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Original Article

Construction and validation of a nomogram to identify risk of sleep disorders in gastrointestinal tumor patients undergoing chemotherapy

Qian Cao[1*], Guowei Zhu[1*], Ruizhi Shen[2*], Jikai Liu[1], Xiao Liang[2], Minmin Zhu[2], Hao Xi[2]

[1]Wuxi Medical School, Jiangnan University, Wuxi 214000, Jiangsu, China; [2]Department of Anesthesiology and Pain Medicine, Jiangnan University Medical Center (Wuxi No. 2 People's Hospital, Wuxi Clinical College of Nantong University), Wuxi 214000, Jiangsu, China. [*]Equal contributors.

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Abstract: Objectives: This study aimed to identify risk factors for sleep disorders in gastrointestinal cancer patients undergoing chemotherapy and to construct a predictive nomogram model, validated both internally and externally. Methods: A prospective study was conducted (ChiCTR2400085854), involving 308 patients from Jiangnan University Affiliated Central Hospital (Oct 2023-Aug 2024) for model development. Sleep quality and symptom burden were assessed using the Pittsburgh Sleep Quality Index (PSQI) and the Memorial Symptom Assessment Scale-Chinese version (MSAS-Ch). Independent risk factors were identified by multivariate logistic regression. A nomogram was constructed using R software and validated internally with 1000 bootstrap resamples and externally with 103 patients (Aug-Dec 2024). Model performance was evaluated by AUC, calibration curves, and decision curve analysis (DCA). Results: The incidence of sleep disorders was 53.8%. Significant influencing factors included longer disease duration, more severe depression, pain, fatigue, and diarrhea, as well as lower social support and physical activity (all $P < 0.05$). Internal validation showed good discrimination (AUC = 0.897, 95% CI: 0.862-0.931) and calibration. External validation confirmed robust performance (AUC = 0.896, 95% CI: 0.837-0.954) with consistent calibration. DCA demonstrated favorable clinical value. Conclusions: Sleep disorders are prevalent among gastrointestinal cancer patients undergoing chemotherapy. The developed nomogram demonstrates high predictive accuracy and is a practical tool to identify high-risk patients.

Keywords: Gastrointestinal cancer, chemotherapy, sleep disorders, prediction model, nomogram

Introduction

Gastrointestinal malignancies, particularly gastric and colorectal cancers, represent some of the most prevalent and lethal cancers globally. According to the 2022 Global Cancer Statistics, their incidence and mortality rates consistently rank among the top five worldwide [1, 2]. Current treatment modalities for gastrointestinal tumors encompass surgery, chemotherapy, radiotherapy, immunotherapy, and targeted molecular therapies. Among these, chemotherapy remains a cornerstone, exerting antitumor effects by targeting rapidly proliferating malignant cells to inhibit progression, reduce recurrence, and extend survival [3-5]. However, these agents also exert cytotoxic effects on healthy proliferating cells, resulting in a range of adverse events. Sleep disturbances, in particular, represent a significant and frequently overlooked complication, affecting up to 60% of patients undergoing chemotherapy for gastrointestinal malignancies [6]. Sleep disturbances can compromise immune function, disrupt hormonal balance, and exacerbate emotional stress, thereby increasing infection risk and reducing treatment adherence. Moreover, their chronic nature can lead to persistent fatigue, cognitive dysfunction, and diminished quality of life [7, 8].

Sleep disorders in patients with gastrointestinal cancers are influenced by a variety of demographic, clinical, and psychological factors. Younger female patients and those with severe complications are particularly susceptible, pos-

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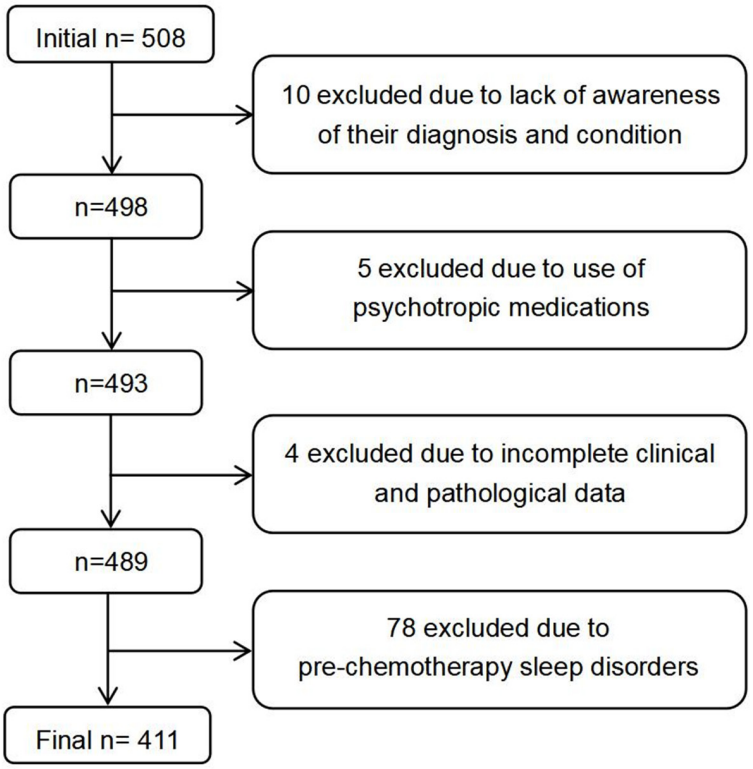

Figure 1. Flowchart of the study selection and inclusion process.

sibly from heightened psychosocial stress. Unemployment and financial strain further elevate the risk of sleep disturbance, whereas being married or partnered may offer a protective effect through social support [9, 10]. Clinical factors such as advanced tumor stage, metastasis, and disease recurrence are all positively correlated with an increased incidence of sleep disturbances [11]. Additionally, chemotherapy-induced symptoms, including nausea, fatigue, and pain, as well as treatment-related toxicities, significantly exacerbate sleep difficulties [12, 13]. Psychological distress, particularly anxiety and depression, may further impair sleep quality through the hypothalamic-pituitary axis (HPA) and by increasing sympathetic nervous system excitability, thereby maintaining a state of physiologic hyperarousal detrimental to normal sleep processes [14, 15]. Although the exact causal mechanisms remain complex and not fully understood, previous studies suggest that chemotherapy may disrupt central sleep-regulating pathways through neurotoxicity and systemic inflammation. Neurotoxic agents such as cisplatin and paclitaxel can affect the central nervous system, impairing brain regions such as the hypothalamus and brainstem. Chemotherapy-induced inflammation increases cytokines that may cross the blood-brain barrier and interfere with circadian centers such as the suprachiasmatic nucleus [16-18].

