ความชุกของความอ่อนล้าและปัจจัยที่เกี่ยวข้องในผู้ป่วยวัยรุ่นและวัยผู้ใหญ่ตอนต้นที่เป็นมะเร็งในประเทศจีน
Prevalence of and Factors Associated with Fatigue in Adolescents and Young Adults with Cancer in China

นิพนธ์ต้นฉบับ **Original Article**

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บทคัดย่อ

วัตถุประสงค์: เพื่อประมาณและเปรียบเทียบความชุกของอาการอ่อนล้าระดับปานกลางถึงรุนแรงในผู้ป่วยมะเร็งวัยรุ่นและวัยหนุ่มสาว และวิเคราะห์ปัจจัยที่เกี่ยวข้องกับความรุนแรงของอาการอ่อนล้า **วิธีการศึกษา:** ณ โรงพยาบาลแห่งหนึ่งในเมือง Zhejiang ประเทศจีน ผู้ป่วยมะเร็งวัยรุ่นและวัยหนุ่มสาว (อายุ 18 – 30 ปีขณะได้รับการวินิจฉัย) จากการสุ่มอย่างง่ายตอบแบบสอบถามดังนี้ แบบประเมินความอ่อนล้าของไพเพอร์-อาร์, ดัชนีคุณภาพการนอนหลับพิตต์สเบิร์ก แบบประเมินความวิตกกังวลแฮมิลตัน แบบประเมินภาวะโภชนาการผู้ป่วย และแบบประเมินความพึงพอใจในครอบครัว ทดสอบความต่างสถิติด้วย t test, Fisher's exact test) และสัมประสิทธิ์สหสัมพันธ์เพียร์สัน **ผลการศึกษา:** ผู้ป่วยมะเร็งวัยรุ่นและวัยหนุ่มสาวรวม 171 คนตอบแบบสอบถาม พบอุบัติการณ์ของอาการอ่อนล้าระดับปานกลางถึงรุนแรงในกลุ่มวัยรุ่นต่ำกว่ากลุ่มวัยหนุ่มสาวอย่างมีนัยสำคัญ (94% และ 99% ตามลำดับ, P-value < 0.05) แต่คะแนนความอ่อนล้าไม่ต่างกัน ปัจจัยที่สัมพันธ์กับความอ่อนล้าอย่างมีนัยสำคัญ (P-value < 0.001) ได้แก่ ความวิตกกังวล ($r_{วัยรุ่น}$ = -0.399, $r_{วัยหนุ่มสาว}$ = -0.587) และคุณภาพการนอนหลับ ($r_{วัยรุ่น}$ = -0.470, $r_{วัยหนุ่มสาว}$ = -0.400) ในกลุ่มวัยรุ่นความอ่อนล้าสัมพันธ์อย่างมากกับภาวะโภชนาการ (r = -0.469, P-value < 0.001) และรายได้ครอบครัว (r = 0.333, P-value < 0.01) ในขณะที่กลุ่มวัยหนุ่มสาวความอ่อนล้าสัมพันธ์กับรายได้ต่อเดือน (r = 0.434, P-value < 0.001) และระยะเวลาตั้งแต่ได้รับการวินิจฉัย (r = -0.206, P-value < 0.05) **สรุป:** อาการอ่อนล้าปานกลางถึงรุนแรงพบบ่อยในผู้ป่วยมะเร็งวัยรุ่นและวัยหนุ่มสาวโดยรุนแรงขึ้นตามอายุ ปัจจัยหลักที่เกี่ยวข้องคือความวิตกกังวลและคุณภาพการนอนหลับ ซึ่งชี้ถึงความสำคัญของการดูแลด้านจิตใจและการจัดการการนอนหลับ

