14]

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Therefore, it is critical to identify those at heightened risk for postoperative pneumonia to allow for timely intervention.[15] Currently, diagnosis is typically made only after the emergence of clinical symptoms, such as persistent cough and fever, with confirmation through imaging techniques like CT scans. At this late stage, the infection is usually well established, and although clinical interventions—such as bronchoscopic sputum aspiration or modifications to antibiotic regimens—may be employed, the opportunity for early treatment is often missed.[16,17] Thus, the development of predictive tools for early identification of postoperative pneumonia based on perioperative clinical data is vital for improving patient outcomes.

Traditionally, prognostic assessments for ESCC have relied on clinical and pathological staging. However, the advent of preoperative laboratory markers has provided new avenues for predictive insights. Markers such as neutrophil, lymphocyte, monocyte, and platelet counts, as well as levels of albumin and C-reactive protein (CRP), have been used to derive various ratios, including the Neutrophil-to-Lymphocyte Ratio (NLR), Platelet-to-Lymphocyte Ratio (PLR), and Lymphocyte-to-Monocyte Ratio (LMR), all of which show promise in forecasting postoperative complications.[18] Investigators have demonstrated the prognostic relevance of these markers in various malignancies. For instance, Ouyang et al found that lower baseline NLR and early NLR reduction correlated with better outcomes in metastatic colorectal cancer patients receiving immunotherapy,[19] while Lu et al identified PLR as a significant predictor of survival in advanced hepatocellular carcinoma patients undergoing immune checkpoint inhibition and kinase inhibitor combination therapy.[20] Additionally, Susiarno et al reported that PLR serves as an independent factor in distinguishing between benign and malignant ovarian tumors.[21] These findings underscore the prognostic capacity of NLR and PLR, supporting their applicability across different cancer types, including ESCC.[22]

The CALLY Index, which integrates albumin, lymphocyte count, and CRP levels, has been highlighted for its prognostic implications in gastric cancer, colorectal cancer, and Non-Small Cell Lung Cancer (NSCLC).[23–25] This index encapsulates the interplay between nutritional status, immune competence, and inflammatory response, providing a composite view of the prognostic landscape. Despite its promising role in other cancers, the potential of the CALLY Index as a predictor of postoperative pneumonia in ESCC remains under-investigated.

This study aims to elucidate the CALLY Index as a pivotal predictive factor for postoperative pneumonia in patients with ESCC. Furthermore, it endeavors to assess individual patient risk factors and facilitate the development of preemptive therapeutic strategies to mitigate the incidence of postoperative complications.

Methods

Study Design and Participants

This study employed a retrospective cohort design, carried out at the Department of Thoracic Surgery, The Affiliated Huai'an No.1 People's Hospital of Nanjing Medical University, over a period spanning from January 2019 to December 2022. The cohort comprised patients diagnosed with resectable ESCC who underwent thoraco-laparoscopic McKeown procedure, as depicted in Figure 1. Patients were selected based on specific inclusion and exclusion criteria. The inclusion criteria included: (1) a confirmed pathological diagnosis of esophageal squamous cell carcinoma; (2) completion of a curative resection meeting R0 resection criteria; and (3) no receipt of preoperative adjuvant therapy, which encompassed chemotherapy, immunotherapy, or targeted therapies. The exclusion criteria were as follows: (1) presence of chronic pulmonary diseases, such as chronic obstructive pulmonary disease; (2) a history of prior thoracic surgeries; (3) incomplete perioperative clinical data; and (4) a previous diagnosis of any other malignancy. Clinical staging of all participants was conducted in accordance with the eighth edition of the TNM classification. The study adhered to the guidelines outlined in the Declaration of Helsinki and received approval from the Ethics Committee of Nanjing Medical University (Reference No: KY-2024-374-01). Informed consent was not required for this retrospective study, as the Ethics Committee granted a waiver based on their assessment that the study met the necessary criteria for exemption from informed consent.

Clinical Parameter Information

In this retrospective study, we meticulously recorded an array of clinical parameters pertinent to our cohort. These included demographic information such as age and gender, as well as pertinent pathological characteristics such as tumor stage and

