Heliyon 9 (2023) e22407

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Symptom clusters and characteristics of cervical cancer patients receiving concurrent chemoradiotherapy: A cross-sectional study

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A R T I C L E I N F O

Keywords:
Cervical cancer
Concurrent chemotherapy
Symptom clusters
Influencing factors
Latent profile analysis

A B S T R A C T

Background: Cervical cancer patients have a high symptom burden during concurrent chemoradiotherapy (CCRT) and urgently need precise symptom management strategies. Nonetheless, the symptom profile and influencing factors are unclear.
Methods: A total of 234 patients with cervical cancer who underwent CCRT in a tertiary care hospital clinical oncology center in Guangxi Zhuang Autonomous Region from March 2022 to March 2023 were included in the study. The general information questionnaire, M.D. Anderson symptom inventory, Fatigue Scale-14, Pittsburgh Sleep Quality Index, and grip strength test were used for the investigation. Symptom clusters were extracted by exploratory factor analysis, and latent profile analysis was performed using Mplus 8.0 software. Multinomial logistic regression was used to explore the factors influencing the potential categories of symptom clusters.
Results: Exploratory factor analysis extracted four symptom clusters: a fatigue-related symptom cluster, a gastrointestinal-related symptom cluster, a mood-related symptom cluster, and a physical-related symptom cluster, of which the fatigue-related symptom cluster was more severe and was divided into three potential categories: low fatigue-good muscle fitness type (25.63%), general fatigue-moderate muscle fitness type (68.37%) and high fatigue-low muscle fitness type (6%). Multinomial logistic regression analysis showed that hemoglobin levels, tumor stage, absence of complications, and unemployment were factors influencing the fatigue-related symptom cluster in patients undergoing CCRT for cervical cancer.
Conclusions: Cervical cancer patients experience multiple symptom clusters during CCRT. Different characteristics appeared in different clusters. Among them, fatigue-related symptom clusters were more severe and heterogeneous. In clinical practice, we should pay attention to and use high symptom feature predictors, focusing on the core symptoms that play a dominant role, achieving early identification and management, and reducing patients' symptom burden.

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https://doi.org/10.1016/j.heliyon.2023.e22407
Received 1 June 2023; Received in revised form 8 November 2023; Accepted 10 November 2023
Available online 17 November 2023

1. Introduction

Cervical cancer is one of the most preventable cancers and the second leading cause of cancer-related death among women aged 20 to 39, according to the latest global cancer statistics (Cancer statistics, 2022), posing a significant global public health problem that seriously endangers women's health [1,2]. Concurrent chemoradiotherapy (CCRT), the standard treatment for locally advanced cervical cancer, not only plays a role in synergistic chemoradiotherapy but also improves overall patient survival. However, its toxic side effects and adverse reactions are increasingly prominent, leading to a cluster of symptoms that includes fatigue, sleep disorders, and decreased muscle strength, which exacerbate symptom burden and severely affect the physical and emotional status and quality of life of patients and may lead to treatment delays or discontinuation [3,4]. Therefore, the effective identification of symptom clusters in cervical cancer patients undergoing CCRT is a prerequisite and foundation for developing precise symptom management strategies, providing a basis for better symptom cluster management [5].

Previous studies have only systematically described the individual symptoms of cervical cancer, lacked in-depth analyses of factors related to symptom clusters from a holistic perspective, and paid less attention to the heterogeneity of specific symptom clusters among individuals, hindering the development and implementation of targeted intervention programs for symptom clusters and limiting intervention effectiveness. Although many studies have examined the relationships between symptom management and quality of life in patients with cervical cancer, the underlying mechanism of latent symptom cluster categories and the influencing factors are still unknown [6–8].

This study focused on symptom clusters in cervical cancer patients receiving CCRT. It aimed to identify their characteristics and explore the latent categories and factors influencing major symptom clusters, providing a scientific reference for developing precise symptom management strategies.

2. Methods

2.1. Study design, setting, and participants

A cross-sectional study was conducted from March 2022 to March 2023. Two hundred and thirty-four patients with cervical cancer who underwent CCRT in a tertiary care hospital clinical oncology center in China were selected as study subjects using a non-probability convenient sampling method. The inclusion criteria were (1) histopathologically diagnosed cervical cancer [9], (2) the use of CCRT treatment protocols, (3) patients at least 18 years old, (4) in stable condition and provided informed consent to participate in this study voluntarily, and (5) had some communication skills and could complete the questionnaire independently. The exclusion criteria were (1) patients with a history of psychiatric-related illness or communication disorders, (2) advanced cervical cancer with a malignant mass or other malignant tumors, (3) palliative care, (4) abandoned or discontinued CCRT treatment midway, or (5) missing ≥20% of the questionnaire responses. This study was carried out in compliance with the STROBE statement and the Declaration of Helsinki [10,11]. This study was approved by the Ethics Committee of the People's Hospital of Guangxi Zhuang Autonomous Region (Ethics Approval No. KY-ZC-2020-93). All participants provided signed informed consent.