คำสำคัญ: มะเร็ง; ความอ่อนล้า; ความชุก; วัยรุ่น; วัยผู้ใหญ่ตอนต้น; ชาวจีน

Abstract

Objective: To determine and compare the prevalence of moderate-to-severe fatigue in adolescent and young adult cancer patients and examine factors associated with fatigue severity. **Method:** At a hospital in Zhejiang, China, cancer patients aged 18 - 30 years at diagnosis were selected by simple random sampling to complete questionnaires including the Piper Fatigue Scale-R (PFS-R), Pittsburgh Sleep Quality Index (PSQI), Hamilton Anxiety Rating Scale (HAMA), Patient-Generated Subjective Global Assessment (PG-SGA©), and the Family APGAR Scale. Statistical comparisons were made using t-test, Fisher's exact test, and Pearson correlation. **Results:** 171 adolescents (A) and young adults (YA) with cancer completed the questionnaires. The incidence of moderate to severe fatigue in adolescents was significantly lower than that in young adults (94% and 99%, respectively, P-value < 0.05). No difference in fatigue scores between the two groups (P-value > 0.05). Anxiety (r_A = -0.399 and r_{YA} = -0.587) and sleep quality (r_A = -0.470 and r_{YA} = -0.400) were strong associated factors of fatigue (P-value < 0.001). In adolescents, fatigue was more affected by nutritional status (r = -.469, P-value < 0.001) and family income (r = 0.333, P-value < 0.01). In young adults, fatigue was significantly correlated with monthly income (r = 0.434, P-value < 0.001) and the duration of diagnosis (r = -0.206, P-value < 0.05). **Conclusion:** Moderate-to-severe fatigue is common in adolescents and young adults with cancer and increases with age. Anxiety and sleep quality are the core related factors, highlighting the importance of psychological intervention and sleep management.

Keywords: cancer; fatigue; prevalence; adolescents; young adults; Chinese

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Introduction

Cancer is a major global public health problem. Although the incidence of cancer in adolescents and young adults is low (1.3 million new cases worldwide in 2022), it has unique biological characteristics and clinical challenges. The top five AYA cancer incidence rates for 15-30-year-olds were: thyroid, leukemia, breast, non-Hodgkin lymphoma (NHL), and brain & central nervous system (CNS), with leukemia having the highest mortality rate.[1] In addition to thyroid cancer, chemotherapy is the mainstay of treatment for four other cancers.[2] The same as adult and child patients, AYA experiences various symptoms during chemotherapy. Moreover, AYA patients who received the same

chemotherapy regimen as children also experienced more severe toxicity. Therefore, the symptoms experienced by AYA are also more severe.[3] These symptoms are associated with poor prognosis, including low survival, reduced treatment compliance, and reduced quality of life.[4] Among many symptoms, fatigue cannot be ignored. Studies have shown that fatigue is a very common and high-scoring symptom in AYA with cancer.[5] In a systematic review of multiple symptoms, fatigue was one of the most frequently reported physical symptoms in 61 studies .[6]

The framework of this study was based on the Piper Integrated Fatigue Model (IFM) and previous research evidence. The IFM model proposes 14 biochemical, physiological, and psychosocial patterns as the most likely factors affecting fatigue. In this study, four possible associated factors of fatigue, sleep quality, anxiety, nutritional status, and family function were identified. The symptoms of sleep disorders in patients seriously affect their daily activities and energy. The more serious the sleep disorder, the higher the degree of fatigue of patients.[7] The quality of nutritional status can be used as one of the criteria for determining the degree of health and disease. Patients with poor nutritional status are more prone to fatigue.[8] The metabolism of energy, carbohydrate, fat, and protein in patients with cancer has changed greatly.[9] In addition, due to the loss of appetite caused by tumor treatment (such as chemotherapy and radiotherapy) and malnutrition, the nutrient supply of the body is lower than that required by the body, resulting in fatigue.[10] However, adolescents and young adults differ in the most common cancer types, treatment options, and gastrointestinal adverse effects. Anxiety is a strong emotional stressor that can activate the hypothalamic-pituitary-adrenal (HPA)axis, leading to abnormal changes in cortisol levels, and finally showing continuous fatigue. Compared with young adults, adolescents have relatively weak emotional regulation. Anxiety is the most abundant of AYAs ‘mental diseases.[11] During chemotherapy, patients may face physical discomfort, mood swings, and lifestyle changes. Social support acts as a buffer and helps patients cope with stressful situations and overcome their challenges. The higher the perceived social support, the lower the level of fatigue.[12] However, East Asians are less willing than Westerners to seek social support when needed, possibly due to cultural differences between East and West.[13] In collectivist cultures, the family is the primary source of support, and its function may have a much greater impact on individual health than generalized social support.[14] If the family can flexibly adjust and effectively cope with these changes, the patient's stress will be reduced, and fatigue will be reduced accordingly.[15] Therefore, good family function can significantly improve the overall state of patients and reduce the degree of fatigue by providing practical and emotional support. However, there was a significant difference in the type of social support between adolescents and young adults during cancer treatment, with adolescents relying more on their parents and young adults valuing support from their spouses.