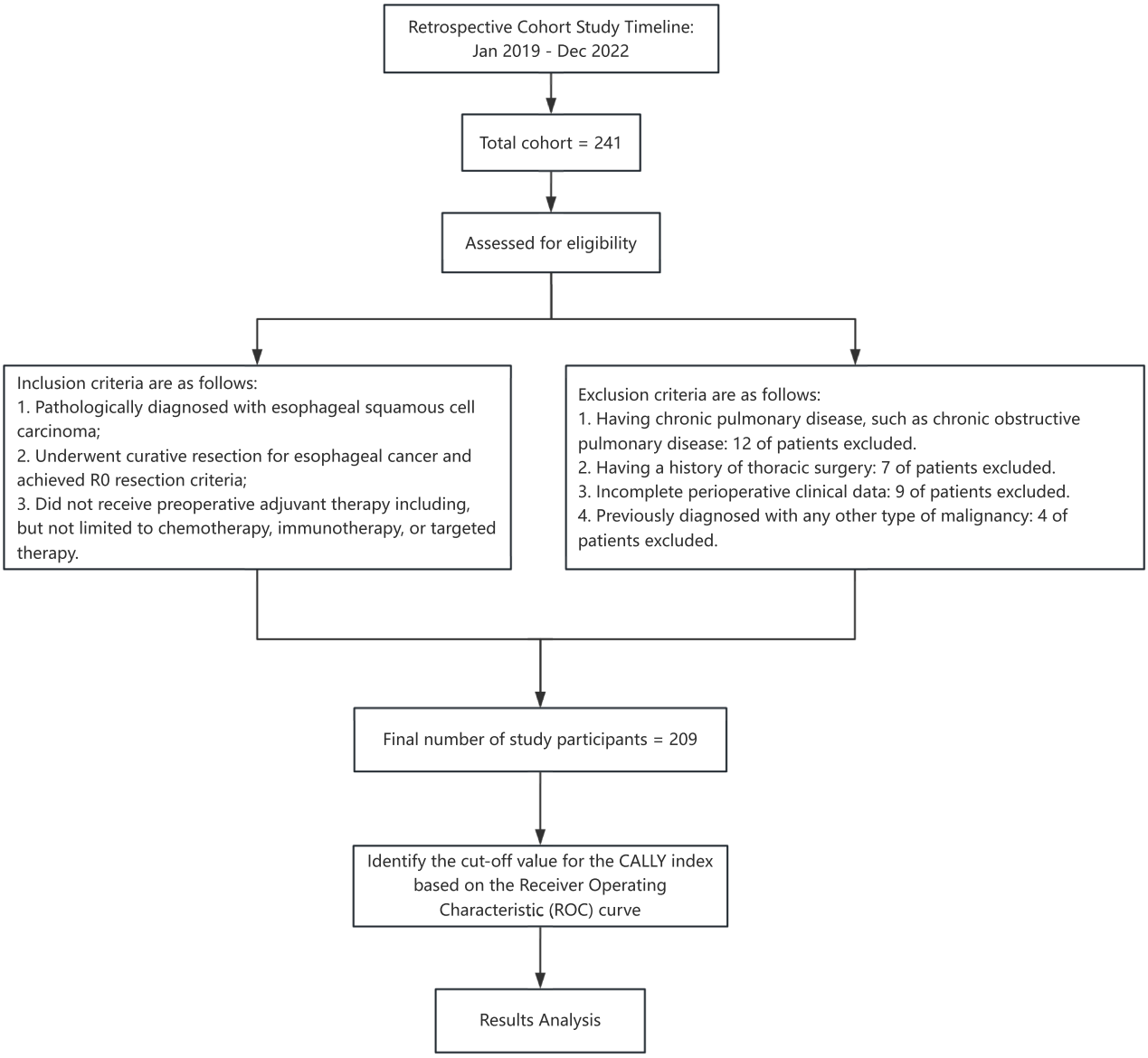

Figure 1 Study Flow Diagram. From an initial cohort of 241 ESCC patients assessed for eligibility, 209 patients were included in the final analysis following the application of strict inclusion and exclusion criteria.

grading. Specifically, we evaluated preoperative albumin levels, which are critical indicators of nutritional status and general health in surgical patients. To comprehensively assess postoperative recovery, we documented various complications that arose during the recovery phase, particularly those that could influence the development of pneumonia.

The diagnosis of postoperative pneumonia within thirty days following surgery adhered strictly to established criteria, requiring the fulfillment of all three of the following conditions: (A) at least two chest radiographs indicating pneumonia, with a definitive diagnosis rendered by the attending physician; (B) a clinical presentation manifesting as either a peripheral blood white blood cell (WBC) count <4 x 10^9/L or >12 x 10^9/L, in conjunction with fever (body temperature >38°C) and altered mental status; and © at least two symptoms such as the production of purulent sputum, alterations in sputum characteristics, increased respiratory secretions necessitating frequent expectoration, or shortness of breath, thereby capturing the clinical spectrum characterizing postoperative pneumonia.[26] All clinical data were extracted from electronic medical records to ensure accuracy and completeness. The systematic approach to data collection aimed to mitigate bias and enhance the reliability of our predictive analyses.

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Measurement of the CALLY Index

The CALLY Index was calculated preoperatively using routinely measured blood parameters obtained within one week prior to surgery. Specifically, we assessed the levels of serum albumin (Alb), lymphocyte count, and CRP for each patient. The CALLY Index score, a composite marker of the inflammatory status and immune competence of the patient, was derived using the following formula: CALLY index score = Alb level (g/dL) * lymphocyte count ($\times 10^9$/L) divided by CRP level (mg/dL) * 10^4. Standardization of the CALLY Index across all samples was conducted to minimize inter-assay variability, with all blood analyses performed at a single accredited laboratory. This methodological rigor ensures the reliability and reproducibility of the CALLY Index as a predictive tool for postoperative pneumonia among patients diagnosed with ESCC.

