



## Original Article

# Symptom profiles and related factors among patients with advanced cancer: A latent profile analysis



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## ABSTRACT

**Objective:** This study aimed to investigate symptom subgroups and associated influencing factors in patients with advanced cancer.

**Methods:** A cross-sectional study was conducted, involving 416 patients with advanced cancer. The study examined five symptoms: fatigue, pain, sleep impairment, anxiety, and depression. Latent Profile Analysis (LPA) was utilized to classify symptom subgroups. A multiple logistic regression analysis was conducted to explore factors associated with the identified symptom subgroups.

**Results:** The analysis revealed three distinct subgroups among the participants: "all low" (58.2%), characterized by normal symptoms except for moderate sleep quality; "all moderate" (35.1%), exhibiting normal symptoms except for poor sleep quality and fatigue; and "all high" (6.7%), experiencing normal pain, moderate depression, moderate anxiety, poor sleep quality, and fatigue. Malnutrition risk, cancer diagnosis, and cancer survivorship duration were found to be associated with a more severe symptom burden.

**Conclusions:** Patients in the "all high" subgroup faced an increased risk of malnutrition and a longer cancer survivorship duration. Additionally, patients in the "all moderate" subgroup were distinguished by having a breast cancer diagnosis. These findings have significant implications for allocating medical resources and implementing person-centered symptom management strategies.

## Introduction

Global cancer statistics indicate that approximately 20 million new total cancer cases are diagnosed per year.<sup>1</sup> More than half of newly diagnosed cancers are at an advanced stage.<sup>2</sup> Numerous reports indicate that patients with advanced cancer experience various symptoms due to treatment in addition to the cancer itself.<sup>3,4</sup> Patients with advanced cancer have reported fatigue (72%), pain (67%), sleep impairment (45%), anxiety (30%), and depression (35%).<sup>5</sup> Symptoms in patients with advanced cancer were related to higher mortality, a longer length of hospital stay, an increased readmission rate, lower quality of life, and a lower ability to participate in activities of daily living<sup>6-8</sup>. The overall survival of advanced cancer patients with low symptom occurrence was more than three times that of those with high symptom occurrence.<sup>9</sup>

A systematic review of 33 studies revealed that symptoms in patients with advanced cancer often co-occur and are correlative.<sup>10</sup> Much work

was performed on exploring the underlying relationships among symptoms and determining the number and type of symptom clusters for patients with advanced cancer.<sup>10,11</sup> Dong et al. formed four symptom clusters based on 1562 advanced cancer patients.<sup>12</sup> Barata et al. identified three symptom clusters based on 318 patients with advanced cancer.<sup>13</sup> However, in the last few years, increasing evidence has shown that the symptom in patients of different sociodemographic and clinical characteristics varies greatly.<sup>14,15</sup>

A person-centered analysis approach can help identify the association between interindividual variability and symptoms. Latent Profile Analysis (LPA) is a person-centered approach that can help classify participants based on different symptom response patterns in order to identify participant heterogeneity.<sup>16,17</sup> This method can identify subgroups with various symptom burdens and can be beneficial for exploring the differences between subgroups in terms of sociodemographic and clinical variables. In addition, interventions developed based on the characteristics of different

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subgroups will contribute to the implementation of patient-centered precision nursing.<sup>18</sup>

Existing studies using LPA have focused on cancer patients, newly diagnosed patients, older patients, adolescent patients, and Chinese-American patients, with only a few focusing on patients with advanced disease<sup>19–24</sup>. One study by Mosher et al. evaluated the relationship between acceptance and commitment therapy constructs and the symptom profiles of advanced cancer patients based on LPA.<sup>25</sup> However, this study did not focus on the relationship between interindividual variability and symptoms. Besides, unlike this study, in addition to patients with stage IV cancer, we recruited patients with stage III cancer. Patients with stages III or IV face similar and severe symptoms, which can better represent advanced cancer.<sup>26</sup> Therefore, we aimed to identify symptom subgroups in patients with advanced cancer and explore the sociodemographic and clinical factors associated with different subgroups.

## Methods

### Study design

This study used a cross-sectional design. Participants were recruited from the cancer treatment center of a tertiary hospital in China between January and December 2022.

### Participants

The participants were identified according to the inclusion and exclusion criteria. Participants were included if they (1) were over 18 years old; (2) were diagnosed with stage III or IV cancer; (3) were receiving cycle therapy, refer to the treatments that were repeated every several weeks; (4) were in an intermittent period, referring to the period between two repeated treatments; and (5) provided informed consent. Besides, participants were excluded if they (1) were unable to communicate due to self-reported hearing impairment or loss of voice; (2) were diagnosed with dementia; and (3) were receiving palliative care at the end of life.