2.2. Procedure

A specific survey team was established, and the team members were trained to unify the instructional language before the survey. The purpose and significance of this study were explained to patients in detail before the survey, and questionnaires were administered after obtaining informed consent from the study subjects. After the investigators collected and verified the questionnaires, if some items and omissions needed to be added, the study subjects were immediately asked to provide them. Two people checked data entry to eliminate logical errors in the questionnaires to ensure validity. A total of 240 questionnaires were distributed in this study, and 234 valid questionnaires were recovered, for a valid recovery rate of 97.5%.

2.3. Measures

2.3.1. General information questionnaire

The investigators developed the questionnaire by drawing on references [12,13]. It included demographic characteristics such as age, education level, marital status, monthly household income per capita, type of medical coverage, and disease-related information, such as pathological type, tumor stage, and complications.

2.3.2. M.D. Anderson symptom inventory (MDASI)

The original section of this scale consists of 19 items, divided into two parts [14]. The first part mainly assesses the patients' 13 common symptoms and their severity in the past 24 h, including pain, fatigue, nausea, sleep disturbance, distress, shortness of breath, forgetfulness, appetite, drowsiness, dry mouth, sadness, vomiting, and numbness, on a scale of 0–10, with higher scores indicating more severe symptoms. The second part assesses the impact of 13 symptoms on patients' daily life, including general activities, mood, work, relationship with others, walking, and enjoyment of life. The Chinese version of the MDASI has good reliability and validity and is suitable for assessing the symptom clusters of Chinese cancer patients [15].

2.3.3. Fatigue Scale-14 (FS-14)

The scale was developed by Trudie Chalder et al. [16] and modified by Morris to measure the severity of fatigue symptoms in individuals and provide a reference for assessing clinical outcomes [17]. The FS-14 contains a total of 2 dimensions and 14 entries. Eight of the items reflect physical fatigue, and 6 reflect mental fatigue. The maximum total score is 14, with higher scores indicating severe fatigue. The reliability of the scale is good, with a Cronbach's α coefficient of 0.88–0.90 and a Spearman-Brown coefficient of 0.86 [18].

2.3.4. Pittsburgh Sleep Quality Index (PSQI)

This scale is a self-reported scale developed by Buysse in 1989 to assess the subjective sleep quality of patients [19]. This scale comprises 19 items that evaluate 7 components (subscale scores range from 0 to 3): sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, the use of sleep medication, and daytime dysfunction. The sum of these 7 component scores yields one global score for subjective sleep quality (range, 0–21). The higher the score, the worse the quality of sleep. A total score of <7 is considered good sleep, and a total score of ≥ 7 indicates a sleep disorder. The assessment takes roughly 5–10 min to complete, has a diagnostic sensitivity of 89.6% and a specificity of 86.5%, and has been widely used in clinical practice and research [20]. The Chinese version of the PSQI has shown good reliability and validity in Chinese cancer patients, which is suitable for clinical sleep quality evaluation studies in China [21].

2.3.5. Grip strength test

This test was conducted using the EH101 electronic hand dynamometer manufactured by CAMRY Guangdong Xiangshan Weighing Equipment Co., Ltd. Before the test, the researcher informed the patient of its purpose, method, and precautions and demonstrated its use. The measurement method had the patient stand naturally in a quiet state, with their feet separated at shoulder width, the upper body straight, arms hanging naturally on both sides of the body, and avoiding the grip strength meter touching the body or clothing of the subject. The test was conducted with the subject's dominant hand. Precautions included the prohibition of arm swinging and squatting or contacting the grip meter with the body when exerting force. The participant was instructed to grip the grip strength meter with maximum force and hold it for 10 s or more to ensure a stable reading. The values were read and recorded by the researcher twice, with a short pause of 10 s between tests. The results were recorded in kilograms with one decimal point. Grip strength is the most commonly used index for assessing reduced muscle fitness, and grip strength tests are simple and convenient and can sensitively reflect changes in muscle fitness in individual skeletal muscles [22,23].