Adolescents are in a period of rapid physiological development, and hormone fluctuations and the maturity of the immune system may affect fatigue perception.[16] They are psychologically dependent on family support and easily affected by family function and economic status. Young adults tend to be physiologically stable but face social pressures such as career development, economic independence, and family formation.[17] Disease treatment may lead to a career crisis and economic burden. There are differences in chemotherapy regimens for adolescents and young adults depending on the type of cancer. Existing studies have focused on the characteristics of AYA population needs, and the pooled study of adolescents and young adults may mask its internal heterogeneity. Narrowing down the age range and subgroup studies can help to accurately identify vulnerable subgroups and provide evidence for the development of targeted interventions.

Although the 5-year survival rate of Adolescents and Young Adults with cancer has greatly improved, there is still a significant gap in the research on the pathological mechanism and intervention of fatigue symptoms in adolescents and young adults with cancer.[18] While undergoing cancer treatment, this group is at a critical stage of physiological development and social role transformation. The interaction of multiple stressors may lead to the complication and chronicity of fatigue.[19] Although current clinical studies have paid attention to the need for special fatigue management programs for the AYA population, there is a lack of personalized strategies for the development needs of the two subgroups. In China, because culture-specific factors have not been fully included in the research, the assessment and intervention system for fatigue needs to be improved urgently.

By comparing the difference in fatigue between adolescent and young adult cancer patients during chemotherapy, this study comprehensively analyzed the predictive effects of demographic characteristics, anxiety, nutritional status, sleep quality, and family function on fatigue, to reveal the influencing mechanism and guide precise intervention.

Materials and methods

Participants were adolescent and young adult cancer patients undergoing chemotherapy at a grade A hospital in Zhejiang, China. Inclusion criteria: (1) Age 15-30 years old; (2) hospitalized patients received at least one course of chemotherapy; (3) able to read and write Chinese and answer the questionnaire. Exclusion criteria: The history of neurological disorders, visual or hearing impairment, motor impairment, and cognitive delay were documented in the patient's health records.

The sample size of this study was estimated based on the number of independent variables.[20] The sample size had been set at 40 for each independent variable. This study included four independent variables. Therefore, the total number of participants was calculated as 160 AYAs with cancer. To account for an anticipated sapless rate and sampling error of 10%, the sample size had been expanded to 176. Ultimately, 171 subjects were recruited. Subjects were selected by simple random sampling. Eligible AYA inpatients were sequentially numbered every week, written on paper, folded into boxes, and drawn the number. Inclusion commenced November 2022 and ended November 2024.

Procedures

AYA had been recruited from hospitalized patients at the Second Affiliated Hospital of Wenzhou Medical University and Yuying Children's Hospital between November 2022 and November 2024. Eligible participants had been identified on the first or second day of admission, prior to the initiation of chemotherapy. Each adolescent (along with their caregiver) or young adult who had agreed to participate had received and signed an informed consent form and completed the corresponding questionnaire. Investigators randomly selected one to two eligible participants daily from 9:00 a.m. to 12:00 a.m.. To minimize fatigue and avoid morning sessions or siesta periods, participants had been asked to complete the questionnaire in the afternoon or evening. The questionnaire had been available in both paper and electronic formats, and segmented testing had been permitted to reduce respondent burden. The research team provided detailed instructions on how to complete the questionnaire and emphasized key considerations to minimize bias. Participants had completed the questionnaire independently in a quiet, private environment within the hospital's reception room. The data collection process took approximately 40 to 50 minutes per participant.