### Measurements

#### (1) Numerical Rating Scale for pain intensity

The Numerical Rating Scale (NRS) was used to evaluate pain intensity in cancer patients.<sup>27</sup> The total score was 10. A higher total score indicated more severe pain intensity. Those who scored 1 to 3 had mild pain, 4 to 6 had moderate pain, 7 to 9 had severe pain, and 10 had very severe pain. NRS revealed high discriminatory capability in distinguishing between background and peak pain intensity, with 14% of patients giving inconsistent evaluations. Besides, NRS showed high reproducibility when measuring different pain intensities for a second time three to 4 h later. (Cohen's K of 0.80 to 0.86).<sup>28</sup>

#### (2) Cancer Fatigue Scale

The Cancer Fatigue Scale (CFS), developed by Okuyama, was used to evaluate fatigue in patients.<sup>29</sup> It comprises 15 items classified into physical, affective, and cognitive subscales. Each item is rated on a 5-point Likert scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, 4 = very much) with a total score of 60. The higher the total score, the more severe the fatigue. Those who scored greater than 18 had symptoms of fatigue. Cronbach's  $\alpha$  was 0.88 in the original research<sup>29</sup> and 0.86 in this study.

#### (3) Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) scale, developed by Buysse, has been widely applied to cancer patients to evaluate sleep quality.<sup>30,31</sup> It consists of 7 subscales, including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping

medications, and daytime dysfunction. Each subscale is scored from 0 to 3, with a total score of 21. A lower total score indicated better sleep quality. Those who scored 0 to 2, 3 to 7, and 8 or higher had good, moderate, and poor sleep quality, respectively. Cronbach's  $\alpha$  was 0.83 in the original research<sup>30</sup> and 0.82 in this study.

#### (4) Hospital Anxiety and Depression Scale

The Hospital Anxiety and Depression Scale (HADS) was developed by Zigmond and used to evaluate anxiety (HADS-A) and depression (HADS-D) status.<sup>32</sup> The HADS can help identify anxiety and depression in cancer

**Table 1**  
Characteristics of participants (N = 416).

Variables	n (%)
Age (years), Mean $\pm$ SD (range)	62.02 $\pm$ 12.08 (20–88)
< 40	31 (7.5)
41–64	184 (44.2)
65–80	187 (45.0)
$\geq$ 81	14 (3.4)
Gender	
Male	212 (51.0)
Female	204 (49.0)
Educational level	
Primary school, or lower	46 (11.1)
Junior high school	118 (28.4)
Senior high school	92 (22.1)
Associate or higher	160 (38.5)
Marital status	
Married	371 (89.2)
Single	45 (10.8)
Resident category	
Urban	350 (84.1)
Rural	66 (15.9)
Resident mode	
Live alone	30 (7.2)
Live with others	386 (92.8)
Family monthly income per capita (yuan)	
< 3000	58 (13.9)
$\geq$ 3000, < 6000	163 (39.2)
$\geq$ 6000, < 10,000	121 (29.1)
$\geq$ 10,000	74 (17.8)
Body mass index (kg/m <sup>2</sup> )	
Underweight (< 18.5)	33 (7.9)
Normal ( $\geq$ 18.5, < 24.0)	225 (54.1)
Overweight ( $\geq$ 24.0, < 28.0)	129 (31.0)
Obesity ( $\geq$ 28.0)	29 (7.0)
Major payment source for medical services	
Insurance	403 (96.9)
Self-payment	13 (3.1)
Malnutrition risk	
Increased	33 (7.9)
Low	383 (92.1)
Cancer type	
Gastrointestinal cancer	127 (30.5)
Lung cancer	138 (33.2)
Breast cancer	61 (14.7)
Urinary cancer	25 (6.0)
Gynecologic cancer	7 (1.7)
Otherwise	58 (13.9)
Cancer survivorships duration (year), Median (IQR)	2 (1–3)
Previous cancer therapy <sup>a</sup>	
Surgery	215 (51.7)
Radiotherapy	102 (24.5)
Chemotherapy	353 (84.9)
Otherwise	39 (9.4)
Comorbidities <sup>a</sup>	
Hypertension	137 (32.9)
Diabetes	74 (17.8)
Cardiovascular disease	57 (13.7)
Kidney disease	13 (3.1)
Liver diseases	22 (5.3)
Otherwise	23 (5.5)
No comorbidities	212 (51.0)

SD: standard deviation, IQR: interquartile range.

