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Esophageal Cancer Symptom Trajectories and High-Risk Phenotypes: A Perioperative Longitudinal Study

Perioperative Symptom Trajectories and High-Risk Phenotypes in Esophageal Cancer

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Abstract

Background Esophageal cancer patients experience a high perioperative symptom burden, and the dynamic evolution of these symptoms exhibits individual heterogeneity. Identifying distinct symptom trajectory classes, along with their influencing factors and clinical outcomes, is essential for achieving precision symptom management.

Objective To characterize the perioperative symptom evolution, identify symptom trajectory latent categories, and explore their influencing factors and associations with clinical outcomes in patients with esophageal cancer.

Methods In this longitudinal study, perioperative symptoms were dynamically assessed in patients undergoing surgery for esophageal cancer. Symptom data were collected through repeated measurements. Latent class growth modeling analysis was used to identify distinct symptom trajectory categories. Data on general characteristics, psychosocial factors, and clinical indicators were also collected for comparative analysis.

Results A total of 264 patients were included. Three distinct symptom trajectories were identified: "High-Symptom Persistent Burden" group (6.3%), "Moderate-Symptom Slow Improvement" group (35.5%), and "Low-Symptom Rapid Recovery" group (58.3%). Age, preoperative BMI, anxiety/depression, and social support were significant factors associated with trajectory categories membership. Statistically significant differences in clinical outcomes were observed among the trajectory groups, including the length of hospital stay, incidence of postoperative complications, and levels of C-reactive protein and red blood cells at discharge. The "High-Symptom Persistent Burden" group consistently demonstrated the least favorable outcomes. **Conclusion** This study delineates three distinct perioperative symptom trajectories in esophageal cancer patients, which are shaped by both biological and psychosocial factors and are predictive of clinical recovery. The findings provide a crucial evidence base for implementing integrated perioperative care and tailored, trajectory-based symptom management strategies, offering significant potential for improving postoperative quality of life in this patient population.

【Keywords】Esophageal Cancer; Symptoms; Latent Class Growth Model; Influencing Factors; Nursing

Key message

This prospective longitudinal study is the first to characterize symptom trajectories in esophageal cancer patients in China. By identifying distinct high-risk phenotypes, we uncovered key predictors and established their significant associations with adverse clinical outcomes, offering novel insights for targeted interventions.

Esophageal cancer, one of the most aggressive malignancies of the digestive tract, is associated with a poor prognosis and imposes a substantial disease burden worldwide[1]. As a high-incidence region, China accounts for nearly half of the global cases and deaths related to this disease[2]. Currently, radical surgical resection remains the cornerstone of curative treatment[3]. Although the advent of minimally invasive techniques such as thoracoscopy has considerably reduced surgical trauma, radical esophagectomy—characterized by three-field lymph node dissection (cervical, thoracic, and abdominal), gastrointestinal tract reconstruction, and extensive lymphadenectomy—continues to rank among the most invasive surgical procedures[4].

Patients undergoing esophagectomy frequently experience a constellation of distressing and dynamically evolving symptoms throughout the perioperative period, including cough, dyspnea, hoarseness, acid reflux, heartburn, and dysphagia[5-7]. Without systematic assessment and effective management, these symptoms can severely impede postoperative recovery and compromise long-term health-related quality of life[8,9]. However, the majority of existing studies have focused on symptom prevalence and severity at isolated time points, thereby overlooking the inherent heterogeneity and temporal dynamics of symptom evolution. Understanding the longitudinal trajectories of perioperative symptoms and identifying distinct subpopulations with varying symptom patterns are critical for developing targeted, patient-centered interventions.

Latent Class Growth Modeling (LCGM) has emerged as a powerful analytical tool for capturing unobserved heterogeneity in longitudinal data, enabling researchers to identify distinct subgroups following similar trajectories of change over time[10]. By applying this method, it is possible to delineate patterns of symptom progression and elucidate the interplay of biological, psychological, and social factors that shape individual recovery pathways.

Given these considerations, the present study aims to systematically characterize the longitudinal trajectories of perioperative symptoms in patients with esophageal cancer, thereby revealing their dynamic patterns and heterogeneous features. Furthermore, we seek to identify factors influencing different symptom trajectory classes and examine their associations with clinical outcomes. The findings are expected to provide an empirical foundation for precision perioperative interventions, ultimately contributing to optimized management strategies and improved patient prognosis and quality of life.