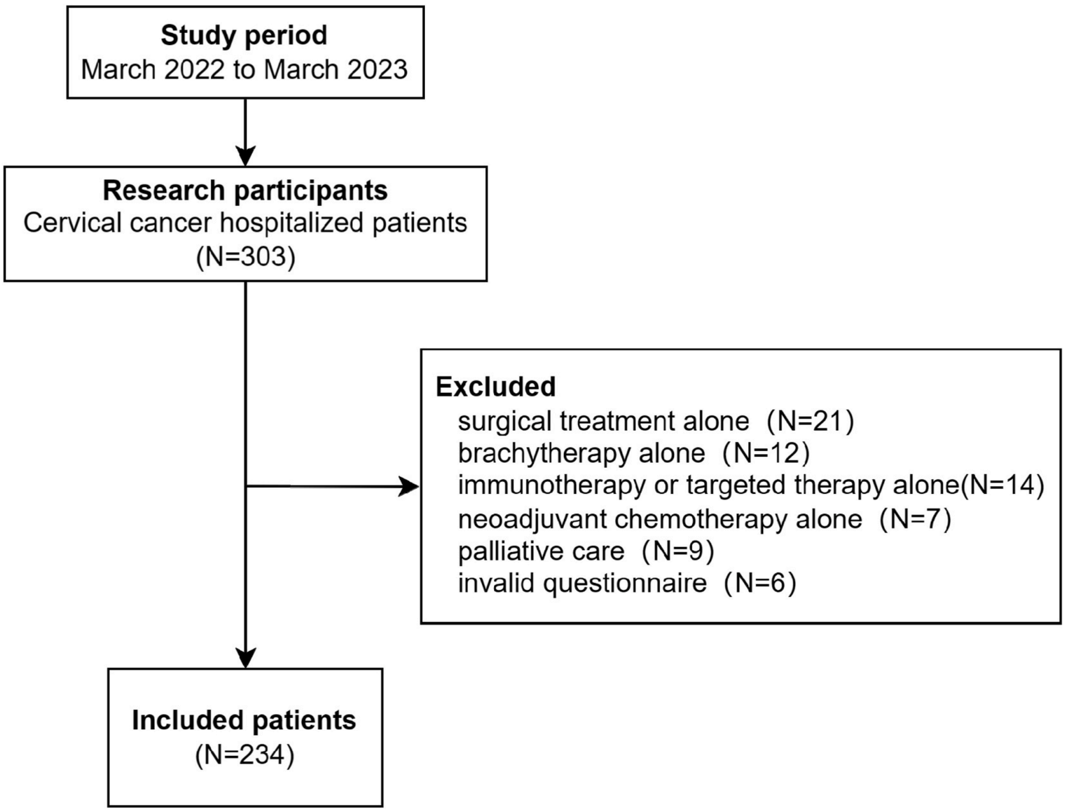

Fig. 1. Flowchart of patient selection.

2.4. Statistical analysis

Data analyses were performed using the Statistic Package for Social Science (IBM SPSS, version 26.0 for Windows, Armonk, NY, USA) and Mplus software (Muthén & Muthén, version 8.0). The results are presented as the mean ± standard deviation (SD) for continuous data and as counts for categorical data. Quantitative data were compared between groups using analysis of variance (ANOVA). The categorical data were compared between groups using the chi-squared test. Exploratory factor analysis was used to identify symptom cluster types, and factor extraction was performed by principal component analysis. Factor rotation was performed by the maximum variance method, and symptoms with factor eigenvalues ≥1 and factor loadings ≥0.4 were extracted to form symptom clusters. Mplus 8.0 software was used for latent profile analysis (LPA), starting with an initial model assuming only one category, gradually increasing the number of model categories until the best model fitness test index was reached, and selecting the optimal model according to the model evaluation index and fitness test. The model fit evaluation indicators included: (1) Akaike Information Criterion (AIC): the smaller the value, the better the model fit; (2) Bayesian Information Criterion (BIC): the smaller the value, the better the model fit; (3) the entropy index: the most sensitive indicator to judge the accuracy of model classification. The values ranged from 0 to 1. Values closer to 1 indicated more accurate model classification; (4) the Bootstrap-based Likelihood Ratio Test (BLRT) and LMR likelihood ratio test (Lo-Mendell-Rubin, LMR): comparing the fit differences of potential category models, if $P < 0.05$ indicates that the k-category model is better than the k-1 category model. Multinomial logistic regression analysis was performed with LPA latent category outcomes as the dependent variable and patient general information as the independent variable. All tests were two-sided, and the statistical significance level for all analyses was defined as $P < 0.05$.

3. Results

3.1. Participant characteristics

The patient selection flow is outlined in Fig. 1. A total of 234 patients undergoing CCRT for cervical cancer were included in this study. They were aged 27–79 (55.21 ± 10.62) years and had an average BMI of 22.71 ± 3.12 (kg/m^2). Patient ethnicity was Han in 117 (50%) patients, Zhuang in 100 (42.7%), and other ethnic groups in 17 (7.3%). Educational levels were below high school in 180 (76.9%), high school in 25 (10.7%), and college and above in 29 (12.4%). Three patients (1.3%) were unmarried, 216 (92.3%) were married, 3 (1.3%) were divorced, and 12 (5.1%) were widowed. Births: Five (2.1%) women had not given birth, 23 (9.8%) had one birth, 131 (56%) had 2 births, and 75 (32.1%) had 3 or more. Forty-one (17.5%) patients were unemployed, 70 (29.9%) were farmers, 25 (10.7%) were staff, 32 (13.7%) were self-employed, and the employment status of 66 (28.2%) was reported as other. The monthly household income per capita was <2000 RMB for 106 (45.3%) patients, 2000–3000 RMB for 98 (41.9%), 3000 RMB for 98 (41.9%), and >3000 RMB for 30 (12.8%). Regarding the medical insurance type, 129 (55.1%) had villagers' medical insurance, 69 (29.5%) had residents' medical insurance, 32 (13.7%) had staff's medical insurance, and 4 (1.7%) were self-payors. The primary caregivers of 79 (33.8%) patients were spouses, and other relatives were the primary caregivers for 155 (66.2%). The pathological type was squamous carcinoma in 183 (78.2%) patients and adenocarcinoma and others in 51 (21.8%). The tumor stage was Ia1-IIa2 in 89 (38%) patients, stage IIb in 36 (15.4%), and stage IIIa-IIIc2 in 109 (46.6%). Forty-two (17.9%) patients had no complications, and 192 (82.1%) had complications.