<sup>a</sup> More than one answer is possible.

patients.<sup>33</sup> It consists of 14 items classified into anxiety and depression subscales. Each item was scored on a 4-point Likert scale, with a total score of 21 for HADS-A and HADS-D. A higher total score indicated a more severe status. Those who scored 0 to 7 had no symptoms, 8 to 10 had mild symptoms, 11 to 14 had moderate symptoms, and 15 had severe symptoms. The Cronbach's  $\alpha$  of HADS-A was 0.68 to 0.93 in the original research<sup>34</sup> and 0.71 in this study. And for HADS-D, the Cronbach's  $\alpha$  was 0.67 to 0.90 in the original research<sup>34</sup> and 0.84 in this study.

(5) Sociodemographic and clinical data questionnaire

The sociodemographic and clinical data questionnaire was designed based on previous studies. Sociodemographic data included gender, age, body mass index (BMI), marital status, educational level, resident category, resident mode, family monthly income per capita, and type of health insurance payment. Clinical data included cancer diagnosis, duration of cancer, therapy, complications, and malnutrition risk. Malnutrition risk was evaluated using nutrition risk screening (NRS 2002). This scale, developed by Kondrup, was used to evaluate the nutritional status of patients.<sup>35</sup> It consists of three components: undernutrition, disease severity, and age, with a total score of 7. A higher total score indicated a poorer nutritional status. Those who scored between 0 and 3 had a low risk of malnutrition, whereas the others had an increased risk.

Data collection

Our study employed a registered nurse in each of the three cancer treatment centers with more than 1-year experience as an evaluator to

collect the data. The employed registered nurses were considered research assistants. Unified training on the questionnaire and data collection was provided to the registered nurses by the researchers. Data were collected using questionnaires on the day of hospitalization. All questionnaires were completed based on self-assessments by patients, assisted by trained nurses.

Data analysis

LPA is an individual-centered algorithm that generates latent class variables to explain the relationship among observable continuous variables. The latent class variables were classified according to the score of observable continuous variables (the score of each symptom). Patients in the same latent class subgroup have similar symptom characteristics. Mplus version 8.0 (Muthen & Muthen, Los Angeles, CA, USA) was used for the LPA. All symptoms were used for LPA to classify patient subgroups. Model fitting started with one latent class and then increased the number of latent classes. Lower Akaike information criteria (AIC) and adjusted Bayesian information criteria (aBIC) indicate better model fitting. Meanwhile, an entropy of 0.8 or higher indicated good model fitting. The Lo-Mendell-Rubin likelihood ratio test (LMRT) and bootstrap likelihood ratio test (BLRT) were used to evaluate the fitting differences between the different latent class models. Statistical significance was set at  $P < 0.05$ . More importantly, the conceptual sense of each subgroup was the most critical factor to consider. Each symptom measurement was standardized into a 10-point questionnaire prior to the LPA to facilitate the interpretation of results.

Statistical Package for the Social Sciences (SPSS) (version 22.0; IBM, Armonk, NY, USA) was used to conduct data analyses. One-way analysis of