1 Objects and Methods

1.1 Study Participants

A convenience sampling method was used to select patients who underwent surgical treatment in the Department of Thoracic Surgery at a tertiary hospital from August 2024 to January 2026. The inclusion criteria were as follows: (1)pathologically confirmed esophageal cancer; (2)age ≥18 years; (3)scheduled for radical esophagectomy; (4)able to complete the questionnaire independently or with the assistance of a researcher; (5)provided informed consent to participate in the study. The exclusion criteria were: (1)presence of other malignant tumors; (2)severe or high-risk comorbidities; (3)mental disorders or consciousness disturbances. The withdrawal criteria were: (1)undergoing palliative surgery; (2)severe postoperative complications; (3)voluntary withdrawal for any reason during the study. Based on the calculation criteria of the Latent Class Growth Model (LCGM) and considering the Bayesian Information Criterion as the primary criterion, the required sample size was 200 cases[11]. Accounting for a 15% loss to follow-up rate, the minimum sample size was calculated to be at least 230 cases. Based on literature review and clinical practice, considering factors such as surgery, occurrence of

complications, and changes in nutritional support, data were collected at four time points: one day before surgery (T1), the first to third day after surgery (T2), the 14th day after surgery (T3), and one month after surgery (T4). This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the the hospital's ethics committee (Approval No. 2024[738]), and all participants voluntarily participated and signed informed consent forms.

1.2 Survey Instruments

1.2.1 General Information Questionnaire Designed by the researchers, this questionnaire collected demographic and disease-related information, including age, gender, weight, marital status, household income, educational level, type of medical insurance, dietary habits, surgical method, postoperative complications, hemoglobin, albumin, C-reactive protein (CRP), and length of hospital stay.

1.2.2 MD Anderson Symptom Inventory Gastrointestinal Cancer Module (MDASI-GI) The MDASI-GI is a symptom assessment scale specifically developed for patients with gastrointestinal cancers[12]. It measures the severity of 18 symptoms and the extent to which these symptoms interfere with six daily life activities (e.g., work, mood) over the past 24 hours, with each item rated on a scale of 0 to 10. As this study focused on perioperative symptoms, after a literature review, consultation with thoracic surgery experts, and discussions within the research team, the first part of the scale was selected, and two additional items—regurgitation and hoarseness—were included, resulting in a total of 20 symptom items. The Cronbach's α coefficient for this scale in the present study was 0.725.

1.2.3 Hospital Anxiety and Depression Scale (HADS) The HADS, originally developed by Zigmond et al.[13] and adapted into Chinese by Sun Zhenxiao et al.[14], consists of two dimensions and 14 items. Odd-numbered items assess anxiety (7 items), while even-numbered items assess depression (7 items).

A 4-point Likert scale is used for scoring. The scoring criteria for each dimension are as follows: 0–7 indicates “no symptoms,” 8–10 indicates “suspicious symptoms,” and 11–21 indicates “definite symptoms.” The overall Cronbach’s α coefficient for the scale was 0.879, and the correlation coefficients for criterion validity between the total score and the two dimensions were all > 0.550.

1.2.4 Multidimensional Scale of Perceived Social Support (MSPSS) The MSPSS, originally developed by Zimet[15] in 1988 and translated and revised into Chinese by Jiang Qianjin[16], assesses the level of social support perceived by individuals. The scale comprises three dimensions and 12 items. The family support dimension includes four items (3, 4, 8, 11); the friend support dimension includes four items (6, 7, 9, 12); and the other support dimension includes four items (1, 2, 5, 10). A 7-point Likert scale is used, with scores ranging from 1 (“strongly disagree”) to 7 (“strongly agree”). The total score ranges from 12 to 84, with higher scores indicating better perceived social support. Total scores are categorized into high (61–84), medium (37–60), and low (12–36) levels of perceived social support. The Cronbach’s α coefficients for the dimensions were 0.800, 0.887, and 0.832, respectively.