Table 1
The severity and prevalence of symptoms and interference (N = 234).

Symptom	Prevalence n (%)	Severity mean ± SD
Fatigue	228 (97.44)	4.75 ± 1.68
Disturbed sleep	216 (92.31)	4.10 ± 1.71
Lack of appetite	205 (87.61)	3.82 ± 1.91
Sadness	201 (85.90)	3.71 ± 1.83
Distress	195 (83.33)	3.61 ± 1.89
Nausea	214 (91.45)	3.54 ± 1.58
Vomiting	204 (87.18)	3.49 ± 1.66
Pain	166 (70.94)	3.19 ± 2.74
Forgetfulness	185 (79.06)	2.69 ± 1.85
Drowsiness	177 (75.64)	2.07 ± 1.48
Dry mouth	162 (69.23)	1.67 ± 1.27
Numbness	131 (55.98)	1.18 ± 1.18
Shortness of breath	162 (69.23)	1.12 ± 0.96
Interference		
Work	208 (88.89)	4.71 ± 1.92
Mood	206 (88.03)	3.88 ± 1.65
Enjoyment of life	204 (87.18)	3.47 ± 1.71
General activity	190 (81.20)	3.22 ± 1.91
Relationships with others	185 (79.06)	2.97 ± 1.77
Walking	185 (79.06)	2.69 ± 1.85

SD, standard deviation.

3.2. Symptom prevalence, severity, and interference

The patients with cervical cancer in this study had 4–13 symptoms, with an average of 10.46 symptoms. The top 5 symptoms were fatigue, sleep disturbance, nausea, loss of appetite, and vomiting. The top 5 symptoms with more serious severity scores were fatigue, sleep disturbance, loss of appetite, sadness, and distress (Table 1). The incidence of each symptom in the daily life of cervical cancer patients was 79.06–88.89%, among which disturbances of work, emotion, and life pleasure were greater, with high severity (Table 1).

3.3. Exploratory factor analysis of symptom clusters

Thirteen symptoms with a single symptom incidence of ≥20% were identified using the inclusion criteria for symptom cluster analysis in previous studies and were subjected to factor analysis [24]. Symptoms with factor eigenvalues ≥1 and factor loadings ≥0.4 were extracted to form symptom clusters. The test of applicability (KMO = 0.763) and Bartlett's sphericity test (approximate $\chi^2 =$ 3498.739; $P = 0.000$) indicated the suitability for exploratory factor analysis. The principal component analysis combined with the maximum variance method was used for factor extraction and rotation. The factor loading matrix after rotation is shown in Table 2. The results showed that four factors were extracted, with a cumulative variance contribution of 83.71%. In this study, we combined the principles of factor extraction and professional knowledge to name each common factor. Factor 1 was called the fatigue-related symptom cluster; factor 2 was the gastrointestinal-related symptom cluster; factor 3 was the mood-related symptom cluster; and factor 4 was the physical-related symptom cluster. Cronbach's α coefficients were 0.758, 0.946, 0.978, and 0.916, respectively.

3.4. Latent profile analysis of fatigue-related symptom clusters

3.4.1. Latent class model fitting and ranking

A total of 1–5 potential category models were fitted in this study. The fit indices are shown in Table 3. AIC, BIC, and aBIC decreased continuously as the number of potential categories increased. When the number of categories was 3, the entropy value was 0.932, and the P-values of LMR and BLRT were statistically significant ($P < 0.05$). When the number of categories was 4, the entropy value was 0.883, and the LMR P-value was not statistically significant ($P > 0.05$). Therefore, 3 categories were selected as the best potential profile model by combining each model fit evaluation index. The probability that patients in each category belonged to each potential category was 0.989, 0.965, and 0.854, respectively, indicating that the potential profile models for the 3 categories were reliable. The potential profiles were plotted according to the classification results (Fig. 2). Fourteen patients (6%) in group C1 had higher fatigue symptoms than the other two groups, and the grip strength was lower, indicating a low level of muscle fitness, so this group was designated as "high fatigue-low muscle fitness." One hundred and sixty patients (68.37%) in group C2 were called the "general fatigue-moderate muscle fitness" group because the overall fatigue and grip strength of the patients in this category were moderate. Sixty patients (25.63%) in group C3 had lower fatigue symptoms than the other two groups, and the grip strength was relatively high, indicating a good level of muscle fitness. Therefore, group C3 was named the "low fatigue-good muscle fitness type".