Research instruments

The demographic record form of AYA included basic information such as age, gender, weight, ethnicity, type of chemotherapy, length of hospital stays, severity of illness, and payment method of medical expenses. The general information of caregivers included age, relationships, education, employment, religious belief, etc.

Fatigue was measured using the revised Piper Fatigue Scale (PFS-R), which included four dimensions (behavior/severity, emotional meaning, feeling, and cognition/emotion), and Likert 11 scoring method.[21] The scoring scale was 0 (no fatigue), 1-3 (mild fatigue), 4-6 (moderate fatigue), and 7-10 (severe fatigue). The PFS-R ranged from 0 to 220, and the result was the meaning of each dimension (total score of the dimension/number of items), with higher scores indicating higher fatigue. The Cronbach alpha coefficient of the scale ranged from 0.87 to 0.89.[22] In this study, the Piper Fatigue Scale-Revised (PFS-R) demonstrated excellent internal consistency, with a Cronbach's alpha coefficient of 0.973.

Sleep quality was measured using the Pittsburgh sleep quality index (PSQI).[23] The PSQI scale was composed of 19 self-rating items and 5 other evaluation items, of which the 19th self-rating item and 5 other evaluation items were not involved in the scoring. All items were divided into seven dimensions: subjective sleep quality, sleep duration, sleep duration, sleep efficiency, sleep disorder, hypnotic medication and daytime function. Each section is scored on a scale of 0-3. The cumulative score of each component was the PSQI total score, which ranged from 0 to 21. The higher the score, the worse the sleep quality. The scale was validated in a Hong Kong study of children with cancer. The Cronbach alpha coefficient of the Chinese version of PSQI was. 71. The

intraclass correlation coefficient was 0.90.[24] In this study, the Pittsburgh Sleep Quality Index (PSQI) showed good internal consistency, with a Cronbach's alpha coefficient of 0.829.

Hamilton Anxiety Scale (HAMA) was used to evaluate the degree of anxiety. There are 14 items. Each item has 5 points (0 = never, 1 = almost never, 2 = sometimes, 3 = often, and 4 = always). The total score ranges from 0 to 56. Higher scores indicate higher levels of anxiety. Its reliability and validity have been demonstrated in AYA.[25] The Cronbach's alpha coefficient of the Hamilton Anxiety Scale was. 92.In this study, the Hamilton Anxiety Rating Scale (HAM-A) showed good internal consistency, with a Cronbach alpha coefficient of 0.804.

Nutritional status was assessed using the patient Subjective Global Assessment (PG-SGAⓒ). It is divided into a patient self-evaluation component and a health care provider evaluation component. Patient self-assessment included weight change, dietary intake, symptoms, and mobility, whereas health care provider assessment included diagnosis, metabolic needs, and physical examination. Numerical scores on the patient-rated portion of the PG-SGA range from 0 (no problem) to 12 (most serious problem). Higher scores indicate more severe nutritional problems and poorer nutritional status. The sensitivity and specificity of the Chinese version PG-SGA score in predicting SGA grade were 98% and 82%.[26] The Cronbach's alpha coefficient of the Patient-generated subjective global Assessment (PG-SGA) was 0.655, and the internal consistency was low. However, given that the PG-SGA is a multidimensional instrument designed to assess complex aspects of nutritional status, this level of reliability was considered acceptable.

Family function was measured by the Family APGAR Scale.[27] The scale contains a total of five items, each assessed on a 3-point scale [0 (almost never), 2 (almost always)], with total scores ranging from 0 to 10, with higher scores reflecting more satisfactory family functioning. Family APGAR was found to be a reliable instrument when used in cancer patients, with Cronbach's alpha reported in a study of bone marrow transplant survivors was 0.88.[28] The Cronbach's alpha coefficient of the Family APGAR scale was .673, indicating a moderate level of internal consistency. As the scale contains only five items, this level of reliability is still acceptable for clinical research as a concise initial screening tool for family function.