Statistical Analysis

Baseline characteristics of the patient cohort were summarized using descriptive statistics. Continuous variables were assessed for normality; those that followed a normal distribution were reported as mean ± standard deviation, while non-normally distributed variables were presented as median and interquartile range. Categorical variables were expressed as frequencies and percentages. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of postoperative pneumonia. The multivariate analysis utilized a stepwise selection approach based on the Akaike Information Criterion (AIC) to refine the model, ensuring that only significant variables remained in the final model. Adjusted odds ratios (adj. OR) were calculated, along with their 95% confidence intervals (CIs), to quantify the strength and precision of the associations. In order to further characterize the relationship between hospital stay length and the risk of pneumonia, we employed multivariate restricted cubic spline (RCS) regression models. This methodological choice allowed for the exploration of potential non-linear relationships, which were adjusted for previously identified confounders to bolster the robustness of our findings. All statistical analyses were conducted using R software (http://www.r-project.org; version 4.2.2, The R Foundation) and Free Statistics (version 2.0). Statistical significance was set at a threshold of $P < 0.05$.

Results

Predictive Validity of the CALLY Index for Postoperative Pneumonia in ESCC Patients

As illustrated in Figure 2, the receiver operating characteristic (ROC) curve analysis for the CALLY index demonstrated an area under the curve (AUC) of 0.784 (95% CI: 0.708–0.861), indicating high predictive accuracy for postoperative pneumonia in patients with resectable ESCC. The optimal cutoff value for the CALLY index was determined to be 3.47, with a sensitivity of 0.721 and specificity of 0.865. This result underscores the CALLY index as a robust predictive tool, outperforming traditional clinical parameters in identifying high-risk patients.

Baseline Characteristics of Participants Stratified by the CALLY Index

A total of 209 patients with esophageal squamous cell carcinoma were included in the study, stratified by their CALLY index. The baseline characteristics of the study population are summarized in Table 1. There were no significant differences between CALLY-Low (n = 69) and CALLY-High (n = 140) groups regarding gender distribution, age, BMI, hypertension, diabetes mellitus, tumor location, tumor grade, pT stage, pN stage, or ASA class (all $p > 0.05$). However, the FEV1% was significantly lower in the CALLY-Low group (87.5 ± 18.4) compared to the CALLY-High group (92.8 ± 18.0, $p = 0.046$), indicating reduced lung function among those with a lower CALLY index. Notably, a significant difference was observed in smoking status ($p = 0.006$), with a higher proportion of smokers in the CALLY-Low group (42%) compared to the CALLY-High group (23.6%). Furthermore, lymphocyte count was significantly lower in the CALLY-High group (1.2 ± 0.34) versus the CALLY-Low group (1.4 ± 0.41; $p = 0.002$). The CALLY index itself demonstrated a striking contrast between the two groups, with a mean score of 2.9 ± 0.8 in the CALLY-Low group and 5.1 ± 1.2 in the CALLY-High group ($p < 0.001$). The incidence of pneumonia postoperatively was significantly higher in the CALLY-Low group (63.8%) versus the CALLY-High group (12.1%; $p < 0.001$). Similarly, the occurrence of esophagocutaneous fistula was exclusively reported in the CALLY-Low group (13%). Additionally, the length of hospital stay was significantly longer for patients in the CALLY-Low group (16.7 ± 9.9 days) compared to those in the CALLY-High group (12.8 ± 5.9 days, $p < 0.001$).