3.4.2. Univariate analysis of different potential categories of fatigue-related symptom clusters

The differences in the 3 latent categories of fatigue-related symptom clusters in patients with cervical cancer were statistically significant ($P < 0.05$) for age, hemoglobin level, white blood cell count, occupation, tumor stage, and complications. The results are shown in Table 4.

3.4.3. Multinomial logistic regression analysis of different potential categories of fatigue-related symptom clusters

A multivariable logistic regression analysis was conducted using the 3 potential categories of fatigue-related symptom clusters in cervical cancer patients as the dependent variable and indicators with P-values of <0.05 in the univariate analysis as independent variables, with the low fatigue-good muscle fitness type serving as the reference group. The results indicated that hemoglobin levels, tumor stage, absence of complications, and unemployment were significant factors influencing different potential categories of fatigue-

Table 2
Exploratory factor analysis of symptom clusters (N = 234).

Symptom	Factor 1	Factor 2	Factor 3	Factor 4
Fatigue	0.782			
Disturbed sleep	0.857			
Pain	0.812			
Nausea		0.934		
Vomiting		0.942		
Lack of appetite		0.909		
Sadness			0.969	
Distress			0.960	
Shortness of breath				0.900
Forgetfulness				0.897
Drowsiness				0.889
Dry mouth				0.906
Numbness				0.679

Table 3
Model fit indices for different latent categories (N = 234).

Model	K	AIC	BIC	aBIC	LMR	BLRT	Entropy	Category Probability
C1	6	3298.989	3319.721	3300.704	–	–	–	–
C2	10	3160.264	3194.817	3163.121	0.000	0.000	0.891	0.274/0.726
C3	14	3113.265	3161.640	3117.266	0.046	0.000	0.932	0.684/0.256/0.06
C4	18	3104.210	3166.406	3109.354	0.156	0.000	0.883	0.256/0.034/0.598/0.112
C5	22	3075.654	3151.671	3081.941	0.001	0.000	0.932	0.171/0.111/0.111/0.034/0.573

K, model-free parameters.

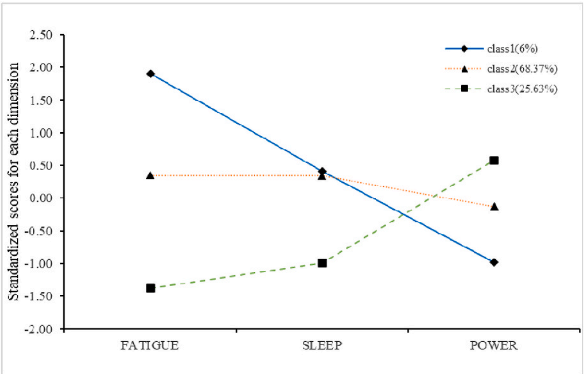

Fig. 2. Characteristics of 3 latent categories of fatigue-related symptom clusters.

related symptom clusters in cervical cancer patients ($P < 0.05$; Table 5).

4. Discussion

4.1. High burden of symptom clusters in patients treated with concurrent chemotherapy for cervical cancer

The results of this study showed that patients with cervical cancer had 4 to 13 co-existing symptoms during CCRT, with an average of 10.46 symptoms. Among them, fatigue had the highest incidence and severity, consistent with the findings of Zhang et al. [5]. The reason for this finding is that simultaneous radiotherapy and chemotherapy treatments tend to superimpose the adverse effects of radiotherapy and the toxic side effects of chemotherapy drugs, causing a decrease in serum potassium and white blood cell counts. In addition, treatment-related myelosuppression may cause a decrease in the immune level of the patient, and many factors, such as sleep disturbances, decreased appetite, psychological stress, and negative emotions, may aggravate the patient's fatigue. In this study, a total of 4 symptom clusters were extracted by exploratory factor analysis, namely the fatigue-related symptom cluster, the gastrointestinal-related symptom cluster, the mood-related symptom cluster, and the physical-related symptom cluster, mostly consistent with the findings of Wang et al. [25], with differences in the naming of symptom clusters and symptom composition. These differences may be due to differences in disease severity, treatment assessment methods, and statistical analysis methods. A systematic review by Harris et al. [26] also showed that symptom cluster studies were prone to differences in naming, differentiation, inclusion, and the number of symptoms, depending on symptom assessment tools, symptom parameters measured, and statistical methods of grouping symptom clusters and study subjects. The incidence and severity of fatigue-related symptom clusters in this study were higher than those of other symptom clusters, which increases the symptom burden of patients and deserves urgent attention, consistent with the results of related domestic and international studies [27,28]. Currently, most studies only focus on single-symptom management, and symptom cluster management in cervical cancer is still at the preliminary exploration stage. Thus, clinical work should focus on the core symptoms that play a dominant role, develop targeted intervention care plans based on the characteristics of the dominant symptoms, integrate the advantages of various intervention models, continuously innovate symptom cluster management strategies based on the best evidence, and vigorously carry out relevant, high-quality randomized controlled trials to improve the quality of life of cervical cancer patients.