In summary, the incidence of sleep disturbances among gastrointestinal cancer chemotherapy patients is influenced by multiple factors. However, targeted screening tools are lacking. Developing prediction models based on patient characteristics woiuld help identify patients at risk of sleep disorders, thereby improving sleep quality and enhancing clinical management.

Materials and methods

Study population

The training cohort comprised 308 gastrointestinal cancer patients undergoing chemotherapy at the Department of Oncology, Wuxi No. 2 People's Hospital, from October 2023 to October 2024. For external validation, 103 gastrointestinal cancer patients receiving chemotherapy between August 2024 and December 2024 were recruited from the Department of Oncology at the Affiliated Hospital of Jiangnan University, another tertiary medical center located in Wuxi. The detailed patient selection flowchart is shown in **Figure 1**. The study protocol was reviewed and approved by the Ethics Committees (Ethics Approval No.: 2023-Y-109).

Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) Hospitalized patients aged ≥ 18 years; (2) Pathologically diagnosed with gastrointestinal cancer (including gastric, colon, and rectal cancer) and currently undergoing chemotherapy, with sleep quality assessed after chemotherapy; (3) Complete clinical and pathologic data available; (4) Awareness of their diagnosis and condition, with informed consent and voluntary participation in the study.

Exclusion criteria included: (1) History of severe mental disorders, cognitive impairment, or inability to communicate normally; (2) History of psychiatric illness or current use of psychotropic medications; (3) Recent major life events, such as divorce or death of a family member; (4) Patients who voluntarily withdrew from treatment and were discharged; (5) Patients with sleep disturbances prior to chemotherapy.

Clinical data collection

General and clinical data were collected including the following: sex, age, height, weight, education level, employment status, household income, marital status, type of medical insurance, past medical history, family history of cancer, smoking and alcohol history, disease diagnosis, disease duration, tumor stage, presence of distant metastasis, stoma status, purpose of chemotherapy, chemotherapy regimen, number of chemotherapy sessions, chemotherapy cycles, surgical treatment, radiotherapy, use of hormones, immunotherapy, and targeted therapy.

Additional assessments included the Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) for anxiety and depression evaluation; the Chinese version of the Memory Symptom Assessment Scale for symptom burden; the Nutritional Risk Screening 2002 (NRS-2002) for nutritional status; the Perceived Social Support Scale (PSSS) for social support level; and the short-form International Physical Activity Questionnaire (IPAQ-SF) for physical activity levels.

Definition of sleep disorders

Sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI), which consists of 19 self-rated and 5 observer-rated items. The self-rated portion covers seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction. Each component is scored from 0 to 3, with a total score ranging from 0 to 21. Higher scores indicate poorer sleep quality. For this study, a total PSQI score greater than 7 was defined as indicative of sleep disturbance.

Statistical analysis

Statistical analyses were performed using SPSS version 26.0. Continuous variables following a normal distribution were expressed as mean ± standard deviation, while categorical data were presented as counts and percentages. Group comparisons for normally distributed continuous variables were conducted using independent-sample t-tests; for non-normally distributed and ordinal data, the Mann-Whitney *U* test was applied. Categorical variables were analyzed using the Chi-square test or Fisher's exact test. Spearman correlation analysis was employed to evaluate the relationship between sleep disturbances and other symptoms in gastrointestinal cancer patients undergoing chemotherapy. Variables with statistical significance ($P < 0.05$) by univariate and correlation analyses were entered into a multivariate logistic regression model to identify risk factors for sleep disturbances. The significance level was set at $\alpha = 0.05$. The model was visualized using a nomogram constructed with R version 4.3.2.

Results

Univariate analysis of sleep disorders in gastrointestinal cancer patients undergoing chemotherapy

Among the 308 gastrointestinal cancer patients undergoing chemotherapy, 172 (55.8%) experienced sleep disturbances, while 136 (44.2%) did not. The mean PSQI score was 9.29 ± 4.326. Univariate analysis was conducted with sleep disturbance as the dependent variable. The results showed that the following factors were statistically significant and may be risk factors for sleep disturbances in this patient population: body mass index ($\chi^2 = 16.293$, $P = 0.001$), disease duration ($\chi^2 = 16.046$, $P < 0.001$), tumor stage ($\chi^2 = 8.839$, $P = 0.032$), chemotherapy regimen ($\chi^2 = 14.469$, $P = 0.043$), nutritional status ($\chi^2 = 7.625$, $P = 0.006$), social support ($\chi^2 = 22.253$, $P < 0.001$), anxiety ($\chi^2 = 58.824$, $P < 0.001$), depression ($\chi^2 = 66.853$, $P < 0.001$), and physical activity ($\chi^2 = 44.435$, $P < 0.001$). Other demographic characteristics and treatment-related variables did not show significant associations with sleep disturbances. Details are presented in **Table 1**.