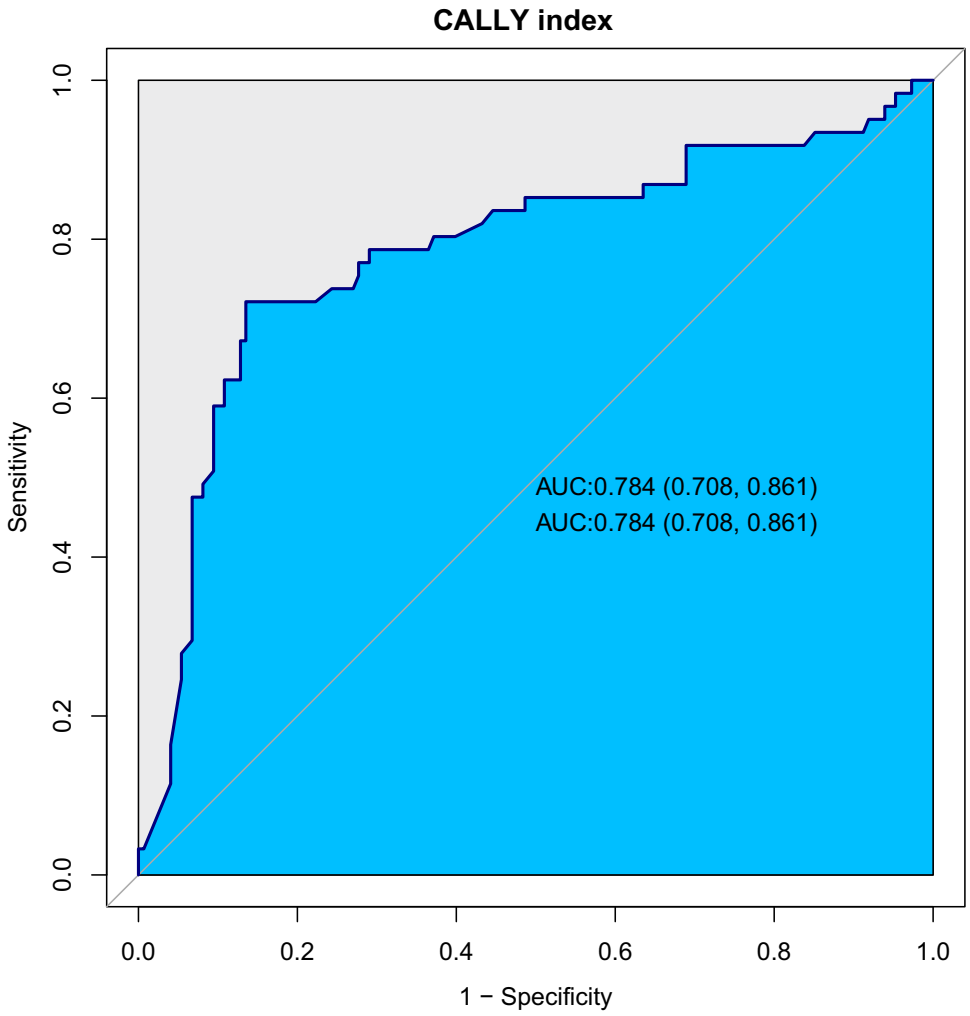

Figure 2 Receiver Operating Characteristic Curve Analysis for the CALLY Index in Predicting Postoperative Pneumonia in ESCC Patients. The ROC curve illustrates the predictive validity of the CALLY Index for postoperative pneumonia among patients with resectable esophageal squamous cell carcinoma. The area under the curve is 0.784 (95% CI: 0.708–0.861), indicating a high level of predictive accuracy. The optimal cutoff value for the CALLY Index is 3.47, which achieves a sensitivity of 0.721 and a specificity of 0.865.

Univariate and Multivariate Logistic Regression Analyses of Postoperative Pneumonia Incorporating the CALLY Index

The univariate and multivariate logistic regression analyses were performed to evaluate the association between various predictors and the incidence of postoperative pneumonia, incorporating the CALLY index as a significant factor. As

Table 1 The Baseline Information of the Study Population Stratified by the CALLY Index

Characteristic	Total (n = 209)	CALLY-Low (n = 69)	CALLY-High (n = 140)	P value
Gender, n (%)				0.884
Female	65 (31.1)	21 (30.4)	44 (31.4)	
Male	144 (68.9)	48 (69.6)	96 (68.6)	
Age (year), Mean ± SD	65.9 ± 6.6	66.6 ± 6.7	65.6 ± 6.5	0.332
BMI (kg/m^2), Mean ± SD	22.6 ± 3.1	22.8 ± 3.3	22.5 ± 3.0	0.519
FEV1%, Mean ± SD	91.1 ± 18.3	87.5 ± 18.4	92.8 ± 18.0	0.046
FEV1/FVC%, Mean ± SD	94.9 ± 13.1	94.6 ± 12.6	95.1 ± 13.3	0.764

(*Continued*)

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Table 1 (Continued).