4.2. Different latent categories of fatigue-related symptom clusters in cervical cancer patients with different characteristics

This study classified the fatigue-related symptom clusters of cervical cancer patients into three latent categories based on latent profile analysis. There were 14 (6%) high fatigue-low muscle fitness type patients, 160 (68.37%) general fatigue-moderate muscle fitness type, and 60 (25.63%) low fatigue-good muscle fitness type, with group heterogeneity in each latent category. Patients with the low fatigue-good muscle fitness type of cervical cancer had low fatigue, good sleep quality, good muscle fitness, and low symptom

Table 4
Univariate analysis of potential categories of fatigue-related symptom clusters (N = 234).

Items	Class1 (n = 14)	Class2 (n = 160)	Class3 (n = 60)	χ^2/F	*P*
Age (years, $\bar{x} \pm s$)	65.86 ± 14.16	56.03 ± 9.71	50.52 ± 9.79	14.982	0.000
BMI ($\bar{x} \pm s$)	21.68 ± 1.93	22.81 ± 3.07	22.70 ± 3.35	0.839	0.433
Hemoglobin (g/L, $\bar{x} \pm s$)	98.86 ± 13.03	103.06 ± 12.08	113.33 ± 11.57	17.960	0.000
White blood cell count ($\times 10^9$/L, $\bar{x} \pm s$)	3.01 ± 1.13	3.14 ± 0.54	3.41 ± 0.42	5.935	0.003
Education level [n (%)]				8.232	0.083
Below high school	13 (92.9)	128 (80)	39 (65)		
High school	0	16 (10)	9 (15)		
College and above	1 (7.1)	16 (10)	12 (20)		
Marital Status [n (%)]				11.302	0.079
Unmarried	1 (7.1)	1 (0.6)	1 (1.7)		
Married	12 (85.8)	147 (91.9)	57 (95)		
Divorce	0	1 (0.6)	2 (3.3)		
Widowed	1 (7.1)	11 (6.9)	0		
Births [n (%)]				6.627	0.357
None	1 (7.1)	3 (1.9)	1 (1.7)		
One	0	15 (9.4)	8 (13.3)		
Two	7 (50)	87 (54.4)	37 (61.7)		
Three or more	6 (42.9)	55 (34.4)	14 (23.3)		
Occupation [n (%)]				24.820	0.000
Farmer	1 (7.1)	49 (30.6)	20 (33.4)		
Self-employed	1 (7.1)	17 (10.6)	14 (23.3)		
Staff	0	14 (8.8)	11 (18.3)		
Unemployed	8 (57.2)	29 (18.1)	4 (6.7)		
Other	4 (28.6)	51 (31.9)	11 (18.3)		
Monthly household income per capita [n (%)]				7.590	0.108
< 2000 RMB	3 (21.4)	77 (48.1)	26 (43.3)		
2000–3000 RMB	9 (64.3)	67 (41.9)	22 (36.7)		
> 3000 RMB	2 (14.3)	16 (10)	12 (20)		
Medical insurance type [n (%)]				8.451	0.207
Villagers' medical insurance	8 (57.2)	94 (58.8)	27 (45)		
Residents' medical insurance	3 (21.4)	45 (28.1)	21 (35)		
Staff's medical insurance	2 (14.3)	18 (11.3)	12 (20)		
Self-payor	1 (7.1)	3 (1.9)	0		
Primary caregiver [n (%)]				2.110	0.348
Spouses	3 (21.4)	52 (32.5)	24 (40)		
Other relatives	11 (78.6)	108 (67.5)	36 (60)		
Pathological type [n (%)]				3.383	0.184
Squamous carcinoma	12 (85.7)	129 (80.6)	42 (70)		
Adenocarcinoma and others	2 (14.3)	31 (19.4)	18 (30)		
Tumor stage [n (%)]				81.990	0.000
I—IIa2	2 (14.3)	35 (21.8)	52 (86.7)		
IIb	4 (28.6)	30 (18.8)	2 (3.3)		
IIIa-IIIc2	8 (57.1)	95 (59.4)	6 (10)		
Complications [n (%)]				76.074	0.000
Yes	12 (85.7)	153 (95.6)	27 (45)		
No	2 (14.3)	7 (4.4)	33 (55)		

Table 5
Multinomial logistic regression analysis of potential categories of fatigue-related symptom clusters (N = 234).