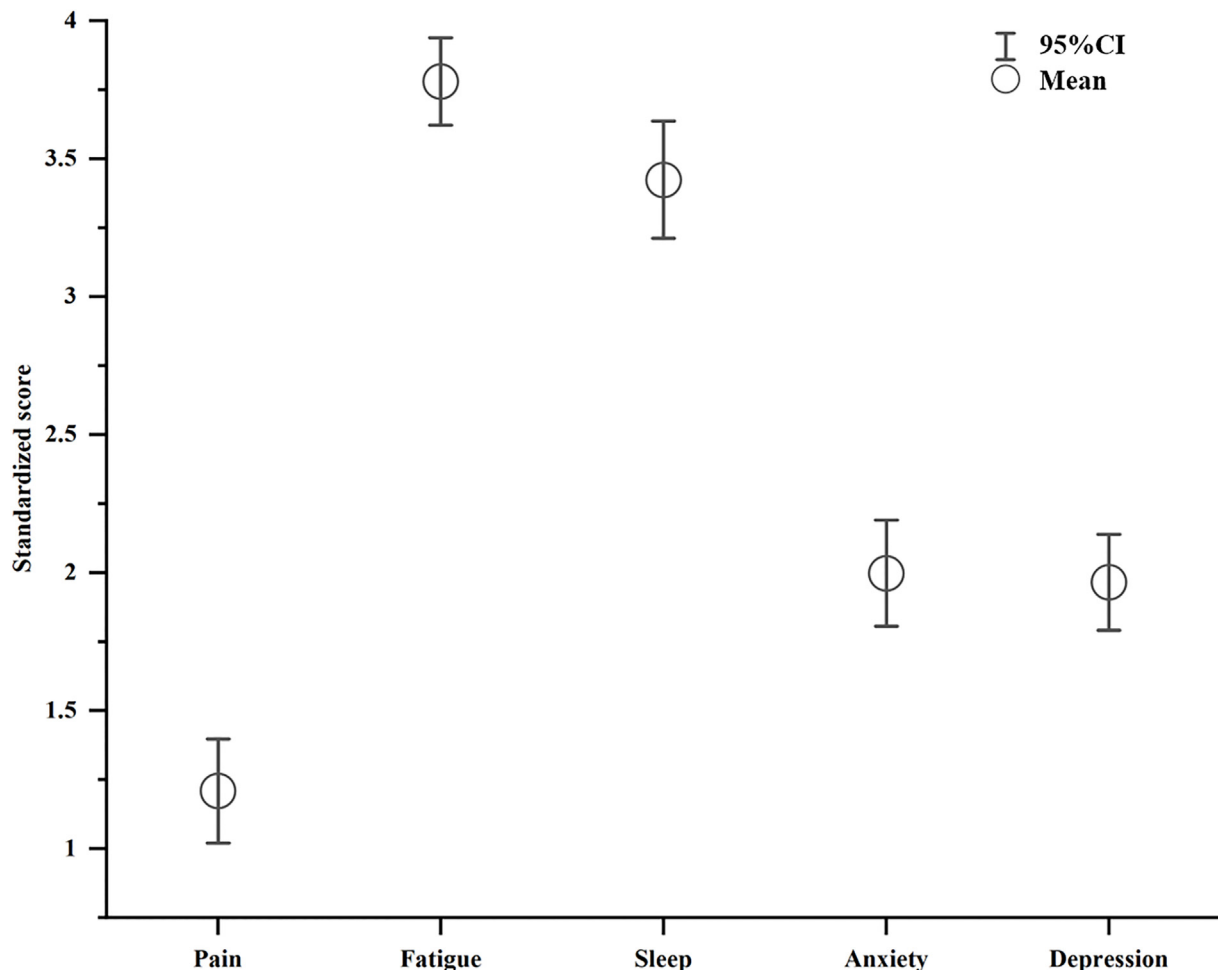


Fig. 1. Standardized symptom scores of participants.

**Table 2**  
Fit indices for latent class group of symptoms ( $N = 416$ ).

Classes	H0 likelihood value	AIC	aBIC	Entropy	LMRT P-value	BLRT P-value
1	-4295.202	8610.404	8618.978	-	-	-
2	-4054.381	8140.763	8154.481	0.838	0.089	< 0.001
3	-3981.621	8007.242	8026.105	0.832	0.166	< 0.001
4	-3916.644	7889.287	7913.295	0.878	0.172	< 0.001
5	-3870.149	7808.298	7837.451	0.876	0.242	< 0.001

AIC, Akaike information criterion; aBIC, sample size-adjusted Bayesian information criterion; LMRT, Lo-Mendell-Rubin adjusted likelihood ratio tests; BLRT, bootstrap likelihood ratio tests.

variance (ANOVA) or chi-square tests were used for univariate analyses. All variables with a  $P$ -value < 0.10 in univariate analyses were included in the multivariate analyses. A multiple logistic regression analysis was used to explore the influencing factors of latent groups, and a  $P$ -value < 0.05 as well as 95% confidence interval (CI) excluding 1 were considered significant. In addition, each symptom measurement was standardized on a 10-point scale to compare the severity of each symptom.

**Ethical considerations**

This study was approved by the Ethics Committee (IRB No. 2021BJYYEC-325-01). All participants received sufficient explanation

about the study and voluntarily participated in it. Informed consent was provided to all participants included in the study.

**Results**

*General characteristics*

In total, 416 patients with advanced cancer were included in our study. The characteristics of the patients with advanced cancers are presented in Table 1. The mean age of the included patients was  $62.02 \pm 12.08$  years (20 to 88 years). Lung cancer accounted for the largest proportion of cases ( $n = 138, 33.2\%$ ), followed by gastrointestinal ( $n = 127, 30.5\%$ ), breast ( $n = 61, 14.7\%$ ), urinary ( $n = 25, 6.0\%$ ), and gynecological cancers ( $n = 7, 1.7\%$ ).

*Cancer symptoms*

Fig. 1 shows the standardized symptom scores of the included patients. Table S1 shows the symptoms and standardized symptom scores of the patients. Fatigue was the most severe symptom ( $3.78 \pm 1.64$ ), followed by sleep disturbance ( $3.42 \pm 2.20$ ), anxiety ( $2.00 \pm 1.99$ ), depression ( $1.96 \pm 1.81$ ), and pain ( $1.21 \pm 1.96$ ).