Table 1. Univariate analysis of sleep disorders in gastrointestinal cancer patients undergoing chemotherapy

Variable name	Non-Sleep Disorders (n = 136)	Sleep Disorders (n = 172)	X^2	P
Gender			2.477	0.116
Male	94 (69.1%)	104 (60.5%)		
Female	42 (30.9%)	68 (39.5%)		
Age (years)			4.958	0.084
≤ 59	32 (23.5%)	25 (14.5%)		
60-69	53 (39%)	66 (38.4%)		
≥ 70	51 (37.5%)	81 (47.1%)		
Body Mass Index (BMI, kg/m^2)			16.293	0.001
< 18.5	11 (8.1%)	40 (23.3%)		
18.5-24	85 (62.5%)	102 (59.3%)		
24-28	35 (25.7%)	26 (15.1%)		
≥ 28	5 (3.7%)	4 (2.3%)		
Education Level			0.811	0.847
Primary school	27 (19.9%)	31 (18%)		
Junior high school	74 (54.4%)	95 (55.2%)		
High school	23 (16.9%)	34 (19.8%)		
College or above	12 (8.8%)	12 (7%)		
Employment Status			6.422	0.093
Employed	5 (3.7%)	2 (1.2%)		
On sick leave	16 (11.8%)	12 (7%)		
Unemployed	11 (8.1%)	24 (14%)		
Retired	104 (76.5%)	134 (77.9%)		
Household Income (Yuan/month)			5.813	0.214
≤ 3000	42 (30.9%)	47 (27.3%)		
3000-5000	55 (40.4%)	85 (49.4%)		
5000-8000	21 (15.4%)	29 (16.9%)		
8000-10000	10 (7.4%)	5 (2.9%)		
≥ 10000	8 (5.9%)	6 (3.5%)		
Marital Status			2.174	0.537
Married	128 (94.1%)	156 (90.7%)		
Unmarried	1 (0.7%)	4 (2.3%)		
Divorced	2 (1.5%)	2 (1.2%)		
Widowed	5 (3.7%)	10 (5.8%)		
Medical Insurance			1.971	0.578
Employee medical insurance	84 (61.8%)	96 (55.8%)		
Resident medical insurance	33 (24.3%)	42 (24.4%)		
Rural cooperative medical insurance	15 (11%)	27 (15.7%)		
Other	4 (2.9%)	7 (4.1%)		
Smoking			1.298	0.255
Yes	21 (15.4%)	19 (11%)		
No	115 (84.6%)	153 (89%)		
Alcohol Consumption			0.085	0.771
Yes	14 (10.3%)	16 (9.3%)		
No	122 (89.7%)	156 (90.7%)		
Medical History			0.400	0.527
Yes	83 (61%)	111 (64.5%)		
No	53 (39%)	61 (35.5%)		

Family History of Cancer			0.242	0.623
Yes	30 (22.1%)	34 (19.8%)		
No	106 (77.9%)	138 (80.2%)		
Cancer Type			3.927	0.140
Gastric cancer	42 (30.9%)	60 (34.9%)		
Colon cancer	53 (39%)	77 (44.8%)		
Rectal cancer	41 (30.1%)	35 (20.3%)		
Disease Duration			16.046	< 0.001
0-6 months	70 (51.5%)	50 (29.1%)		
6 months-1 year	22 (16.2%)	42 (24.4%)		
> 1 year	44 (32.4%)	80 (46.5%)		
Tumor Stage			8.839	0.032
I	5 (3.7%)	2 (1.2%)		
II	5 (3.7%)	10 (5.8%)		
III	52 (38.2%)	44 (25.6%)		
IV	74 (54.4%)	116 (67.4%)		
Presence of Distant Metastasis			3.034	0.082
Yes	72 (52.9%)	108 (62.8%)		
No	64 (47.1%)	64 (37.2%)		
Purpose of Chemotherapy			6.741	0.081
Neoadjuvant chemotherapy	8 (5.9%)	12 (7%)		
Adjuvant chemotherapy	48 (35.3%)	41 (23.8%)		
First-line chemotherapy	43 (31.6%)	52 (30.2%)		
Second-line and above	37 (27.2%)	67 (39%)		
Chemotherapy Regimen			14.469	0.043
CAPEOX	44 (32.4%)	40 (23.3%)		
FOLFOX	25 (18.4%)	23 (13.4%)		
FOLFIRI	20 (14.7%)	25 (14.5%)		
SOX	17 (12.5%)	18 (10.5%)		
XELOX	2 (1.5%)	14 (8.1%)		
XP	4 (2.9%)	5 (2.9%)		
FLOT	10 (7.4%)	20 (11.6%)		
Other	14 (10.3%)	27 (15.7%)		
Chemotherapy Sessions			6.883	0.229
T1	19 (14%)	14 (8.1%)		
T2	11 (8.1%)	12 (7%)		
T3	10 (7.4%)	15 (8.7%)		
T4	22 (16.2%)	18 (10.5%)		
T5	8 (5.9%)	17 (9.9%)		
T6 and above	66 (48.5%)	96 (55.8%)		
Chemotherapy Cycle			5.542	0.063
14 days	26 (19.1%)	17 (9.9%)		
21 days	86 (63.2%)	118 (68.6%)		
28 days	24 (17.6%)	37 (21.5%)		
Surgery			0.202	0.653
Yes	105 (77.2%)	129 (75%)		
No	31 (22.8%)	43 (25%)		
Radiotherapy			0.266	0.606
Yes	21 (15.4%)	23 (13.4%)		
No	115 (84.6%)	149 (86.6%)		

Hormone Therapy			2.935	0.087
Yes	47 (34.6%)	76 (44.2%)		
No	89 (65.4%)	96 (55.8%)		
Immunotherapy			0.478	0.489
Yes	37 (27.2%)	53 (30.8%)		
No	99 (72.8%)	119 (69.2%)		
Targeted Therapy			0.364	0.546
Yes	57 (41.9%)	78 (45.3%)		
No	79 (58.1%)	94 (54.7%)		
Stoma			2.382	0.123
Yes	28 (20.6%)	24 (14%)		
No	108 (79.4%)	148 (86%)		
Nutritional Status			7.625	0.006
Good	114 (83.8%)	121 (70.3%)		
Poor	22 (16.2%)	51 (29.7%)		
Social Support			22.253	< 0.001
Low	1 (0.7%)	12 (7%)		
Medium	90 (66.2%)	137 (79.7%)		
High	45 (33.1%)	23 (33.1%)		
Anxiety Status			58.824	< 0.001
Yes	20 (14.7%)	99 (57.6%)		
No	116 (85.3%)	73 (42.4%)		
Depression Status			66.853	< 0.001
Yes	7 (5.1%)	82 (47.7%)		
No	129 (94.9%)	90 (52.3%)		
Physical Activity (MET-minutes/week)			44.435	< 0.001
Low	51 (37.5%)	129 (75%)		
Medium	84 (61.8%)	43 (25%)		
High	1 (0.7%)	0 (0%)		

Note: CAPEOX: Oxaliplatin combined with capecitabine treatment; FOLFOX: Oxaliplatin combined with fluorouracil treatment; FOLFIRI: Fluorouracil, leucovorin, and irinotecan combination treatment; SOX: Oxaliplatin combined with tegafur-gimeracil-oteracil potassium treatment; XELOX: Oxaliplatin combined with capecitabine treatment; XP: Cisplatin combined with capecitabine treatment; FLOT: Fluorouracil, leucovorin, oxaliplatin, and docetaxel combination treatment.