1.3 Data Collection and Quality Control Methods

Data were collected by two investigators who received unified training and passed assessments. The survey was conducted at four key perioperative time points using paper-based questionnaires. The investigators explained the purpose of the study to the patients on-site and, after obtaining informed consent, guided them in completing the questionnaires. All questionnaires were collected on the spot and immediately reviewed. Any missing items were addressed promptly by patiently inquiring and assisting patients in supplementing or correcting the information. Disease-related data and post-discharge metabolic biochemical indicators were collected by the investigators through the hospital’s medical record system. To ensure data quality, all questionnaires were independently verified

and entered by two individuals.

1.4 Statistical Methods

Statistical analysis was performed using SPSS 27.0 software. Normally distributed measurement data were expressed as mean±standard deviation, while count data were presented as frequencies, percentages, or rates. Univariate analyses were conducted using the chi-square test, Fisher's exact test, one-way ANOVA, and the Kruskal-Wallis H test. Multivariate logistic regression was used to analyze factors influencing trajectory categories. A P-value<0.05 was considered statistically significant.

Latent class growth modeling was performed using Mplus 8.0 software to identify perioperative symptom burden trajectories in patients with esophageal cancer, based on total symptom scores. The number of latent classes was gradually increased starting from one. The most appropriate model was selected based on fit indices and practical interpretability. The primary fit indices included the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and adjusted BIC (aBIC), with smaller values indicating better model fit. The BIC was generally used as the primary criterion for determining the optimal model. Classification accuracy was evaluated using Entropy, with values closer to 1 indicating higher precision. The Lo-Mendell-Rubin (LMR) and bootstrap likelihood ratio test (BLRT) were used to compare the fit differences between models with n-1 and n classes, with $P < 0.05$ indicating that the model with n classes was significantly better than the model with n-1 classes. Each class was required to account for at least 5% of the sample. After identifying the optimal model, posterior probabilities for each participant's trajectory group were calculated to assess classification accuracy.

2 Results

2.1 General Information, Anxiety, Depression, Social Support, and Symptom Scores of the Patients

A total of 287 patients were initially enrolled in this study at baseline (T1). During follow-up, one patient was lost to follow-up at T2 due to transfer to the ICU, three voluntarily withdrew at T3, and 18 were lost to follow-up at T4, resulting in a loss-to-follow-up rate of 7.67%. There were no statistically significant differences in baseline characteristics between patients who completed the entire follow-up and those who were lost to follow-up ($P > 0.05$), indicating that sample attrition did not introduce significant selection bias. A total of 265 patients completed all four follow-up assessments. Their ages ranged from 45 to 86 years, with a mean of 67.99 ± 7.18 years. The sample included 218 males (82.58%). The majority had an educational level of junior high school or below (78.79%). Squamous cell carcinoma accounted for 78.5% of cases, and 20.3% of patients received neoadjuvant therapy. The three-incision surgical approach was used in 67.05% of cases. The mean length of hospital stay was 29.17 ± 15.19 days, and the mean time to oral intake was 17.67 ± 14.02 days. At baseline (T1), the mean perceived social support score was at a high level, while the mean Hospital Anxiety and Depression Scale scores indicated definite anxiety and suspected depression.

The symptom scores of esophageal cancer patients at the four perioperative time points were as follows: 19.33 ± 8.56 at T1, 34.12 ± 7.24 at T2, 25.36 ± 9.06 at T3, and 17.61 ± 11.06 at T4. The distribution of mean symptom scores at each time point is shown in Figure 1. Repeated measures ANOVA revealed a significant main effect of time ($F = 134.08$, $P < 0.001$). Post hoc multiple comparisons indicated statistically significant differences in symptom scores between all adjacent time points (all $P < 0.001$), suggesting that symptoms exhibited dynamic changes across treatment stages. Additional details are presented in Table 1.

Table 1 General characteristics and univariate analysis outcomes of peroperative symptom trajectory latent categories in Patients with

Esophageal Cancer (n=264)