*Identification of symptom subgroups*

The latent groups were classified using LPA based on the severity of the five symptoms. Standardized scores for the above five symptoms

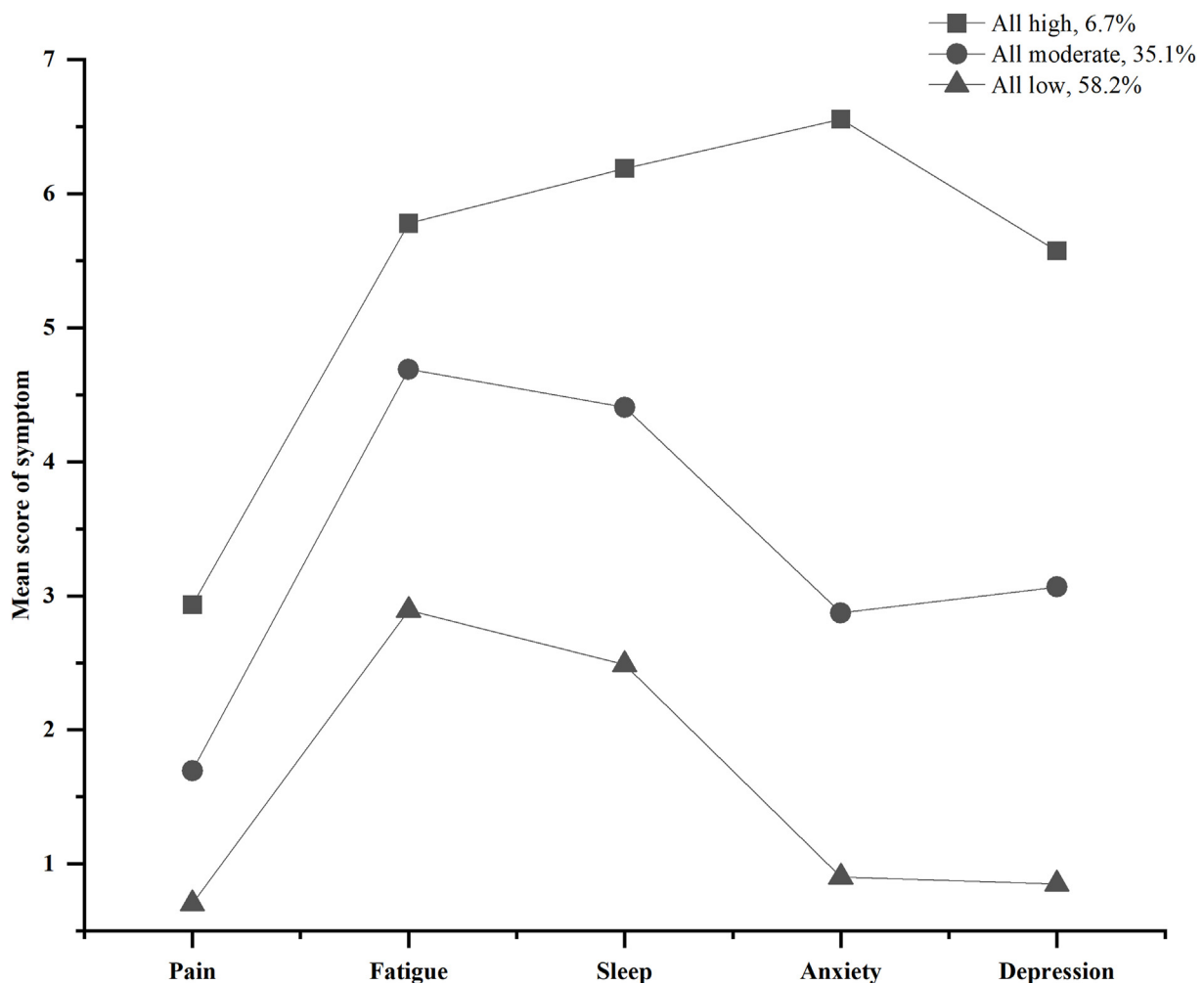


Fig. 2. Characteristics distribution of 3 latent subgroup.