Correlation analysis between sleep disturbance and symptoms in gastrointestinal cancer patients undergoing chemotherapy

To explore the relationship between sleep disturbance scores and the severity of various symptoms in gastrointestinal cancer patients undergoing chemotherapy, Spearman correlation analysis was conducted. Symptoms with an incidence rate below 20%, including cough, bloating, difficulty urinating, shortness of breath, pruritus, dysphagia, mouth ulcers, and limb edema (Supplementary Table 1), were excluded from the analysis to prioritize more prevalent and clinically significant symptoms. The correlation heatmap allows for the quick identification of variables strongly associated with sleep disorders. The color bar on the right represents the range of correlation coefficients, from -1 (perfect negative correlation) to 1 (perfect positive correlation). Red indicates positive correlation, blue indicates negative correlation, and white suggests a correlation close to 0 (no correlation). The results revealed that sleep disturbance scores were positively correlated with the following symptoms: Difficulty concentrating (S1), Pain (S2), Fatigue (S3), Nervousness (S5), Diarrhea (S15), Distress (S18), Loss of appetite (S21), Irritability (S24) and Changes in taste (S26) ($P < 0.005$). These variables may be significant factors influencing the PSQI. These findings are illustrated in **Figure 2**.

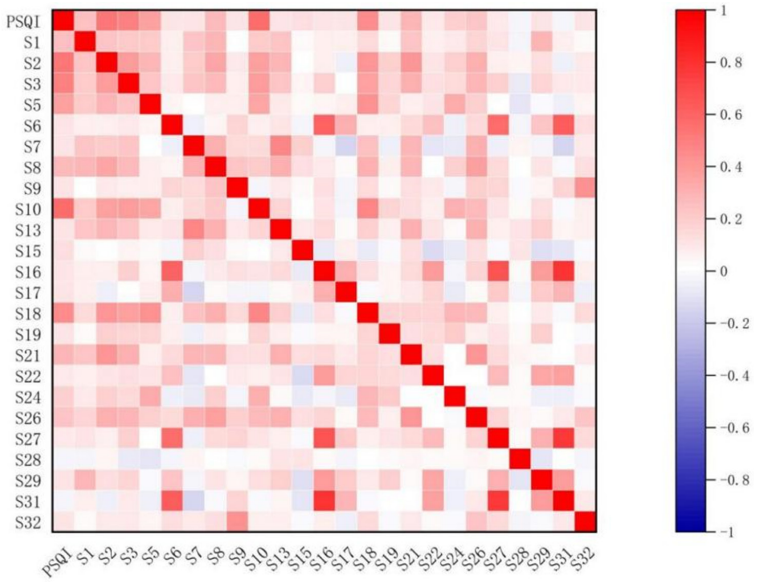

Figure 2. Heatmap of the correlation between sleep disturbances and symptoms in gastrointestinal cancer patients undergoing chemotherapy.

Table 2. Multivariate regression analysis results of sleep disorders in gastrointestinal cancer patients undergoing chemotherapy

Characteristics	*β*	*SE*	*Wald*	*P*	OR [95% CI]
Time	0.558	0.180	9.624	0.002	1.748 [1.228, 2.487]
Depression	1.810	0.515	12.33	0.000	6.110 [2.225, 16.780]
Pain	0.756	0.236	10.214	0.001	2.129 [1.340, 3.385]
Fatigue	0.652	0.160	16.683	0.000	1.919 [1.403, 2.623]
Diarrhea	0.802	0.205	15.325	0.000	2.229 [1.492, 3.330]
Support	-1.046	0.361	8.394	0.004	0.351 [0.173, 0.713]
Activity	-1.163	0.335	12.074	0.001	0.312 [0.162, 0.602]
Constant	1.003	1.026	0.956	0.328	

Multivariate regression analysis of sleep disorders in gastrointestinal cancer patients undergoing chemotherapy

Based on the results of univariate and correlation analyses, variables with statistical significance were included in a multivariate regression analysis. The results showed that disease duration (OR = 1.748, 95% CI: 1.228-2.487, $P < 0.05$), pain (OR = 2.129, 95% CI: 1.340-3.385, $P < 0.05$), fatigue (OR = 1.919, 95% CI: 1.403-2.623, $P < 0.05$), diarrhea (OR = 2.229, 95% CI: 1.492-3.330, $P < 0.05$), social support (OR = 0.351, 95% CI: 0.173-0.713, $P < 0.05$), depression (OR = 6.110, 95% CI: 2.225-16.780, $P < 0.05$), and physical activity level (OR = 0.312, 95% CI: 0.162-0.602, $P < 0.05$) had significant effects on sleep. Detailed results are presented in **Table 2**.

Construction of a nomogram prediction model

The final logistic regression model for predicting sleep disturbance was established as follows: logit(P) = 1.003 + 0.558 × disease duration + 1.810 × depression + 0.756 × pain + 0.652 × fatigue + 0.802 × diarrhea - 1.046 × social support - 1.163 × physical activity level. A multivariate logistic regression model predicting sleep disturbances in gastrointestinal cancer patients undergoing chemotherapy was constructed using R software. The nomogram includes key predictive factors. Each factor corresponds to a calibrated line segment, where the length of the segment reflects the relative impact of that factor on the risk of sleep disturbance. By drawing vertical lines from the patient's values on each predictor to the corresponding point scale, the individual scores are summed to obtain a total score. This total score can then be mapped to the bottom scale to estimate the predicted probability of experiencing sleep disturbances (**Figure 3**).