Data analysis

SPSS 22 software was used for statistical analysis. The significance level for correlation and multivariate analysis was set at .05. Data analysis was performed after rechecking the data input. Descriptive statistics were used to analyze the demographic characteristics, general information of the subjects, and the general information of the caregivers, and the normal distribution test was performed on each variable. The difference of fatigue between adolescent group and young adult group was tested by independent sample T test. Fisher's exact test was used to compare the proportion of moderate to severe fatigue between the adolescent and young adult groups. Pearson and point-biserial correlations were calculated to examine associations between continuous variables or continuous and dichotomous variables, respectively.

Results

A total of 188 questionnaires were distributed and 171 valid questionnaires were collected, with an effective recovery rate of 91.0%. Table 1 shows the social characteristics, disease and treatment-related characteristics, and caregiver situation of 171 AYAs with cancer in the final sample, stratified by the severity of fatigue. For participants with moderate to severe fatigue, the ratio of males to females tended to be even among adolescents, and the young adult group was dominated by females (74%). 47% of young adults with moderate to severe fatigue had a high school education. Most young adults are employed (69%) and married (62%). The cancers in adolescents were mainly of the hematological system (90%), while the most common cancers in young adults were of the gastrointestinal cancer (33%), breast cancer (23%), and hematological system (17%). Most participants in both groups had a monthly household income of more than 10,000 yuan (38%). Most participants had intermediate or high risk - 84% in the adolescent group and 98% in the young adult group. The mean Body Mass Index (BMI) of the participants was 20.97 (SD=3.82).

Most of the patients in the adolescent group were treated with consolidation chemotherapy (56%), while the patients in the young adult group were treated with adjuvant chemotherapy (32%). Almost no surgery was performed in the

adolescent group due to the type of disease (73%), while most of the young adult group had surgery (85%). Most participants in both groups stayed in the hospital for less than a week (mean, 5.61; SD =7.22), and had received a cancer diagnosis for less than 6 months (mean, 6.18; SD =7.11). Caregivers for the adolescent group were primarily mothers (82%), whereas caregivers for young adults were spouses (58%). As a result, caregivers in the young adult group had a college education (43%), while caregivers in the adolescent group had a high school education or less (75%).

Table 1 Characteristics of adolescents and young adults stratified by fatigue severity (N = 171).

Character-istics	**Adolescents** [n=67(%)]			**Young Adults** [n=104(%)]		
	Mild	Moderate	Severe	Mild	Moderate	Severe
	4(6%)	59(88%)	4(6%)	1(1%)	94(90%)	9(9%)
Gender						
Male	4 (100%)	32(54%)	3(75%)		25(26%)	2(22%)
Female		27(46%)	1(25%)	1(100%)	69(74%)	7(78%)
Education						
Junior High School	4(100%)	59(100%)	4(100%)		11(12%)	
High School					41(43.5)	7(78%)
College				1(100%)	39(41%)	2(22%)
Master's Degree					33.5%)	
Family Monthly income (RMB)						
< 1000			1(25%)			
1000-2999		35%)			1(1%)	
3,000- 4999		16(27%)	1(25%)		18(19%)	5(55%)
5,000 - 9999	2(50%)	10(17%)			31(33%)	1(11%)
>10,000	2(50%)	18(30%)	2(50%)	1(100%)	40(42%)	3(34%)
Not known		12(21%)			45%)	
BMI Kg/m2 (Range =12.5-31.2, mean =20.97, SD =3.82)						
<18.5	1(25%)	25(42%)	1(25%)		14(15%)	4(44%)
18.5-25	2(50%)	30(51%)	3(75%)	1(100%)	65(69%)	3(33%)
> 25	1(25%)	4(7%)			15(16%)	2(23%)
Types of cancer						
Hematologic Cancers	4(100%)	50(85%)	4(100%)	1(100%)	15(16%)	2(23%)
Gastrointestinal Cancers		2(3%)			29(31%)	5(55%)
Cancers of the Reproductive System		1(2%)			8(9%)	1(11%)
Breast Cancer		1(2%)			24(25%)	
Lung Cancer					5(5%)	
Other		5(8%)			13(14%)	1(11%)
Surgery						
Yes		18(31%)			80(85%)	8(89%)
No	4(100%)	41(69%)	4(100%)	1(100%)	14(15%)	1(11%)
Current Chemotherapy Cycle						
Intensive		34(58%)	2(50%)		12(13%)	1(11%)
Consolidation	4(100%)	16(27%)	2(50%)	1(100%)	8(8%)	1(11%)
Salvage		1(2%)			13(14%)	6(67%)
Multimodal		3(5%)			27(29%)	1(11%)
Adjuvant		5(8%)			33(35%)	
Neoadjuvant					1(1%)	
Hospitalization Period (Day) (Range =1-42, mean =5.61, SD =7.22)						
<7	3(75%)	37(63%)	1(25%)	1(100%)	69(73%)	5(55%)
7-14	1(25%)	6(10%)	2(50%)		11(12%)	3(33%)
> 14		16(27%)	1(25%)		14(15%)	1(12%)
Time of Diagnosis (Month) (Range =1-40 mean = 6.18, SD =7.11)						
< 6		38(64%)	2(50%)		69(73%)	3(33%)
6 - 12	3(75%)	13(22%)	1(25%)	1(100%)	15(16%)	3(33%)
>12	1(25%)	8(14%)	1(25)		10(11%)	3(33%)