Characteristics	Number of cases （*n*=264）	Symptom trajectory classes			Test statistics	*P*
		High Symptom-Persistent Burden Group (n=16)	Moderate Symptom-Slow Improvement Group (n=96)	Low Symptom-Rapid Recovery Group (n=152)		
Gender [No. (%)]					1.182[2)]	0.411
Female	46（17.42）	1(6.25)	14(14.58)	31(11.74)		
Male	218（82.58）	15(93.75)	82(31.06)	121(45.83)		
Age [n (%)]						
＜60years~	12（4.55）	1(6.25)	10(10.42)	27(17.76)	19.141[2)]	＜0.001
60years~	161（60.98）	12(75.00)	42(43.75)	75(51.32)		
＞70years~	91（34.47）	3(18.75)	44(45.83)	50(32.89)		
Residence [n (%)]					2.736[1)]	0.255
Rural	128（48.49）	11(68.75)	45(46.88)	72(47.37)		
Urban	136（51.51）	5(31.25)	51(53.12)	80(53.95)		
Education Level [n (%)]					3.726[3)]	0.157
Junior high school or below	217（82.20）	11(68.75)	76(79.17)	130(85.53)		
High school or above	47（17.80）	5(31.25)	20(20.83)	22(14.47)		
Monthly Family Income per Capita [n (%)]					11.059[2)]	0.051
＜3 000RMB	45（17.05）	2(12.5)	12(12.50)	31(20.39)		

3 000RMB~	72（27.27）	5(31.25)	35(36.46)	32(21.05)		
5 000RMB~	95（35.98）	7(43.75)	32(33.33)	56(36.84)		
>8 000RMB	52（19.70)	2(12.50)	17(17.71)	33(21.72)		
Smoking History [n (%)]					1.415[1)]	0.506
Yes	148(56.06)	11(68.75)	52(54.17)	85(55.92)		
No	116(43.94)	5(31.25)	44(45.83)	67(44.08)		
Alcohol Consumption History [n (%)]					5.336[1)]	0.069
Yes	140(53.03)	11(68.75)	46(47.92)	83(54.61)		
No	124(46.97)	5(31.25)	50(52.08)	69(45.39)		
Comorbidities [n (%)]					2.876[1)]	0.237
Yes	153(57.95)	10(62.50)	50(52.08)	93(61.18)		
No	111(42.05)	6(37.5)	46(47.92)	59(38.82)		
Neoadjuvant Therapy [n (%)]					2.787[2)]	0.255
Yes	54(20.45)	2(12.50)	20(20.83)	32(21.05)		
No	210(79.55)	14(87.50)	76(79.17)	120(78.95)		
Lung Cancer Histology [n (%)]					6.215[3)]	0.177
Adenocarcinoma	40(15.15)	1(6.25)	12(12.5)	27(17.76)		
Squamous cell carcinoma	209(79.17)	11(68.75)	82(85.42)	116(76.32)		
Other	15(5.68)	4(25.00)	2(2.08)	9(5.92)		
Lymph Node Metastasis [n (%)]					2.624[2)]	0.269

Yes	82(31.06)	4(25.00)	27(28.13)	51(33.55)		
No	182(68.94)	12(75.00)	69(71.87)	101(66.45)		
BMI [kg/m², n (%)]					17.448[3]	＜0.001
<18.5	12(4.55)	1(6.25)	10(10.42)	1(0.66)		
18.5~	161(60.98)	6(37.5)	58(60.42)	97(63.82)		
24.0~	91(34.47)	9(56.25)	28(29.17)	54(35.52)		
HADS Score [points, Mean ± SD]	22.65±5.48	23.31±5.06	24.16±4.64	21.62±5.80	6.677[4]	＜0.001
Anxiety	13.13±4.28	14.13±4.26	13.98±3.72	12.49±4.51	4.143	0.017
Depression	9.52±2.17	9.19±1.38	10.18±1.93	9.14±2.30	7.252	＜0.001
MSPSS Score [points, Mean ± SD]	61.95±9.58	56.31±6.09	59.94±7.82	63.82±10.41	8.19[4]	＜0.001
Family Support	24.40±2.46	23.87±1.784	24.48±1.86	24.40±2.83	0.412	0.663
Friend Support	18.32±4.51	15.81±2.83	17.05±4.01	19.38±4.66	11.298	＜0.001
Significant Other Support	19.23±14.1556	16.63±3.10	19.23±4.16	20.03±4.38	8.3	＜0.001
Admission Indicators						
Red Blood Cell Count [$\times10^{12}$/L, M (P_{25}, P_{75})]	4.23(3.88，4.635)	4.18(3.855，4.67)	4.18(3.88，4.60)	4.28(3.88，4.66)	0.078[5]	0.962
White Blood Cell Count [$\times10^{9}$/L, M (P_{25}, P_{75})]	5.455(4.54，7.27)	5.29(4.37，7.775)	5.545(4.31，7.73)	5.45(4.67，6.77)	0.183[5]	0.912
Hemoglobin [g/L, M (P_{25}, P_{75})]	132(119.75，141.25)	128(117.5，141)	134(118，144)	132(120，140)	0.573[5]	0.751
Albumin [g/L, M (P_{25}, P_{75})]	39.7(36.80，42.15)	41.5(37.65，43.8)	39.65(36.55，41.53)	39.65(36.80，42.33)	2.863[4]	0.239