Items	High fatigue-poor muscle.				General fatigue-moderate muscle			
	β	P	OR	95%CI	β	P	OR	95%CI
Age	1.217	0.243	3.377	0.439–25.998	0.106	0.869	1.111	0.318–3.881
Hemoglobin level	−1.344	0.035	0.261	0.075–0.909	−0.493	0.207	0.611	0.284–1.314
White blood cell count	−0.944	0.077	0.389	0.137–1.108	−0.554	0.121	0.575	0.285–1.158
Tumor stage	2.089	< 0.001	8.077	2.555–25.531	1.403	< 0.001	4.069	2.269–7.298
No complications	−0.033	0.981	0.968	0.067–14.043	−2.128	0.001	0.119	0.036–0.396
Unemployed	17.376	< 0.001	7.27	5.653–8.714	1.546	0.128	4.691	0.641–34.339

distress. Most patients with the average fatigue-medium muscle fitness type of cervical cancer had moderate fatigue and average sleep quality. They needed targeted care measures to improve their muscle fitness further. Patients with the high fatigue-low muscle fitness type of cervical cancer had higher fatigue levels, poor sleep quality, and low muscle fitness, consistent with the findings of other scholars in China [29], and urgently need focused attention. These findings may be due to the clustering of fatigue, sleep, and grip strength symptoms, which affect each other and tend to exert a synergistic superposition effect and increase patients' symptom burden

[30]. Lee et al. [31] found that patients with cervical cancer had severe loss of skeletal muscle volume and mass during the treatment phase and often showed pathological and physiological changes, mainly characterized by decreased muscle volume and muscle contraction, weight loss, and frailty. Muscle strength is an independent predictor of progression-free survival and overall survival in patients with cervical cancer, as well as a significant predictor for evaluating the toxicity of radiation therapy and chemotherapy, suggesting that attention should be paid to grip strength and related functional changes in patients with cervical cancer to identify potential risks of treatment at an early stage. Therefore, precise symptom cluster management plans should be adopted for different latent categories of the fatigue-related symptom clusters of cervical cancer patients. Personalized nursing intervention plans should be implemented for the general fatigue-moderate muscle fitness type and high fatigue-low muscle fitness types of cervical cancer patients, taking symptom clusters as the smallest nursing unit and fully utilizing the advantages of symptom cluster management to boost its effect.

4.3. Factors influencing latent categories of fatigue-related symptom clusters in patients with cervical cancer

The results of this study showed that hemoglobin levels are an essential risk factor and risk indicator for fatigue-related symptom clusters in cervical cancer patients, suggesting that the lower the hemoglobin level, the greater the probability of being the high fatigue-low muscle adaptability type, similar to the results of Xu et al. [32]. The reason for this is that while radiotherapy reduces the volume of tumor lesions and improves the therapeutic effect, the adverse effects of the treatment become more prominent and, when coupled with platinum-based chemotherapy, can cause hematologic toxicity. A decline in hemoglobin levels due to anemia is a high-incidence symptom in patients with cervical cancer undergoing simultaneous radiotherapy and chemotherapy. These physiological events decrease the patient's immunity, aggravate fatigue and sleep disorders, and reduce muscle fitness. Previous studies showed [33] that the degree of fatigue in cancer patients receiving chemotherapy was negatively correlated with hemoglobin levels, which, to a certain extent, reflects the trend of dynamic changes in the internal environment of the patient during treatment, indicating the correlation between the occurrence and development of fatigue and blood indices. Thus, serum biomarkers can predict the occurrence and development of fatigue-related symptom clusters. The findings suggest that different potential categories of fatigue-related symptom clusters in cervical cancer patients can be dynamically assessed in clinical nursing practice by the real-time monitoring of hematological indicators, using hemoglobin levels as a predictor to help identify and manage fatigue-related symptom clusters.

The results of this study showed that tumor stage was an early warning factor for fatigue-related symptom clusters in patients with cervical cancer, suggesting that the later the tumor stage, the higher the probability of being the high-fatigue-low-muscle-adaptation type, consistent with the findings of Stanca et al. [6]. The reason for this finding is that the later the tumor stage is, the greater the depth and scope of infiltration of cervical cancer, and the easier it is to involve neighboring organs, accompanied by metastasis to local or distant lymph nodes. Tumor staging reflects the degree of progression of the primary tumor and is an essential indicator for evaluating tumor invasion and the prognosis of cervical cancer patients [34]. Patients with later tumor stages have rapid disease progression and multiple complications, experience intense symptoms and high psychological pressure, and are prone to self-regulation and cognitive fatigue. They also have more worries and fears about disease treatment and prognosis, which makes their symptom burden heavier and reduces their quality of life [9]. Therefore, clinical nursing workers are prompted to focus on patients with middle and advanced cervical cancer in the process of symptom management; assess, identify, and manage symptom clusters on time, and formulate targeted symptom cluster management measures and nursing care plans according to the patient's individualized situation to reduce their symptom burden.