Differences in scores and severity of fatigue between adolescents and young adults

There were no significant differences in fatigue scores reported by adolescent cancer patients compared with younger cancer patients (M = 5.854, SD =0.967 vs. M = 6.069, SD = 0.694, p >.05, respectively). Adolescents with cancer had a lower prevalence of moderate to severe fatigue than young adults with cancer (94%, n = 63/67 vs 99%, n = 103/104, p <.05), and adolescents had a higher tendency of mild fatigue. (See Tables 2 and 3)

Table 2 Comparison of fatigue scores between adolescents and young adults.

	Number (n)	**Mean**	**SD**	**T**[a]	**p-value**
Adolescents	67	5.854	0.967	-1.573	.119
Young adults	104	6.069	0.694		

[a]t-test

Table 3 Comparison of the severity of fatigue in adolescents and young adults

	Mild fatigue	**Moderate to severe fatigue**	**p-value**	**OR**[b]
Adolescents	4	63	.046	6.54
Young adults	1	103		

[b]Fisher's Exact test

Sociodemographic, treatment-related, and correlated variable correlations of fatigue severity

This study aimed to compare the influencing factors of fatigue during cancer chemotherapy in adolescents and young adults. Therefore, in addition to the core study variables such as anxiety, sleep quality, nutritional status, and family function, some demographic and clinical characteristics variables were also included. This was based on the existing literature and clinical observations, considering its possible impact on fatigue, and controlling for it as a potential confounding factor, to reveal the relationship between the main independent variables and fatigue more comprehensively.

Table 4 lists the correlations. Anxiety, insomnia quality, and nutritional status were all strongly associated with fatigue severity in adolescents with cancer (p <.001). Household income was a moderate factor (p <.01). Monthly household

income had a weaker correlation (p <.05). The factors associated with the severity of fatigue in young adults were slightly different: monthly household income, anxiety, and sleep quality were strongly correlated with the severity of fatigue (p <.001). Nutritional status had a moderate correlation (p <.01). Age and time from diagnosis were weakly associated with the severity of fatigue in young adults with cancer (p <.05). No significant associations were observed between fatigue severity and other sociodemographic characteristics and disease - and treatment-related variables (see Table 4; p >.05).

Table 4 Correlates fatigue severity in AYAs with cancer

	Adolescents (N= 67)	**Young Adults** (N=104)
	Correlation coefficients	**Correlation coefficients**
Sociodemographic variables		
Gender	.003/.983	-.070/.636
Age	.156/.206	.202/.040*
Hospitalization Period (Day)	.249/.001*	-.071/.475
Duration of Illness (Month)	-.046/.547	-.206/.036*
BMI	.071/.568	.106/.284
Family Monthly income	.333/.006*	.434/.000004**
Disease- and treatment-related variables		
Types of cancer	.056/.651	-.047/.638
Surgery	-.102/.411	.015/.879
Current Chemotherapy Cycle	.150/.226	-.080/.417
Main factors		
Family function	.308/.011*	.170/.084
Anxiety	.399/.00082**	.587/.000263**
Sleep quality	-.470/.00006**	-.400/.000025**
Nutritional status	-.469/.000061**	-.266/.006*