Characteristic	Total (n = 209)	CALLY-Low (n = 69)	CALLY-High (n = 140)	P value
Hypertension, n (%)				0.812
No	137 (65.6)	46 (66.7)	91 (65)	
Yes	72 (34.4)	23 (33.3)	49 (35)	
Diabetes mellitus, n (%)				0.281
No	191 (91.4)	61 (88.4)	130 (92.9)	
Yes	18 (8.6)	8 (11.6)	10 (7.1)	
Smoking, n (%)				0.006
No	147 (70.3)	40 (58)	107 (76.4)	
Yes	62 (29.7)	29 (42)	33 (23.6)	
Smoking pack years, n (%)	32.1 ± 5.1	32.8 ± 6.4	31.9 ± 5.8	0.153
Tumor location, n (%)				0.159
Upper	35 (16.7)	7 (10.1)	28 (20)	
Middle	118 (56.5)	44 (63.8)	74 (52.9)	
Low	56 (26.8)	18 (26.1)	38 (27.1)	
Tumor grade, n (%)				0.985
I	50 (23.9)	16 (23.2)	34 (24.3)	
II	117 (56.0)	39 (56.5)	78 (55.7)	
III	42 (20.1)	14 (20.3)	28 (20)	
pT, n (%)				0.397
T1	85 (40.7)	24 (34.8)	61 (43.6)	
T2	92 (44.0)	32 (46.4)	60 (42.9)	
T3	32 (15.3)	13 (18.8)	19 (13.6)	
pN, n (%)				0.541
N0	149 (71.3)	52 (75.4)	97 (69.3)	
N1	42 (20.1)	13 (18.8)	29 (20.7)	
N2	13 (6.2)	2 (2.9)	11 (7.9)	
N3	5 (2.4)	2 (2.9)	3 (2.1)	
ASA class, n (%)				0.797
1	129 (61.7)	42 (60.9)	87 (62.1)	
2	57 (27.3)	18 (26.1)	39 (27.9)	
3	23 (11.0)	9 (13)	14 (10)	
Lymphocyte count ($\times 10^9$/L), Mean ± SD	1.4 ± 0.4	1.4 ± 0.41	1.2 ± 0.34	0.002
Albumin (g/dL), Mean ± SD	36.8 ± 15.2	36.1 ± 14.4	37.1 ± 15.5	0.651
CRP (mg/dL), Mean ± SD	5.2 ± 1.8	5.4 ± 2.1	3.7 ± 1.3	0.903
CALLY index, Mean ± SD	4.3 ± 1.6	2.9 ± 0.8	5.1 ± 1.2	< 0.001
NLR, Mean ± SD	3.82 ± 1.03	3.98± 1.17	3.71 ± 0.87	0.061
Pneumonia, n (%)				< 0.001
No	148 (70.8)	25 (36.2)	123 (87.9)	
Yes	61 (29.2)	44 (63.8)	17 (12.1)	
Esophagocutaneous fistula, n (%)				< 0.001
No	200 (95.7)	60 (87)	140 (100)	
Yes	9 (4.3)	9 (13)	0 (0)	
Length of hospital stay (day), Mean ± SD	14.1 ± 7.6	16.7 ± 9.9	12.8 ± 5.9	< 0.001
Microvascular invasion, n (%)				0.492
No	134 (64.1)	42 (60.9)	92 (65.7)	
Yes	75 (35.9)	27 (39.1)	48 (34.3)	

presented in Table 2, several variables were analyzed to identify their impact on pneumonia risk. In the univariate analysis, the CALLY index was determined to be a strong predictor of pneumonia, with a crude odds ratio (OR) of 0.59 (95% CI: 0.51–0.79, $p < 0.001$). This association remained significant in the multivariate model, yielding an adjusted

Table 2 Results of Univariable/Multivariable Logistic Regression Analysis and Predictors of Pneumonia

Variable	Crude.OR (95% CI)	Crude.P value	Adj.OR (95% CI)	Adj.P value
Gender				
Female	Ref			
Male	1.41 (0.69~2.47)	0.31		
Age	1.21 (0.82~1.35)	0.29		
BMI	0.97 (0.89~1.11)	0.661		
FEV1/FVC%	1.03 (0.95~1.06)	0.252		
Hypertension				
No	Ref			
Yes	0.9 (0.48~1.49)	0.727		
Diabetes mellitus				
No	Ref			
Yes	2.11 (0.71~5.39)	0.136		
Smoking				
No	Ref			
Yes	1.44 (0.79~2.33)	0.152		
Smoking pack years	1.35 (0.93~3.07)	0.137		
Tumor location				
Upper	Ref			
Middle	1.53 (0.69~4.21)	0.271		
Low	2.11 (0.71~4.91)	0.125		
Tumor grade				
I	Ref		Ref	
II	1.44 (0.68~3.17)	0.347	1.15 (0.31~2.42)	0.761
III	2.15 (0.85~5.41)	0.091	1.49 (0.44~5.02)	0.517
pT				
T1	Ref		Ref	
T2	2.33 (1.19~4.78)	0.013	3.01 (1.21~7.56)	0.011
T3	4.09 (1.57~9.81)	0.006	5.91 (1.92~18.77)	0.012
pN				
N0	Ref			
N1	1.41 (0.62~2.93)	0.341		
N2	0.49 (0.12~2.13)	0.273		
N3	1.69 (0.33~9.92)	0.661		
ASA class				
1	Ref		Ref	
2	1.64 (0.32~1.27)	0.191	1.54 (0.21~1.27)	0.149
3	1.31 (0.67~1.37)	0.059	1.27 (1.11~1.58)	0.047
CALLY index	0.59 (0.51~0.79)	<0.001	0.64 (0.51~0.77)	<0.001
NLR	1.12 (0.98~1.31)	0.079	1.07 (0.97~1.26)	0.063
Esophagocutaneous fistula				
No	Ref		Ref	
Yes	5.22 (1.29~22.12)	0.022	2.07 (0.39~14.11)	0.427
Length of hospital stay	1.17 (1.06~1.23)	<0.001	1.12 (1.03~1.16)	0.003
Microvascular invasion				
No	Ref			
Yes	1.5 (0.82~2.77)	0.192		