Total Protein [g/L, M (P_{25}, P_{75})]	66.8(62.9，71.30)	66(63.75，74.25)	66.8(62.85，71.60)	66.75(62.88，70.73)	1.046[5)]	0.593
Discharge Indicators						
Red Blood Cell Count [$\times10^{12}$/L, M (P_{25}, P_{75})]	3.59(3.26，3.96)	3.7(2.78，3.9)	3.46(3.11，3.91)	3.68(3.32，4.00)	6.063[5)]	0.048
White Blood Cell Count [$\times10^{9}$/L, M (P_{25}, P_{75})]	6.96(5.6，8.33)	6.04(5.62，9.14)	6.455(5.24，8.45)	7.28(5.69，8.27)	2.344[5)]	0.310
Hemoglobin [g/L, M (P_{25}, P_{75})]	110(98，120)	109(89，117)	107(94，119)	111(100.25，121.75)	4.875[5)]	0.087
Albumin [g/L, M (P_{25}, P_{75})]	36.7(34.425，39.9)	38(35.8，39)	36.3(33.55，39.95)	37.2(34.60，39.95)	1.403[5)]	0.496
Total Protein [g/L, M (P_{25}, P_{75})]	63.95(59.425，67.6)	64.4(59.4，68.1)	63.7(59.28，68.40)	64(59.45，67.30)	0.506[5)]	0.776
CRP[mg/L，$M(P_{25}, P_{75})$]	12.7(6.67，24.3)	24.18(11.31，47.01)	11.90(5.68，18.64)	13.01(7.35，25.89)	6.258[5)]	0.044
Length of Hospital Stay [days, M (P_{25}, P_{75})]	26(21，29)	31.5(29，72.75)	29(24.3，30.75)	23(19，28)	52.824[5)]	＜0.001
Complications					36.76[2)]	＜0.001
Yes	76(28.79)	14(87.5)	39(40.63)	23(15.13)		
No	188(71.21)	2(12.5)	57(59.37)	129(84.87)		

Note: HADS refers to the Hospital Anxiety and Depression Scale, and SSRS refers to the Social Support Rating Scale. Bold formatting indicates statistical significance.

1) χ^2 value; 2) Continuity-corrected χ^2 value; 3) Fisher's exact test; 4) F value; 5) z value



196 **Figue1. Radar chart of symptom mean distribution at different perioperative time points in patients with**

197 **esophageal cancer(n = 264)**

198

199 2.2 Identification and Naming of Perioperative Symptom Trajectory Classes in Patients with

200 Esophageal Cancer

201 Based on group-based trajectory modeling, one- to four-class trajectory models were fitted, as shown in

202 Table 2 and Figure 2. The results indicated that as the number of classes increased, the AIC, BIC, and

aBIC values gradually decreased. When the number of classes reached three, the BIC was minimized, the LMR and BLRT tests were statistically significant, and the entropy value was closest to 1, indicating optimal classification accuracy. Additionally, the three classes demonstrated greater discriminability in clinical characteristics. Therefore, the three-class model was selected as the final model. The trajectory plot for the three-class model is presented in Figure 2. Based on symptom levels and change patterns, the three classes were named as follows: the low-symptom rapid-recovery group (N=152, 57.6%), characterized by mild symptoms and rapid postoperative recovery (slope = -8.432, P < 0.001); the moderate-symptom slow-improvement group (N=96, 36.4%), characterized by moderate symptom levels and a slow postoperative improvement trend (slope = -4.122, P < 0.001); and the high-symptom persistent-burden group (N = 16, 6.1%), characterized by high symptom burden and limited improvement over time (slope = -1.772, P < 0.001). The posterior probabilities for the three classes were all above 0.89, indicating high classification accuracy and clear between-group discrimination.