* p <.05, ** p <.001

Discussions and Conclusion

In this study, fatigue was divided into two groups: "mild fatigue" and "moderate to severe fatigue". Due to the small number of samples reporting mild fatigue, if fatigue is divided into three levels for analysis, the statistical results will be unstable due to the uneven distribution of samples. Therefore, moderate and severe fatigue were combined to maintain adequate statistical power and improve the explanatory power of the results. Nevertheless, the combined groups may mask differences between moderate and severe fatigue, and this should be considered with caution when interpreting the results. Future studies can further refine the comparative analysis of fatigue levels with a larger sample size and a more balanced distribution.

This study suggests that the severity of fatigue in adolescents with cancer is correlated with the length of hospital stay and family income. Fatigue in young adults with cancer is significantly associated with household income, but less so with duration of illness and age. Adolescent patients have poor adaptability to the hospital environment. Adolescent patients have poor adaptability to the hospital environment.[29] Previous studies have suggested an association between fatigue and hospitalization.[30] Long-term hospitalization may lead to increased bedridden time, resulting in muscle atrophy and decline in cardiopulmonary function.[31] It also removes adolescents from school and peer groups, triggering feelings of loneliness and depression, which can indirectly lead to fatigue.[32] In addition, economic stress may bring family conflict and weaken family function, thereby affecting fatigue.[33] A study focusing on chemotherapy patients also showed that household income was lower in patients with high levels of fatigue.[34] For adolescents, family is the core channel to obtain resources, and family income directly determines the quality of medical care. Young adults who are in a critical period of separation from their family of origin are also career upward, their careers are interrupted because of their illness, and they are financially dependent on their family, which may trigger feelings of shame and thus exacerbate fatigue through psychological stress.[35,36] This socioeconomic strain may increase with age. As others have shown, there is a correlation between the duration of treatment and the degree of fatigue.[37] There is a correlation between the severity of fatigue and the duration of illness in young adults, which may be related to the accumulation of fatigue.[38]

The results demonstrated that anxiety levels in AYA patients during chemotherapy significantly correlated with fatigue. This finding is consistent with studies involving patients with colorectal cancer, which reported that patients with significantly more anxiety symptoms experienced more fatigue.[39] One possible explanation is that anxiety increases cognitive burden, as persistent worry consumes substantial psychological resources, leading to Cognitive fatigue.[40] Additionally, anxiety can interfere with working memory and attention allocation, making it more challenging to concentrate on daily activities and thereby exacerbating feelings of fatigue. Anxiety is often accompanied by persistent negative emotions, such as fear, helplessness, and hopelessness, which drain psychological energy. According to the Emotion Regulation Theory, individuals need to expend additional emotional regulation efforts to manage anxiety, and the long-term

accumulation of these efforts can lead to emotional exhaustion, further increasing fatigue.[41] While anxiety is frequently studied alongside depression about fatigue, some scholars argue that anxiety and depression are interrelated, with anxiety sometimes being overshadowed by depression, and depression representing a progression of anxiety.[42] However, other studies have identified anxiety as an independent factor with a distinct association with fatigue.[43] From a physiological perspective, anxiety activates the sympathetic nervous system, triggering the release of stress hormones such as cortisol and adrenaline.[44]