were included in the analysis. Table 2 presents the fit indices for the latent symptom classes. According to the AIC and aBIC, the 5-class model was the best model. However, the results of LMRT were not significant in all models. Furthermore, the proportions of one subgroup using a 4-class model (53.1%, 7.7%, 0.5%, and 38.7%) and a 5-class model (52.6%, 0.5%, 34.1%, 5.3%, and 7.5%) did not reach the minimum requirement of 3%.<sup>11</sup> Moreover, the conceptual sense of the 3-class model is more significant than that of the 2-class model. Therefore, we chose the 3-class model. In this model, 58.2% of the included patients were divided into subgroup 1 (named “all low”), of which all symptoms were at normal levels except moderate sleep quality. For subgroup 2, 35.1% of patients included (named “all moderate”) had normal symptoms except poor sleep quality and fatigue. Finally, 6.7% of patients allocated to subgroup 3 (named “all high”) had normal pain, moderate depression besides anxiety, poor sleep quality, and fatigue. Fig. 2 shows the characteristic distribution of the three latent symptom subgroups.

### Factors associated with symptom subgroups

A univariate analysis was performed for variable screening. Table 3 presents the demographic and clinical characteristics of each group and the results of the univariate analyses. Variables including breast cancer and malnutrition risk were considered in the multiple logistic regression analyses. In addition to significant variables in univariate analysis, clinically significant variables identified by the research team (age, income, marriage, cancer survivorship duration, treatment, and comorbidities) were included in logistic regression analysis. Table 4 presents the results of the multiple logistic regression analyses. Increased malnutrition risk (OR = 5.572; 95% CI, 1.683–18.450) and cancer survivorship duration (OR = 1.099; 95% CI, 1.001–1.206) were significantly related to the “all high” subgroup. In addition, increased malnutrition risk (OR = 3.083; 95% CI, 1.353–7.024), breast cancer (OR = 2.345; 95% CI, 1.259–4.368), and cancer survivorship duration

**Table 3**  
Compare the sample characteristics in three subgroups (N = 416).

Variables	All low, n = 242, 58.2%	All moderate, n = 146, 35.1%	All high, n = 28, 6.7%	F/ $\chi^2$ /H (P)
Age (years), n (%)				1.910 (0.385)
< 65	120 (49.6)	82 (56.2)	13 (46.4)	
≥ 65	122 (50.4)	64 (43.8)	15 (53.6)	
Gender, n (%)				1.913 (0.384)
Male	128 (52.9)	68 (46.6)	16 (57.1)	
Female	114 (47.1)	78 (53.4)	12 (42.9)	
Educational level, n (%)				6.199 (0.397) <sup>a</sup>
Primary school, or lower	29 (12.0)	15 (10.3)	2 (7.1)	
Junior high school	71 (29.3)	41 (28.1)	6 (21.4)	
Senior high school	44 (18.2)	40 (27.4)	8 (28.6)	
Associate or higher	98 (40.5)	50 (34.2)	12 (42.9)	
Marital status, n (%)				3.599 (0.164) <sup>a</sup>
Married	213 (88.0)	135 (92.5)	23 (82.1)	
Single	29 (12.0)	11 (7.5)	5 (17.9)	
Resident category, n (%)				2.167 (0.343) <sup>a</sup>
Urban	198 (81.8)	127 (87.0)	25 (89.3)	
Rural	44 (18.2)	19 (13.0)	3 (10.7)	
Resident mode, n (%)				2.834 (0.217) <sup>a</sup>
Live alone	18 (7.4)	8 (5.5)	4 (14.3)	
Live with others	224 (92.6)	138 (94.5)	24 (85.7)	
Family monthly income per capita (yuan), n (%)				6.465 (0.368) <sup>a</sup>
< 3000	34 (14.0)	22 (15.1)	2 (7.1)	
≥ 3000, < 6000	89 (36.8)	61 (41.8)	13 (46.4)	
≥ 6000, < 10,000	75 (31.0)	35 (24.0)	11 (39.3)	
≥ 10,000	44 (18.2)	28 (19.2)	2 (7.1)	
Major payment source for medical services, n (%)				0.357 (1.000) <sup>a</sup>
Insurance	234 (96.7)	141 (96.6)	28 (100.0)	
Self-payment	8 (3.3)	5 (3.4)	0 (0.0)	
Body mass index (kg/m <sup>2</sup> ), n (%)				4.743 (0.568) <sup>a</sup>
Underweight (< 18.5)	14 (5.8)	15 (10.3)	4 (14.3)	
Normal (≥ 18.5, < 24.0)	134 (55.4)	76 (52.1)	15 (53.6)	
Overweight (≥ 24.0, < 28.0)	77 (31.8)	45 (30.8)	7 (25.0)	
Obesity (≥ 28.0)	17 (7.0)	10 (6.8)	2 (7.1)	
Malnutrition risk, n (%)				10.316 (0.004)
Increased	11 (4.5)	17 (11.6)	5 (17.9)	
Low	231 (95.5)	129 (88.4)	23 (82.1)	
Cancer type, n (%)				
Gastrointestinal cancer	79 (32.6)	40 (27.4)	8 (28.6)	1.236 (0.539)
Lung cancer	87 (36.0)	40 (27.4)	11 (39.3)	3.511 (0.173)
Breast cancer	24 (9.9)	33 (22.6)	4 (14.3)	11.349 (0.003) <sup>a</sup>
Urinary cancer	18 (7.4)	6 (4.1)	1 (3.6)	1.737 (0.430) <sup>a</sup>
Gynecologic cancer	4 (1.7)	3 (2.1)	0 (0.0)	0.249 (1.000) <sup>a</sup>
Cancer survivorships duration (year), Median (IQR)	2 (1–3)	2 (1–3)	2 (1–3.75)	1.899 (0.387)
Number of previous cancer therapy, n (%)				1.251 (0.874) <sup>a</sup>
1	103 (42.6)	57 (39.0)	12 (42.9)	
2	111 (45.9)	67 (45.9)	13 (46.4)	
≥ 3	28 (11.6)	22 (15.1)	3 (10.7)	
Number of comorbidities, n (%)				1.690 (0.951) <sup>a</sup>
0	127 (52.5)	71 (48.6)	14 (50.0)	
1	64 (26.4)	43 (29.5)	8 (28.6)	
2	32 (13.2)	22 (15.1)	3 (10.7)	
≥ 3	19 (7.9)	10 (6.8)	3 (10.7)	