Table 2 Model Fit Indices for peroperative symptom trajectory latent categories in Patients with Esophageal Cancer (n=264)

Number of classes	AIC	BIC	aBIC	Entropy	LMRT(*P*)	BLRT(*P*)	Class probability (%)
1	8052.715	8074.171	8055.148	-	-	-	100
2	7908.941	7941.124	7912.590	0.814	0.0005	0.0007	65.6/35.4
3	7865.628	7908.539	7870.493	0.843	0.0012	0.0017	58.3/6.3/35.5
4	7861.603	7915.242	7867.684	0.758	0.5401	0.5515	53/5.7/19.1/22.2

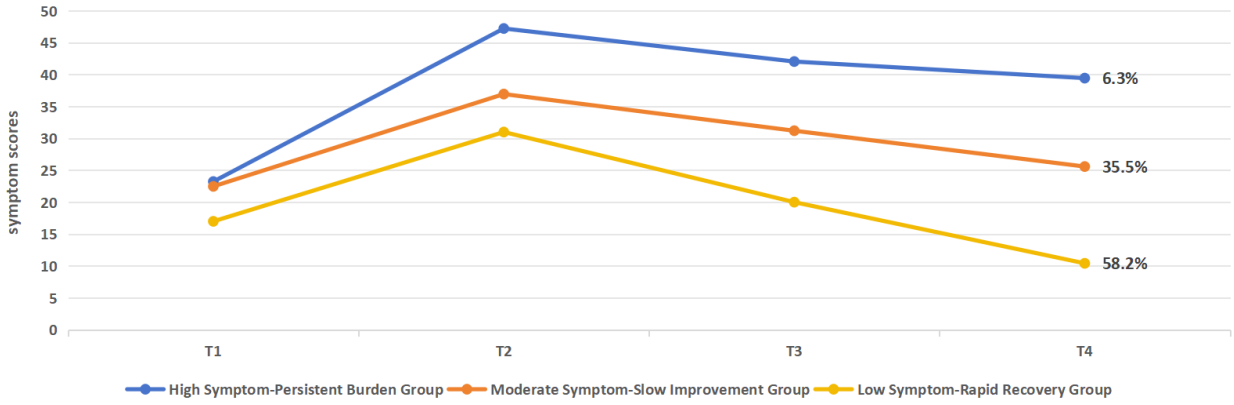


Figure 2 Plots of the perioperative symptom trajectories by latent categories with esophageal cancer patients

2.3 Factors Influencing Perioperative Symptom Trajectory Classes in Esophageal Cancer Patients

2.3.1 Univariate Analysis Results

Age, preoperative BMI, anxiety and depression, social support level, length of hospital stay, postoperative complications, red blood cell count at discharge, and CRP were significantly associated with the symptom trajectory classes (Table 1).

2.3.2 Multivariate Logistic Regression Analysis Results

Using symptom trajectory class as the dependent variable (low symptom-rapid recovery group=1, moderate symptom-slow improvement group=2, high symptom-persistent burden group=3), logistic regression analysis was performed on the variables that were statistically significant in the univariate analysis. The assignment of independent variables is shown in Table 3. The results indicated that anxiety and depression, social support, length of hospital stay, and red blood cell count at discharge were significant factors influencing the perioperative symptom trajectory classes in esophageal cancer patients (Table 4).

Table 3 Independent variable assignment

Independent variable	Assignment
Age (years)	＜60=1；60～=2；70～=3
BMI	<18.5=1；18.5～=2；24～=3
Complications	No=0；Yes=1
Continuous variables	Entered as original values
Symptom trajectory	Low symptom-rapid recovery group = 1; Moderate symptom-slow improvement group = 2; High symptom-persistent burden group = 3

Table 4　Multivariate logistic regression analysis of perioperative symptom trajectory categories in esophageal cancer patients(n=264)

Variable	*B*	SE	Walds χ^2	*P*	*OR*	95%*CI*
Moderate symptom-slow improvement group[2)]						
Length of hospital stay	0.127	0.035	13.139	<0.001	1.136	1.06～1.217
Anxiety and depression	0.12	0.049	6.156	0.013	1.128	1.026～1.24
Social support	-0.148	0.042	12.182	<0.001	0.863	0.794～0.937
High symptom-persistent burden group[3)]						
Red blood cell count (discharge)	-4.981	1.927	6.681	0.01	0.007	0.001-0.300
Length of hospital stay	0.222	0.054	17.121	<0.001	1.248	1.124～1.387

Note: The low symptom-rapid recovery group served as the reference category.