Comparison of baseline data between training and validation groups

A total of 103 patients were included in the external validation dataset, comprising 71 men (68.9%) and 32 women (31.1%). Among them, 57 patients (18.5%) were under 60 years old, 119 patients (38.6%) were aged 60-69, and 132 patients (42.9%) were 70 years or older. In terms of cancer types, there were 24 patients (23.3%) with gastric cancer, 52 patients (50.5%) with colon cancer, and 52 patients (50.5%) with rectal cancer. There were no significant differences ($P > 0.05$) between the validation dataset and the model development

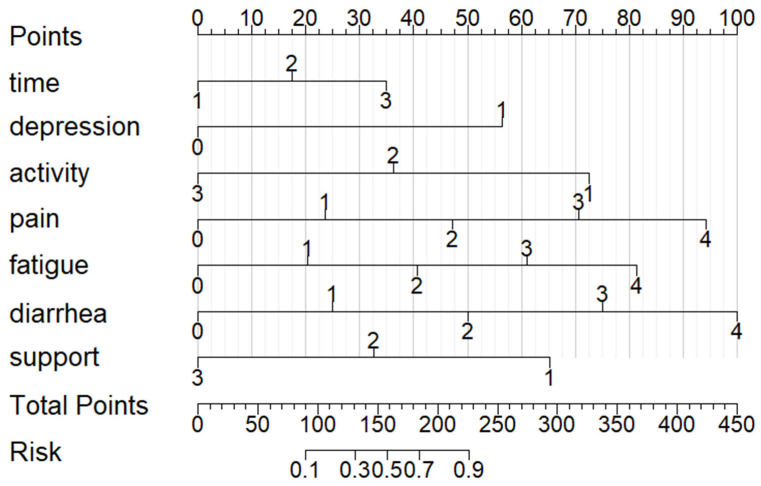

Figure 3. Nomogram for predicting sleep disorders in gastrointestinal cancer patients undergoing chemotherapy.

cohort in terms of demographic variables, including gender, age, body mass index, education level, employment status, income, marital status, health insurance type, smoking and drinking history, medical history, or family history of cancer. Similarly, disease- and treatment-related variables, such as diagnosis, disease duration, tumor stage, distant metastasis, chemotherapy regimen, purpose of chemotherapy, number of chemotherapy cycles, chemotherapy duration, radiotherapy, use of hormones, immunotherapy, targeted therapy, and presence of a stoma, also showed no significant differences between the two groups ($P > 0.05$). These findings indicate good homogeneity and comparability between the modeling and validation cohorts, supporting use of the validation dataset to assess the performance of the predictive model. Detailed results are shown in **Table 3**.

Validation of the sleep disorders risk prediction model in gastrointestinal cancer patients undergoing chemotherapy

Discrimination: We performed internal validation of the model using the Bootstrap method. **Figure 4A** shows that the AUC of the model's ROC curve is 0.897 (95% CI: 0.862-0.931), indicating good discriminatory ability. The results showed that the AUC/sensitivity/specificity values for the seven variables: disease duration, depression, pain, fatigue, diarrhea, social support, and physical activity level were 0.610/70.9%/51.5%, 0.713/47.7%/94.9%, 0.709/51.2%/0.87.5%, 0.783/82.6%/60.3%, 0.584/33.7%/82.4%, 0.619/86.6%/33.1%, 0.688/75.0%/62.5% respectively, as shown in Supplementary Table 2. External validation results show that the AUC of the ROC curve is 0.896 (95% CI: 0.837-0.954) (**Figure 4D**).

Calibration: In the calibration curve of the training set (**Figure 4B**), the calibration curve obtained after 1,000 resampling iterations almost perfectly overlaps with the curve fitted based on the actual observed values (Apparent). The calibration curve shows that the actual curve closely aligns with the ideal curve, and the slope of the calibration line is near 1, indicating good calibration performance. The external validation Brier score was 0.131, which is less than 0.25, indicating good accuracy. The calibration curve for the external validation dataset is shown in **Figure 4E**.

Clinical applicability: In **Figure 4C**, **4F**, the red solid line represents the actual net benefit of the predictive model, the black solid line indicates the net benefit when assuming that no samples experience sleep disturbances, and the gray solid line shows the net benefit assuming that all samples experience sleep disturbances. The further the red solid line deviates from the black and gray solid lines, the greater clinical applicability of the model. Results showed, whether by internal or external validation, that taking targeted treatment or intervention measures for these patients resulted in greater net benefit compared to strategies of "universal intervention" or "no intervention", suggesting that the model has significant clinical application value.

Discussion

This study showed that the incidence of sleep disturbances in gastrointestinal cancer chemotherapy patients is high, reaching 53.8%. Previous studies have also reported that more than 50% of gastrointestinal cancer chemotherapy patients experience sleep disturbances [19, 20]. However, prior research has mainly focused on exploring the trajectory of sleep

Table 3. Comparison of baseline characteristics between development set and validation set