<sup>a</sup> Fisher's exact test; IQR, interquartile range.



**Table 4**  
Multiple logistic regression analyses of symptom subgroup.

Variables	B	Standard error	Odds ratio	95% CI	p-value
All high vs All low					
Malnutrition risk (low)	Reference				
Malnutrition risk (increased)	1.718	0.611	5.572	1.683, 18.450	0.005
Cancer survivorships duration (year)	0.094	0.047	1.099	1.001, 1.206	0.046
All moderate vs All low					
Malnutrition risk (low)	Reference				
Malnutrition risk (increased)	1.126	0.420	3.083	1.353, 7.024	0.007
Cancer type (breast cancer)	0.852	0.317	2.345	1.259, 4.368	0.007
Cancer survivorships duration (year)	0.074	0.033	1.077	1.010, 1.148	0.023

CI, confidence interval.

(OR = 1.077; 95% CI, 1.010–1.148) were significantly related to the “all moderate” subgroup.

## Discussion

This study used LPA, a person-centered approach, to classify symptom subgroups of patients with advanced cancer. Increased malnutrition risk and longer cancer survivorship duration were risk factors for “all high” subgroups. And increased malnutrition risk, breast cancer diagnosis, and a longer duration of cancer survivorship were relevant in the “all moderate” subgroup. These results will be beneficial for implementing person-centered nursing for patients with advanced cancer.

Three subgroups were identified in this study. The symptoms of patients in the “all low” (58.2%) group were normal except for moderate sleep quality. “all moderate” patients (35.1%) had normal symptoms, except for poor sleep quality and fatigue. The “all high” subgroup (6.7%) had normal pain, moderate depression, anxiety, poor sleep quality, and fatigue. Symptom characteristics of the three subgroups were similar to those reported by Mosher<sup>25</sup> (subgroup 1: normal symptoms; subgroup 2: normal symptoms except for mild sleep problems and moderate fatigue; subgroup 3: mild sleep problems, anxiety, and depression, moderate fatigue, and normal pain). However, the proportions of the three subgroups (32%, 19%, and 48%) in the study by Mosher differed from the results of our study. One possible explanation for this might be that the cancer patients in the study by Mosher et al.<sup>25</sup> were at stage IV. The cancer stage may be related to symptom severity. In addition, this outcome differed from those reported by Marilyn et al. (44.0%, 45.1%, and 10.8%).<sup>24</sup> This inconsistency may be due to cancer diagnosis and treatment.<sup>36</sup> In the study by Marilyn, over 40% of the patients were diagnosed with breast cancer, and all patients received chemotherapy. In summary, for the five symptoms in advanced cancer patients mentioned in our study, the composition of subgroups was stable. But the proportion of different subgroups was influenced by cancer diagnosis, stage, and treatment. One potential explanation for these is that all of these common symptoms are the result of the activation of neuroimmune pathways and their associated regulation by inflammatory cytokines.<sup>37,38</sup> The release of these inflammatory mediators activates hypothalamic neuronal activity that induces a state of sickness behavior that is manifested by fatigue, sleep disturbance, and negative emotion.<sup>39</sup> And physiological changes such as levels of proinflammatory cytokine production, in cancer patients with different diagnoses, stages and treatments offer a possible explanation for the difference in subgroup proportion.<sup>40,41</sup> Further longitudinal studies could be implemented to explore the change in symptom subgroups so as to identify the optimal tailoring of symptom management methods for cancer patients at different stages of diagnosis, and treatment.