3 Discussion

3.1 Perioperative Symptom Distress and Trajectories in Esophageal Cancer Patients

Extending beyond traditional cross-sectional assessments, this study systematically characterized the longitudinal landscape of perioperative symptom burden in esophageal cancer patients. We identified three distinct, heterogeneous developmental trajectories, which were significantly associated with preoperative psychosocial status and postoperative clinical outcomes. These findings deepen our understanding of the dynamic process of postoperative recovery. Our findings indicate that patients with esophageal cancer experience multiple symptom distresses prior to surgery, which peak at 1–3

days postoperatively and gradually diminish as recovery progresses—a trend consistent with previous studies[17,18]. Preoperatively, patients often present with eating-related symptom clusters centered on "choking sensation, dysphagia, and foreign body sensation," intricately intertwined with psychological symptom clusters such as "sadness, distress, and sleep disturbance," attributable to tumor-induced mechanical obstruction, nerve invasion, and the anxiety and psychological stress following diagnosis. In the early postoperative period, symptoms including pain, fatigue, dry mouth, and sleep disturbance typically reach their peak due to surgical trauma, stress response, and physiological adaptation following gastrointestinal tract reconstruction[19]. During subsequent treatment and recovery phases, symptom distress exhibits a declining trend, with the predominant symptoms shifting to anorexia, chronic fatigue, and persistent sleep disturbance. By one month post-surgery, symptom levels generally return to below preoperative baseline. Previous research has demonstrated that while role function and emotional function dimensions of quality of life recover relatively quickly after esophageal cancer surgery, cognitive function, social function, and physical function require extended periods for improvement(17). This suggests that although symptom distress may alleviate in the short term, the comprehensive restoration of patients' quality of life necessitates sustained, systematic attention and support due to alterations in dietary structure, potential nutritional challenges, and the impact of subsequent adjuvant therapies.

This study identified a subset of patients classified into the "high symptom-persistent burden group," whose symptom levels remained elevated throughout the follow-up period, presenting a critical challenge in clinical management. This finding is consistent with previous research[20]. Latent profile analyses conducted domestically have also suggested that such patients often exhibit a comorbid state characterized by "high somatic symptoms–high psychological symptoms"[21]. The refined identification

of heterogeneous symptom trajectories and the recognition of a persistently high-symptom subgroup among perioperative esophageal cancer patients refines the conventional view of symptom improvement as a uniform process, highlighting the inter-group heterogeneity underlying differences in postoperative recovery. Consequently, there is an urgent need in clinical practice to enhance the early identification of these patients to implement more precise, personalized symptom management and rehabilitation support.

3.2 Age, Preoperative BMI, Anxiety/Depression, and Social Support Are Factors Differentiating Symptom Trajectory Classes

Elderly patients, characterized by poor physiological function and multiple comorbidities, exhibit reduced tolerance to major surgery and consequently experience more pronounced postoperative physical symptoms—a finding consistent with previous research[22]. Preoperative BMI typically reflects patients' nutritional status and metabolic reserve. A lower BMI may indicate malnutrition and prolonged disease duration, which not only compromises immune function and repair capacity but may also directly contribute to and exacerbate postoperative symptoms such as fatigue and weakness, predisposing these patients to a high symptom-persistent burden trajectory. The present study identified anxiety and depression levels as significant differentiators of symptom trajectory classes. The low symptom-rapid recovery group exhibited the lowest anxiety and depression scores, further confirming the critical role of emotional state in shaping postoperative symptom evolution. This finding aligns with research by Lyu et al.[21], which demonstrated that patients with higher perceived stress and lower self-efficacy are more likely to experience concurrent high somatic and high psychological symptom burden. Social support emerged as an independent factor influencing symptom trajectory classification in esophageal cancer patients: lower social support was associated with greater likelihood of

assignment to more severe symptom trajectory groups. Among the three dimensions of social support—family, friends, and significant others—family support received the highest scores yet showed no significant differences across symptom trajectory groups. This suggests that family support, as a universally available and relatively stable resource, exhibits a consistently high baseline level that diminishes its discriminatory power in differentiating symptom trajectories. These findings have important clinical implications for perioperative management of esophageal cancer patients. While recognizing the importance of family support, healthcare providers should place greater emphasis on constructing diversified, multidimensional social support networks. Through systematic assessment, implementation of tiered interventions, and integration of continuous hospital-community-home support resources, the rehabilitation needs of patients following distinct symptom trajectory patterns can be addressed in a targeted manner.