Variable name		Development Set	Validation Set	χ^2/F	*P*
Gender	Male	198 (64.3%)	71 (68.9%)	0.737	0.391
	Female	110 (35.7%)	32 (31.1%)		
Age	≤ 59	57 (18.5%)	18 (17.5%)	0.837	0.658
	60-69	119 (38.6%)	45 (43.7%)		
	≥ 70	132 (42.9%)	40 (38.8%)		
BMI	< 18.5	51 (16.6%)	14 (13.6%)	3.320	0.345
	18.5-24	187 (60.7%)	58 (56.3%)		
	24-28	61 (19.8%)	29 (28.2%)		
	≥ 28	9 (2.9%)	2 (1.9%)		
Education Level	Primary school	58 (18.8%)	19 (18.4%)	6.553	0.088
	Junior high school	169 (54.9%)	69 (67%)		
	High school	57 (18.5%)	11 (10.7%)		
	College or above	24 (7.8%)	4 (3.9%)		
Employment Status	Employed	7 (2.3%)	3 (2.9%)	3.539	0.316
	Sick leave	28 (9.1%)	4 (3.9%)		
	Unemployed	35 (11.4%)	11 (10.7%)		
	Retired	238 (77.3%)	85 (82.5%)		
Income	≤ 3000	89 (28.9%)	17 (16.5%)	7.540	0.110
	3000-5000	140 (45.5%)	53 (51.5%)		
	5000-8000	50 (16.2%)	21 (20.4%)		
	8000-10000	15 (4.9%)	8 (7.8%)		
	≥ 10000	14 (4.5%)	4 (3.9%)		
Marital Status	Married	284 (92.2%)	101 (98.1%)	7.347	0.062
	Unmarried	5 (1.6%)	0 (0.0%)		
	Divorced	4 (1.3%)	0 (0.0%)		
	Widowed	15 (4.9%)	2 (1.9%)		
Medical Insurance	Employee medical insurance	180 (58.4%)	55 (53.4%)	4.578	0.205
	Resident medical insurance	75 (24.4%)	25 (24.3%)		
	Rural cooperative medical insurance	42 (13.6%)	14 (13.6%)		
	Other	11 (3.6%)	9 (8.7%)		
Alcohol Consumption	No	278 (90.3%)	90 (87.4%)	0.684	0.408
	Yes	30 (9.7%)	13 (12.6%)		
Smoking Status	No	268 (87.0%)	86 (83.5%)	0.800	0.371
	Yes	40 (13.0%)	17 (16.5%)		
Medical History	No	114 (37.0%)	45 (43.7%)	1.450	0.228
	Yes	194 (63.0%)	58 (56.3%)		
Family History	No	244 (79.2%)	89 (86.4%)	2.593	0.107
	Yes	64 (20.8%)	14 (13.6%)		
Disease Diagnosis	Gastric cancer	102 (33.1%)	24 (23.3%)	3.693	0.158
	Colon cancer	130 (42.2%)	52 (50.5%)		
	Rectal cancer	76 (24.7%)	27 (26.2%)		
Disease Duration	0-6 months	120 (39.0%)	40 (38.8%)	2.912	0.233
	6 months-1 year	64 (20.8%)	29 (28.2%)		
	> 1 year	124 (40.3%)	34 (33.0%)		

Tumor Stage	I	7 (2.3%)	0 (0.0%)	5.745	0.125
	II	15 (4.9%)	6 (5.8%)		
	III	96 (31.2%)	26 (25.2%)		
	IV	190 (61.7%)	71 (68.9%)		
Distant Metastasis	No	128 (41.6%)	33 (32.0%)	2.936	0.087
	Yes	180 (58.4%)	70 (68.0%)		
Chemotherapy Regimen	CAPEOX	84 (27.3%)	45 (43.7%)	12.698	0.08
	FOLFOX	48 (15.6%)	14 (13.6%)		
	FOLFIRI	45 (14.6%)	13 (12.6%)		
	SOX	35 (11.4%)	8 (7.8%)		
	XELOX	16 (5.2%)	7 (6.8%)		
	XP	9 (2.9%)	1 (1.0%)		
	FLOT	30 (9.7%)	5 (4.9%)		
	Others	41 (13.3%)	10 (9.7%)		
Purpose of Chemotherapy	Neoadjuvant chemotherapy	20 (6.5%)	7 (6.8%)	1.568	0.667
	Adjuvant chemotherapy	89 (28.9%)	36 (35.0%)		
	First-line chemotherapy	95 (30.8%)	27 (26.2%)		
	Second-line and above	104 (33.8%)	33 (32.0%)		
Chemotherapy Cycle	T1	33 (10.7%)	3 (2.9%)	8.931	0.112
	T2	23 (7.5%)	11 (10.7%)		
	T3	25 (8.1%)	11 (10.7%)		
	T4	40 (13%)	11 (10.7%)		
	T5	25 (8.1%)	13 (12.6%)		
	T6 and above	162 (52.6%)	54 (52.4%)		
Chemotherapy Interval	14 days	43 (14.0%)	23 (22.3%)	5.054	0.080
	21 days	204 (66.2%)	66 (64.1%)		
	28 days	61 (19.8%)	14 (13.6%)		
Surgery	No	74 (24.0%)	16 (15.5%)	3.255	0.071
	Yes	234 (76.0%)	87 (84.5%)		
Radiotherapy	No	264 (85.7%)	83 (80.6%)	1.546	0.214
	Yes	44 (14.3%)	20 (19.4%)		
Hormone Therapy	No	185 (60.1%)	58 (56.3%)	0.450	0.502
	Yes	123 (39.9%)	45 (43.7%)		
Immunotherapy	No	218 (70.8%)	77 (74.8%)	0.603	0.437
	Yes	90 (29.2%)	26 (25.2%)		
Targeted Therapy	No	173 (56.2%)	52 (50.5%)	1.006	0.316
	Yes	135 (43.8%)	51 (49.5%)		
Stoma	No	256 (83.1%)	86 (83.5%)	0.008	0.929
	Yes	52 (16.9%)	17 (16.5%)		

pattern changes during chemotherapy, without evaluating the patients' responses to chemotherapy side effects and symptoms. The influencing factors considered in those studies were limited, and they did not comprehensively include variables that may affect sleep quality.

Multivariate regression analysis revealed that longer disease duration was significantly associated with an increased risk of sleep disturbances, aligning with previous findings that sleep problems tend to persist over time following a cancer diagnosis [21-24]. Social support, which refers to the material and emotional help obtained from various social relationships in a network, is important for maintaining good emotional experiences [25]. The findings suggest that greater social support is associated