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odds ratio (adj. OR) of 0.64 (95% CI: 0.51–0.77, p < 0.001), indicating that higher CALLY index scores are associated with a reduced risk of developing postoperative pneumonia. Other notable predictors identified in the multivariate analysis included the pT stage. Specifically, patients with a pT2 stage had an adj. OR of 3.01 (95% CI: 1.21–7.56, p = 0.011), while those with a pT3 stage had an adj. OR of 5.91 (95% CI: 1.92–18.77, p = 0.012), highlighting a significantly increased risk of pneumonia associated with more advanced tumor stages. Additionally, the ASA class 3 presented a marginally significant association with pneumonia (adj. OR: 1.27, 95% CI: 1.11–1.58, p = 0.047). The length of hospital stay was also a significant predictor of postoperative pneumonia risk, with both crude and adjusted odds ratios of 1.17 (95% CI: 1.06–1.23, p < 0.001) and 1.12 (95% CI: 1.03–1.16, p = 0.003), respectively. Furthermore, patients who developed an esophagocutaneous fistula had a higher crude OR of 5.27 (95% CI: 1.27–21.82, p = 0.022) in the univariate analysis; however, this association was not significant in the adjusted model (adj. OR: 2.07, p = 0.427).

Curve Fitting for Assessing Postoperative Pneumonia Risk in ESCC Patients in Relation to Length of Hospital Stay

Figure 3 presents the curve-fitting analysis that correlates the length of hospital stay with the odds ratio for postoperative pneumonia in patients with ESCC. The findings indicate a non-linear increase in pneumonia risk associated with longer hospital stays, as evidenced by a p-value of 0.065 for non-linearity. Importantly, the risk becomes particularly significant when the hospital stay exceeds the reference period of 12 days. The OR curve, together with the confidence interval band, demonstrates that extended hospital stays are correlated with an increasing risk of pneumonia.

Discussion

In this retrospective cohort study, we aimed to validate the efficacy of the CALLY Index as a predictive tool for postoperative pneumonia in patients with resectable ESCC. Our analysis included a well-defined cohort of 209 patients, from whom we meticulously gathered baseline clinical and pathological data to ensure homogeneity among participants. The results indicated a significantly higher incidence of postoperative pneumonia in patients categorized with a low CALLY Index (63.8%) compared to those with high scores (12.1%), underscoring the predictive value of the CALLY Index in identifying at-risk individuals. Through univariate and multivariate logistic regression analyses, we established the CALLY Index as an independent predictor of pneumonia, with an adjusted odds ratio of 0.62 (95% CI: 0.51–0.76, p < 0.001). In addition to the CALLY Index, tumor pT stage and prolonged hospital stays were identified as critical risk factors for postoperative pneumonia. Notably, higher pT stages complicate the risk of pneumonia, with patients at stage pT3 demonstrating an adjusted odds ratio of 6.30, highlighting the intricate relationship between postoperative risk and disease progression. Furthermore, our findings emphasize the length of hospital stay as a significant predictor of pneumonia risk, indicating that an increased duration positively correlates with the likelihood of developing this complication. The non-linear relationship observed between hospital stay and pneumonia risk further underscores the necessity for vigilant monitoring of patients during their postoperative phase, particularly when hospital stays exceed 12 days. Our study offers valuable insights for the early identification of individuals at high risk for postoperative pneumonia, enabling clinicians to implement tailored therapeutic interventions to preempt complications.

Our approach differentiates itself by uniquely integrating the CALLY index within ESCC, reflecting nutritional status, immune response, and inflammatory activity. Unlike traditional indicators that rely on postoperative clinical signs or basic preoperative risk factors, the CALLY index offers a preoperative hematological assessment for more timely interventions. Existing indicators typically focus on specific factors like age, gender, smoking history, comorbid conditions, and tumor characteristics. For instance, research by Kato et al highlights the importance of respiratory function tests and related respiratory comorbidities.[27] Our methodology improves upon this by incorporating comprehensive blood parameters that reflect systemic health, extending beyond just respiratory function. Additionally, our results are especially pertinent for areas with high ESCC incidence, offering a tailored predictive tool that may be more accurate for these populations.

The CALLY index, as a comprehensive hematological medical index, has been shown to have important utility value in prognostic analysis of various malignant tumors.[28,29] For example, studies have demonstrated a close relationship