The findings of this study showed that the absence of complications was a protective factor for fatigue-related symptom clusters in patients with cervical cancer, suggesting that patients with an absence of complications had a higher probability of being low fatigue-good muscle fitness type. Due to the uncertain effect of changing the radiotherapy dose gradient on the absorbed dose in the bladder and rectum and the exceptional location of the bladder and rectum about the clinical target area, complications such as radiation proctitis, radiation cystitis, radiation dermatitis, and bone marrow suppression commonly occur in patients with cervical cancer [35]. In addition, platinum-based chemotherapeutic drugs are mainly metabolized by the liver and kidney organs, which can cause liver and kidney function damage to patients and increase symptom burden. Studies showed that the incidence of complications related to cervical cancer patients during treatment reached 48.08%, among which myelosuppression, acute gastrointestinal reactions (nausea, vomiting, and loss of appetite), and radiation proctitis all aggravated patients' subjective fatigue to varying degrees [36]. In addition, radiotherapy-related complications are often accompanied by a sustained inflammatory response, which indirectly affects patients' sleep, pain, anxiety, and other discomfort symptoms [37]. Therefore, clinical workers care for radiotherapy-related complications during the treatment of cervical cancer patients, focusing on patients' existing or potential risk symptoms, especially diet, nutrition, and sleep status. Patients should be closely monitored for routine blood and inflammatory factor indicators. Infection should be prevented and controlled from various aspects, such as intravenous lines, skin mucosa, and diet.

The study showed that unemployment was a risk factor for fatigue-related symptom clusters in cervical cancer patients, suggesting that lacking stable income increased the probability of being categorized as the high fatigue-low muscle fitness type, consistent with the findings of Smith et al. [38]. The reason for this is that the disease itself and the adverse effects of treatment tend to aggravate the psychological pressure of patients, coupled with the lack of stable economic support and security due to joblessness. Economic pressure creates a sense of shame and low self-esteem, which makes the treatment effect unsatisfactory. Previous studies showed that clinical treatment decisions and options overwhelmingly depended on the patient's financial status and subjective wishes [39]. As the cost of treatment far exceeds the patient's monthly income, patients have limited treatment options, considering their financial status. Adequate medical insurance conditions can alleviate the economic burden of patients to a certain extent, reducing the economic toxicity of cancer. Therefore, patients' occupational status and economic level should be evaluated, with emphasis on those who are jobless and in poor economic conditions, coordinating and communicating with relevant departments, seeking appropriate support and preferential policies, assisting patients in applying for medical insurance reimbursement, and giving them specific support and assistance to reduce their economic burden and psychological fatigue.

4.4. Limitations

It is important to note that this study was conducted as a cross-sectional study in only one tertiary hospital in Guangxi Province, resulting in a small sample size and potential selection bias. Furthermore, the study was limited by its cross-sectional design, precluding the determination of causal relationships between factors. Future research should aim to expand the sample size and include more potential influencing factors. Multi-center, large-scale longitudinal studies should be conducted to explore the longitudinal changes in symptom clusters during CCRT in cervical cancer patients, further validate and refine the conclusions of this study, comprehensively analyze the risk factors and potential influencing mechanisms of symptom clusters, and develop comprehensive intervention plans for symptom cluster management in cervical cancer patients based on evidence, to minimizing symptom burden and optimizing quality of life.

5. Conclusions

Patients undergoing concurrent chemoradiotherapy for cervical cancer experience multiple symptoms that are interrelated and interactive, often in the form of symptom clusters. Four symptom clusters were explored in this study: the fatigue-related symptom cluster, the gastrointestinal-related symptom cluster, the mood-related symptom cluster, and the physical-related symptom cluster. Among them, the fatigue-related symptom clusters had a higher incidence and severity and group heterogeneity, with different characteristics among different categories. Three potential categories could be classified according to symptom characteristics: the low fatigue-good muscle fitness type, general fatigue-moderate muscle fitness type, and high fatigue-low muscle fitness type. Different latent categories were influenced by factors such as age, hemoglobin level, white blood cell count, occupation, tumor stage, and complications. Therefore, clinical nursing workers should identify and manage different latent categories of fatigue-related symptom clusters in cervical cancer patients, focusing on the predictors and risk factors for the development of symptom clusters and better formulate precise nursing intervention plans to reduce the burden of symptom clusters and improve the quality of life of patients.

Ethical approval

Written informed consent was obtained from all participants.

Funding

No external funding

Data availability statement

The data that support the findings of this study are available on request from the corresponding author.

CRediT authorship contribution statement

Hao Tie: Conceptualization, Formal analysis, Investigation, Methodology, Software, Writing – original draft, Writing – review & editing. **Limei Shi:** Investigation, Methodology. **Li Wang:** Conceptualization, Data curation, Formal analysis. **Xinyu Hao:** Formal analysis, Investigation. **Hongyan Fang:** Data curation, Investigation. **Lirong Li:** Conceptualization, Methodology, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The study expresses its sincerest gratitude to all those who participated in the questionnaire. In addition, we highly appreciate Dr. Kong's dedicated guidance for this study.

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