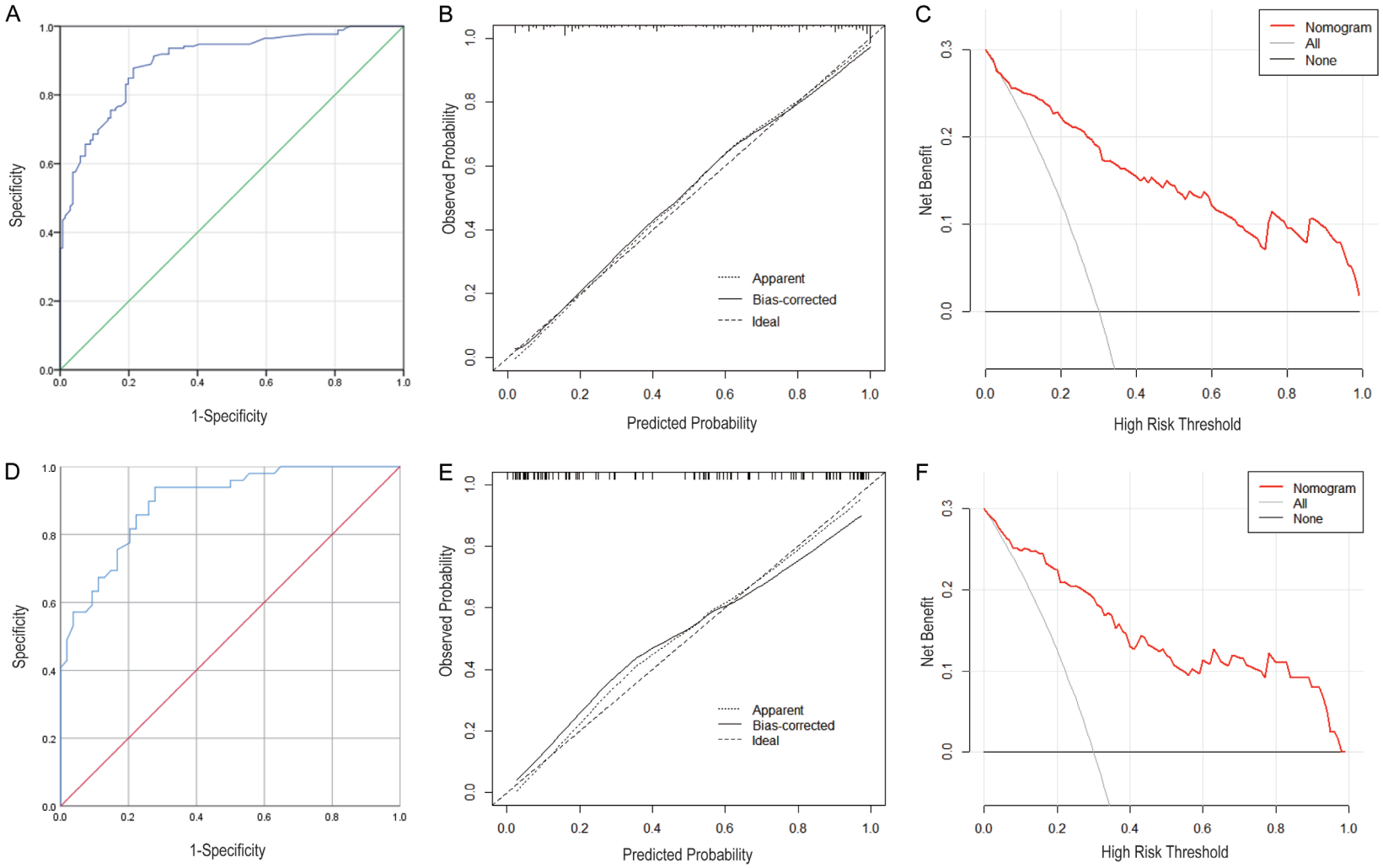

Figure 4. Validation of risk prediction model for sleep disorders in gastrointestinal cancer patients undergoing chemotherapy.

with a lower risk of sleep disorders and significantly contributes to improved sleep quality [26, 27]. The study further demonstrated a positive association between depression and sleep disturbances. Patients experiencing negative emotional states, such as excessive concern about cancer prognosis, anxiety regarding sleep, cognitive rumination, and increased environmental sensitivity, are more prone to maladaptive coping mechanisms, which may contribute to the onset and persistence of chronic sleep disturbances [28, 29]. Additionally, some colorectal cancer patients may experience body image changes due to ostomy surgery, leading to a sense of disease-related shame and exacerbating negative emotions [30]. Negative emotions like depression can interfere with the normal feedback mechanism of the HPA, increasing sympathetic nervous system excitability and leading to elevated levels of norepinephrine and cortisol, which can disrupt circadian rhythms and ultimately cause sleep disturbances [31, 32].

In this study, patients' overall activity levels were low, and those with lower activity levels had a higher likelihood of sleep disturbances. Chemotherapy disrupts sleep and activity patterns, leading to increased wakefulness during the night [33]. Regular physical activity is a safe and effective means of alleviating various treatment-related symptoms, improving sleep duration, sleep efficiency, sleep latency, and circadian rhythm of rest activity [34, 35]. Moderate exercise not only promotes the release of neurotransmitters like dopamine and serotonin but also improves overall emotional states, indirectly enhancing sleep quality [36]. Pain is a complex subjective experience involving both sensory and emotional components, typically associated with actual or potential tissue damage. It can result from tumor compression of surrounding tissues, the release of chemicals such as prostaglandins and bradykinin, or ischemia and necrosis due to inadequate blood supply to tumors [37]. Chemotherapy drugs such as oxaliplatin, used in gastrointestinal cancer treatment, may cause cold-induced numbness, tingling, and muscle tension or spasms, resulting in acute sensory neuropathy [38, 39]. The study found that the severity of pain is positively correlated with the occurrence of sleep disturbances, consistent with previous studies by Pachman et al., where higher pain severity increased the likelihood of sleep disturbances [40, 41]. Fatigue is a common symptom associated with insomnia in cancer patients and is one of the most common factors contributing to cancer-related insomnia [42]. Cancer progression and chemotherapy activate the immune system, releasing pro-inflammatory factors that induce fatigue, while also affecting sleep regulation. Sleep quality deterioration may exacerbate inflammation, thereby intensifying fatigue, creating a vicious cycle [43].

This study also found that the severity of diarrhea is positively correlated with the occurrence of sleep disturbances. Previous studies have shown that poorer sleep quality and shorter sleep duration are closely related to a higher incidence of gastrointestinal symptoms [44-46]. In a meta-analysis involving 540 patients with gastrointestinal cancer chemotherapy regimens, the incidence of diarrhea was 19.1% [47]. In this study, the incidence of diarrhea was slightly higher, possibly due to the different patient populations in the two studies. The meta-analysis included patients at various stages of cancer, whereas our study included more stage IV patients. Advanced cancer patients often exhibit more significant side effects during chemotherapy, which could explain the higher incidence of diarrhea. Velda et al. [48] conducted a sleep disturbance survey in 18 newly diagnosed rectal cancer patients and used stool genetic sequencing during chemotherapy. Their findings indicated that chemotherapy patients had a significant increase in sleep disturbances due to a reduction in bacterial diversity and abundance.