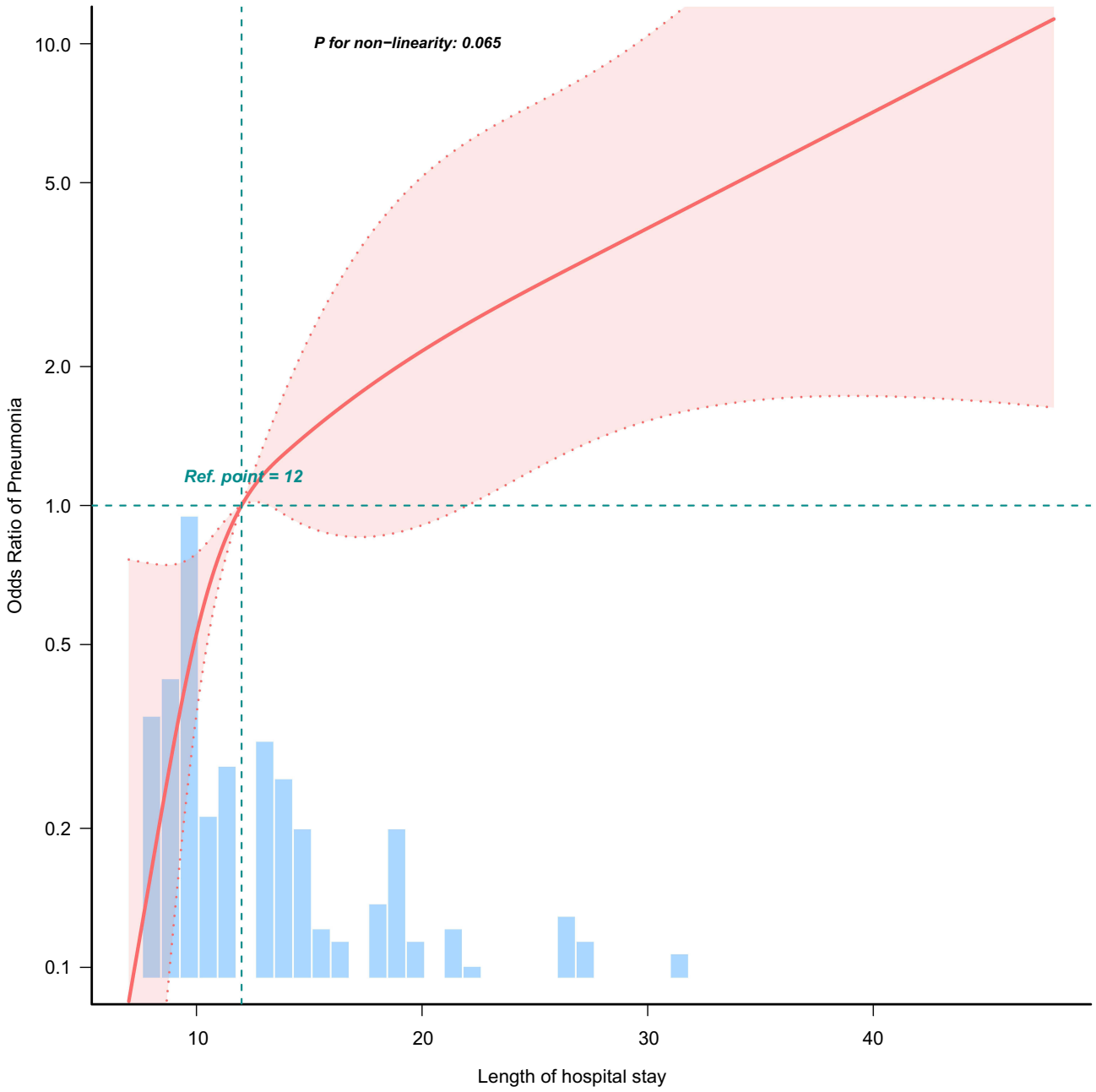

Figure 3 Curve Fitting Analysis of Postoperative Pneumonia Risk Related to Hospital Stay Length in ESCC Patients This figure displays the relationship between the length of hospital stay and the odds ratio for postoperative pneumonia in patients with esophageal squamous cell carcinoma. The analysis reveals a non-linear increase in pneumonia risk as hospital stay extends beyond the reference point of 12 days (P for non-linearity = 0.065). The curve illustrates that longer hospital stays correlate with a higher risk of pneumonia, highlighted by the red line representing the OR and the shaded area indicating the confidence interval.

between the CALLY index and patient prognosis in gastric cancer, colorectal cancer, and non-small cell lung cancer. In the context of gastric cancer, findings by Fukushima et al have elucidated that a preoperative CALLY index below 2 is conspicuously associated with diminished overall and relapse-free survival post-gastrectomy, marking it as a potent indicator of adverse prognoses.[30] Similarly, Takeda et al have recognized the index's utility in colorectal cancer, establishing a CALLY index score under 2 as an independent harbinger of improved disease-free survival.[24] Liu et al's research in non-small cell lung cancer further underscores the CALLY Index's viability, with their CALLY-based nomogram exhibiting commendable proficiency—evidenced by a C-index of 0.697—in forecasting overall survival.[31] These findings support the CALLY index's potential as a valuable tool for prognostication and management

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across various cancer types. Wei Wang et al found that using a cut-off value of 3 to classify patients into groups with CALLY indices below and above 3, a CALLY index of 3 or higher was associated with better survival outcomes in their study cohorts.[32] Both univariate and multivariate COX regression analyses identified the CALLY index as a prognostic factor for OS and DFS. These studies emphasize the potential role of the CALLY index in predicting disease progression and long-term outcomes in malignant tumors. Despite this, in-depth research on the CALLY index in esophageal squamous cell carcinoma remains scarce.[33] Therefore, our findings provide a new perspective for postoperative management of esophageal squamous cell carcinoma and emphasize the importance of early identification of the CALLY index, which may promote personalized prognostic risk assessment and precise treatment.