Multivariate regression analysis in this study revealed that psychosocial factors exerted significant independent predictive effects on trajectory class membership distinguishing the moderate symptom-slow improvement group from the low symptom-rapid recovery group; however, these factors did not demonstrate statistical significance in differentiating the high symptom-persistent burden group. When considered alongside the observed differences across trajectory groups in clinical outcomes—including complication rates, length of hospital stay, and inflammatory markers—these findings suggest that the recovery process in patients with high symptom burden may be more directly governed by biomedical factors. These results indicate that a tiered strategy should be adopted for postoperative symptom management in esophageal cancer patients. For patients with moderate to low symptom burden, interventions such as psychological counseling and strengthening of social support systems may effectively promote recovery. In contrast, for patients with persistently high symptom

burden, clinical priorities should be proactively focused on perioperative medical risk prevention and control, meticulous management of complications, and close monitoring and intervention of inflammatory responses. Future symptom management practices should integrate biological, psychological, and social factors comprehensively, implementing differentiated, multidisciplinary, and coordinated whole-course management plans tailored to patients' specific symptom trajectory classes. Such an approach would facilitate a genuine paradigm shift toward individualized rehabilitation.

3.3 Association Between Symptom Burden Trajectory Typology and Clinical Outcomes and Its Implications

This study identified significant differences across symptom trajectory classes in key clinical outcome indicators. The "high symptom-persistent burden group" exhibited particularly unfavorable characteristics in terms of length of hospital stay, complication rates, red blood cell count, and CRP levels. The high concordance between patient-reported symptom burden and objective physiological abnormalities validates the clinical and biological significance of symptom trajectory typology. These aberrant indicators suggest that patients in this group may experience prolonged physiological stress and impaired tissue repair. The coexistence of low red blood cell count and elevated CRP levels reflects the simultaneous presence of malnutrition and chronic inflammation, which mutually reinforce each other and may represent the core biological mechanism driving poor prognosis in these patients[23].

Therefore, in the clinical care of esophageal cancer patients, those with significant preoperative symptom distress should undergo early systematic evaluation including functional status and surgical tolerance, with enhanced optimization interventions centered on prehabilitation. For patients with persistently elevated postoperative symptoms, dynamic monitoring of nutritional status, inflammatory indicators, and overall recovery progress is warranted, along with multidimensional, integrated

management strategies to interrupt the vicious cycle of "physiological disturbance—high symptom burden—adverse outcomes." During the long-term rehabilitation phase, evidence-based comprehensive strategies—including smoking cessation, progressive exercise, and weight maintenance—should be employed to alleviate symptom burden and improve long-term quality of life[24-26].

4 Conclusion

This study employed a prospective design with intensified follow-up and utilized latent class growth analysis to identify three heterogeneous trajectories of perioperative symptom evolution in patients with esophageal cancer. These trajectories were jointly shaped by biological, nutritional, and psychosocial factors and were significantly associated with postoperative clinical outcomes. Our findings provide a theoretical foundation for dynamic, individualized management strategies based on risk stratification. By identifying the "high-symptom persistent" phenotype preoperatively, healthcare professionals can proactively allocate intervention resources to high-risk patients, potentially flattening symptom trajectories, promoting overall recovery, and ultimately improving patients' postoperative quality of life while reducing the risk of adverse outcomes.

Nevertheless, this study has certain limitations. Although loss-to-follow-up analysis revealed no significant bias, the single-center sample may limit the generalizability of the findings, warranting future multicenter validation. Additionally, symptom burden trajectories may be influenced by unmeasured factors such as tumor molecular characteristics. Future research should expand the scope of preoperative assessment to include additional potential biomarkers, thereby refining predictive models and providing a more precise basis for early identification and intervention in high-risk trajectories.

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2. Competing interests: The authors declare no competing interests.

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