This study constructed a predictive model for sleep disturbance risk in gastrointestinal cancer chemotherapy patients using regression analysis and further visualized the model with a nomogram. The model's AUC value, ranging from 0.7 to 0.9 [49], suggests a certain level of diagnostic value. The model demonstrated strong predictive performance and high clinical application value, providing a scientific basis for assessing the risk of sleep disturbances in gastrointestinal cancer chemotherapy patients and assisting clinicians in developing personalized intervention measures to improve patients' sleep quality and quality of life.

This study had several limitations. First, sleep assessment relied on scales, which may have introduced subjective bias. Future studies should use polysomnography or wearable devices to assess sleep and circadian rhythms in chemotherapy patients. Second, the diversity of chemotherapy regimens could affect the results, and no subgroup analysis was conducted. Future research should include a larger sample size for further analysis. Additionally, some predictors, such as social support, anxiety, and depression, were measured simultaneously with sleep disturbances, limiting causal conclusions. The model, however, aims to identify high-risk patients using easily accessible clinical and psychosocial data. Longitudinal studies are needed to validate these findings and clarify temporal relationships.

Conclusion

Longer disease duration, greater severity of depression, fatigue, pain, and diarrhea, along with lower social support and physical activity, were identified as independent predictors of sleep disturbances in gastrointestinal cancer patients receiving chemotherapy. The nomogram based on these factors demonstrated good identification ability and offers a simple, user-friendly tool for the clinical assessment of sleep problems in this patient population.

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Disclosure of conflict of interest

None.

Address correspondence to: Hao Xi, Minmin Zhu and Xiao Liang, Department of Anesthesiology and Pain Medicine, Jiangnan University Medical Center (Wuxi No. 2 People's Hospital, Wuxi Clinical College of Nantong University), Wuxi 214000, Jiangsu, China. Tel: +86-18601482516; E-mail: jgs8686-99@163.com (HX); Tel: +86-13921292032; E-mail: minminzhu2024@163.com (MMZ); Tel: +86-182-62278182; E-mail: 9862023142@jiangnan.edu.cn (XL)

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Supplementary Table 1. Symptom occurrence in patients with gastrointestinal tumors undergoing chemotherapy

Number	Symptom Item	Incidence n (%)	Frequency Mean ± SD	Severity Mean ± SD	Distress Mean ± SD
S1	Difficulty concentrating	85 (27.6%)	1.99±0.84	1.41±0.52	1.28±0.62
S2	Pain	105 (34.1%)	2.54±0.91	1.93±0.90	2.32±0.65
S3	Fatigue	229 (74.4%)	2.72±1.11	2.00±0.96	2.30±1.09
S4	Cough	53 (17.2%)	1.53±0.64	1.27±0.45	1.57±0.54
S5	Nervousness	81 (26.3%)	1.70±0.49	1.21±0.44	2.09±0.48
S6	Dry mouth	121 (39.3%)	2.11±0.66	1.55±0.61	2.15±0.54
S7	Nausea	103 (33.4%)	2.42±0.69	1.97±0.65	2.31±0.60
S8	Drowsiness	108 (35.1%)	1.81±0.73	1.61±0.64	1.34±0.75
S9	Numbness or tingling in hands/feet	112 (36.4)	2.12±0.67	1.79±0.64	2.13±0.63
S10	Sleep disturbance	178 (57.8%)	2.45±0.64	2.34±0.62	2.43±0.66
S11	Feeling bloated/abdominal distension	49 (15.9%)	2.06±0.75	1.88±0.67	2.12±0.63
S12	Difficulty urinating	18 (5.8%)	2.00±0.00	1.61±0.50	2.33±0.49
S13	Vomiting	77 (25%)	1.84±0.52	1.61±0.59	1.86±0.58
S14	Shortness of breath	49 (15.9%)	1.65±0.63	1.59±0.57	2.18±0.49
S15	Diarrhea	82 (26.6%)	1.93±0.68	1.76±0.66	2.33±0.59
S16	Feeling sad	76 (24.7%)	2.22±0.83	1.72±0.75	1.68±0.71
S17	Sweating	67 (21.8%)	1.60±0.49	1.07±0.27	1.22±0.42
S18	Anxiety	101 (32.8%)	2.22±0.77	1.77±0.70	2.24±0.74
S19	Loss of interest in sexual activity	85 (27.6%)	1.65±0.57	1.92±0.32	1.52±0.50
S20	Itchy skin	39 (12.7%)	1.93±0.47	1.78±0.42	2.24±0.44
S21	Loss of appetite	155 (50.3%)	2.61±0.71	2.09±0.67	2.10±0.66
S22	Dizziness	64 (20.8%)	1.72±0.45	1.61±0.49	2.25±0.47
S23	Difficulty swallowing	26 (8.4%)	1.88±0.33	1.69±0.47	2.62±0.50
S24	Irritability	87 (28.2%)	2.00±0.55	1.43±0.50	2.18±0.62
S25	Oral ulcers	28 (9.1%)	1.99±0.84	1.68±0.48	2.39±0.63
S26	Taste changes	135 (43.8%)	-	1.77±0.42	2.19±0.58
S27	Weight loss	90 (29.2%)	-	1.84±0.39	2.19±0.45
S28	Hair loss	62 (20.1%)	-	1.64±0.48	1.98±0.43
S29	Constipation	79 (25.6%)	-	1.82±0.45	2.18±0.55
S30	Swelling of arms or legs	33 (10.7%)	-	1.64±0.60	2.24±0.61
S31	Feeling that one's appearance has changed	67 (21.8%)	-	1.76±0.43	2.13±0.46
S32	Skin changes such as pigmentation	68 (22.1%)	-	1.84±0.37	2.28±0.57

Supplementary Table 2. ROC curves of various factors

Factor	AUC	Sensitivity	Specificity
Disease Duration	0.610	0.709	0.515
Depression	0.713	0.477	0.949
Pain	0.709	0.512	0.875
Fatigue	0.783	0.826	0.603
Diarrhea	0.584	0.337	0.824
Social Support	0.619	0.866	0.331
Physical Activity	0.688	0.750	0.625