A growing body of evidence underscores the crucial role of nutritional status, immune-inflammatory responses, and cancer behavior in determining the prognosis of cancer patients. Albumin, widely acknowledged for its predictive value in assessing nutritional status, has been implicated in forecasting the prognosis of cancer patients.[34] Tumor necrosis factor (TNF) is known to enhance microvascular permeability, while interleukin-1 (IL-1) and interleukin-6 (IL-6) can inhibit albumin synthesis, leading to marked reductions in serum albumin levels among cancer patients.[35,36] Concurrently, serum C-reactive protein is a recognized marker of systemic inflammation, inducing the secretion of pro-inflammatory cytokines such as IL-1, IL-6, and TNF-α.[37–40] This inflammatory cascade can result in significant protein loss, culminating in mortality in cancer patients.[41] Notably, studies have established a close correlation between elevated CRP levels and advanced TNM cancer staging, reflecting a broader scale of the inflammatory response inherent to malignancies. Lymphocytes (LYMs), serving as indicators of immune function, possess the capacity to infiltrate the tumor microenvironment, influencing the proliferation and metastasis of tumor cells.[42] Their regulatory role in this environment is pivotal for mounting an effective defense against tumor cells. In light of the interactions between cancer, nutrition, and inflammation, the CALLY index emerges as a potentially superior prognostic tool compared to traditional indices.[43] By integrating albumin levels, lymphocyte count, and CRP, the CALLY index holistically mirrors a patient's nutritional status, immune competence, and inflammatory state.[44] Specifically, low albumin levels may signal poor nutritional health, influencing postoperative recovery.[45] A diminishing lymphocyte count, indicative of weakened immune defenses, could impair the body's resistance to pathogens.[46] Elevated CRP levels act as biomarkers for acute inflammation, providing insights into systemic inflammatory responses.[47] Thus, by amalgamating these critical parameters, the CALLY index serves as an integrative predictor for the risk of postoperative infections, offering a mechanistic framework for understanding patient outcomes in the context of both the tumor microenvironment and systemic health.

While our retrospective study offers valuable insights, certain limitations should be considered in interpreting the results. A key limitation is the small sample size, with only 209 patients from a single institution, which may compromise the generalizability of our findings. ESCC has significant variability in clinical presentations and treatment responses, and data from a single center may not fully capture this diversity. Therefore, the external validity of our study may be limited, emphasizing the need for multicenter prospective studies with larger cohorts to confirm our findings and enhance the applicability of our predictive model. Additionally, while we excluded patients with chronic pulmonary disease and prior malignancies to improve homogeneity and predictive accuracy, this may reduce the generalizability of our conclusions. Older ESCC patients with such comorbidities are a significant group and face a heightened risk of postoperative pneumonia, suggesting our predictive indicators may not be universally applicable. Future studies should adopt broader inclusion criteria to validate and refine our model. We also acknowledge that our study lacked data on postoperative interventions, such as antibiotics and rehabilitation therapy, which could influence the incidence and severity of postoperative pneumonia. The retrospective nature of our research limited comprehensive data collection on these factors, hindering our ability to adjust for all variables that affect postoperative outcomes and restricting the extrapolation of our findings. We recognize the need to address this limitation in future research. In summary, while the CALLY index shows promise for assessing the risk of postoperative pneumonia in ESCC resection patients, we admit our study did not adequately consider the potential confounding effects of postoperative interventions. Thus, we plan to expand our research to include a more thorough analysis of postoperative care, aiming to gather detailed information about these interventions to clarify their significance and improve risk stratification, ultimately enhancing patient care. Our ongoing research efforts will focus on deepening our understanding of the risk factors for postoperative pneumonia in ESCC management.

Conclusion

In this study, we establish the CALLY Index as a reliable and effective predictive tool for postoperative pneumonia in patients with esophageal squamous cell carcinoma (ESCC). Our findings indicate a significant disparity in pneumonia rates between patients classified as CALLY-low (index score < 3.47) and CALLY-high (index score ≥ 3.47), with the former exhibiting a pneumonia incidence of 63.8% versus just 12.1% in the latter group ($p < 0.001$). This cutoff point of 3.47 demonstrates the prognostic value of the CALLY Index in clinical practice. The integration of the CALLY Index with tumor stage and length of hospital stay enhances risk stratification, allowing for timely interventions tailored to patients' needs. By identifying patients at higher risk for postoperative pneumonia based on their CALLY Index scores, clinicians can implement proactive measures aimed at mitigating complications, ultimately improving patient outcomes.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author, Xinkui Xiong.

Ethics Approval and Consent to Participate

The study adhered to the guidelines outlined in the Declaration of Helsinki and received approval from the Ethics Committee of Nanjing Medical University (Reference No: KY-2024-374-01). Informed consent was not required for this retrospective study, as the Ethics Committee granted a waiver based on their assessment that the study met the necessary criteria for exemption from informed consent. Specifically, the waiver was granted because the study involved the review of anonymized clinical data that did not allow for individual identification of patients. We have ensured strict measures to maintain patient data confidentiality, and all clinical information was anonymized and securely stored to protect the privacy of individuals involved in this study.

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Disclosure

The authors declare that they have no competing interests.

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