The “all high” subgroup had characteristics of increased malnutrition risk and a longer duration of cancer survivorship. Malnutrition is always accompanied by clinical features, including insufficient dietary intake, poor appetite, muscle wasting, and weight loss,<sup>42</sup> which overlap with fatigue.<sup>43</sup> Moreover, a previous study showed that several inflammatory biomarkers, such as soluble-receptor-for-TNF- $\alpha$ , interleukin-8, and interleukin-18, were associated with malnutrition risk.<sup>44</sup> The relationships between inflammatory biomarkers and depression, anxiety, sleep, and fatigue have also been reported<sup>45–48</sup>. Therefore, inflammation may be the core element of these variables. Advanced cancer patients with a longer duration of cancer survivorship may experience more types or cycles of treatment, which may affect their symptoms adversely.<sup>26,49</sup> Previous studies showed that as the number of prior cancer treatments increased, the odds of moving one point higher on the pain severity scale were 1.32 times more likely, and numbness/tingling in the hands/feet was 1.36 times more likely.<sup>50</sup> As such, advanced cancer patients with an increased risk of malnutrition and a longer duration of cancer survivorship should receive more attention and healthcare resources.<sup>50,51</sup> To copy more severe symptom burden, higher-intensity interventions such as web symptom monitoring, oncology nurse-led person-centered symptom management, and nutrition support, could be implemented for patients in the “all high” subgroup.<sup>52–54</sup>

The “all moderate” subgroup was characterized by increased malnutrition risk, breast cancer, and a longer duration of cancer survivorship. The relationship between breast cancer, a particular factor in this subgroup, and moderate symptoms has also been reported in a previous study.<sup>24</sup> Further study could explore the change in symptom burden for different diagnoses of cancer so as to contribute to symptom monitoring and management in cancer treatment centers.

## Limitations

Our study had some limitations. First, the cross-sectional design limited the exploration of symptom profiles at all cancer stages. A longitudinal study is required in the future. Second, the data from one cancer treatment center may limit the generalizability of our findings. Multi-center, large-sample studies are needed in the future. Third, the exclusion of patients who could not communicate due to self-reported hearing impairment or loss of voice may lead to an underestimation of the symptom severity of advanced cancer patients.

## Conclusions

This study identified three subgroups of patients based on five symptoms (fatigue, sleep disturbance, anxiety, depression, and pain) in a sample of patients with advanced cancer. This study is unique due to the individualization of the treatment and the symptom experience of the participants. Our results revealed that over forty percent of patients were classified into more severe subgroups (“all moderate” and “all high”). Increased risk of malnutrition, breast cancer diagnosis, and longer duration of cancer survivorship were relevant to the above subgroups. These findings can be used to identify those who are at risk of experiencing more severe symptoms. In addition, this study may lead to the development of person-centered interventions that can improve symptoms for patients with advanced cancer. For example, for patients with increased malnutrition risk, early symptom monitoring and more attention should be paid. Besides, early implementation of oncology nurse-led, person-centered symptom management will be a good idea for improving the progression of symptoms.

## CRedit author statement

**Huixiu Hu:** Conceptualization, Methodology, Data curation, Software, Visualization, Writing – Original draft preparation. **Yajie Zhao:** Conceptualization, Methodology, Data curation, Software, Visualization, Writing – Original draft preparation. **Chao Sun:** Conceptualization, Methodology, Supervision, Writing – Reviewing and Editing. **Pei Wang:**

Investigation, Supervision, Writing – Reviewing and Editing. **Lijuan Yu:** Investigation, Writing – Reviewing and Editing. **Ke Peng:** Software, Writing – Original draft preparation. All authors read and approved the final manuscript.

### Declaration of competing interest

All authors have no conflicts of interest to declare. The corresponding author, Professor Chao Sun, is a member of the editorial board of the Asia-Pacific Journal of Oncology Nursing. The article underwent the journal's standard review procedures, with peer review conducted independently of Professor Sun and their research groups.

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### Ethics statement

This study was approved by Ethics Committee (IRB No. 2021BJYYEC-325-01). All participants received sufficient explanation about the study and voluntarily participated in the study. Informed consent was provided to all participants included in the study.

### Data availability statement

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

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.apjon.2023.100296>.

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