The results showed that the worse the sleep quality, the worse the fatigue. This finding is consistent with a study conducted in Iran, which reported the average sleep quality of cancer patients as a positive influencing factor for fatigue.[45] Similarly, a study in China confirmed that sleep quality affects fatigue levels in breast cancer patients.[46] Sleep is a critical process for physical and cognitive recovery. Poor sleep quality directly impairs the body's ability to recover, both physically and psychologically. Deep sleep, particularly slow-wave sleep, plays a vital role in energy restoration and immune system function. Reduced sleep quality decreases the time spent in deep sleep, leading to insufficient physical recovery and increased daytime fatigue.[47] Additionally, poor sleep quality negatively affects cognitive functions such as attention, memory, and decision-making.[48] These cognitive impairments can exacerbate feelings of fatigue, particularly during tasks requiring high levels of concentration. Furthermore, decreased sleep quality disrupts emotional regulation, contributing to increased negative emotions such as anxiety and depression.[49] These emotions can further intensify fatigue, creating a vicious cycle. Prolonged activation of this state can result in physical fatigue. Furthermore, anxiety is a leading cause of sleep disturbances. Sleep deprivation directly impairs the body's ability to recover, leading to increased daytime fatigue.[50] This relationship is further supported by Korean scholars who found a significant correlation between anxiety and sleep disturbances.[51] Studies have shown that improving sleep quality can alleviate fatigue, and patients with cancer may benefit from interventions aimed at regulating sleep patterns and optimizing sleep quality. A randomized controlled trial in 36 patients with breast cancer showed that melatonin for insomnia significantly improved sleep quality and reduced fatigue levels compared with controls.[52]

Although there was a negative correlation between nutritional status and fatigue during AYA chemotherapy (the better nutritional status, the less fatigue), there was a difference between adolescents and young adults. The correlation between fatigue severity and nutritional status was stronger in adolescents. Adolescents are in a stage of rapid growth and development, with higher basal metabolic rates and nutritional requirements than young adults.[53] Studies have shown that nutritional supplementation is an important proposition for adolescents with cancer.[54] In contrast, meta-analyses of adults and young adults suggest that nutrition therapy does not have a significant effect on fatigue.[55] Therefore, adolescents are more likely to develop nutritional deficiencies in response to chemotherapy, leading to energy deficit and fatigue.[56] Malnutrition disrupts energy metabolism, leading to an inadequate energy supply. Protein-energy malnutrition reduces muscle mass and strength, contributing to fatigue.[57] Another possible reason is that most of the adolescents' diets are arranged by their caregivers. Lack of family nutrition knowledge, financial constraints, or neglect of special needs may lead to deterioration of nutritional status.[54] Young adults can actively adjust their diet, use nutritional supplements, or seek professional guidance, and there are more ways to compensate for nutritional deficiency.

This study confirms that family functioning is weakly associated with fatigue in adolescents (the higher the family function score, the lower the degree of fatigue) with cancer but not in young adults. Family function was conceptually defined as the daily processes families engage in to achieve goals and to support family members' health and development. Studies have shown that family dysfunction increases the risk of anxiety and depression, which in turn aggravate fatigue in cancer patients.[58] Another study confirmed that family function indirectly affected fatigue by affecting quality of life.[59] A study of adults with cancer showed no significant association between family functioning and fatigue.[60] A possible explanation for these findings is Piper's integrated fatigue model, which posits that fatigue is perceived through three dimensions: psychological, physiological, and behavioral. Family function may mainly affect emotional fatigue, while the correlation between physical fatigue and family function is weak, and it is more prominent in cancer patients. For adolescents, family support often manifests as direct care and management by parents, while young adults may prioritize

emotional support and involvement in decision-making. In some theoretical models, spousal support is categorized as partner support, which combines elements of family support and peer support.[61,62] This distinction may explain why family function's impact on fatigue varies depending on the patient's age and relationship dynamics.

The present study has certain limitations. This study focused specifically on AYA with cancer, a population that is often underrepresented in research but faces unique developmental, psychosocial, and medical challenges. By comparing two different subgroups, adolescents vs. young adults, the study provides valuable insights into age-specific factors associated with cancer-related fatigue. This study has several limitations. As a single-center study with a relatively small sample size, the findings may not be representative of the broader AYA population in China. The limited sample size may also reduce statistical power, potentially affecting the generalizability of the results. Additionally, the cross-sectional design precludes the establishment of causal relationships between the studied variables. Future research should consider multicenter, longitudinal studies with larger sample sizes to validate these findings and explore causal mechanisms. Meanwhile, this study only focused on four core variables and could not comprehensively cover all the factors that might affect fatigue. Due to sample size limitations, only the main psychosocial and physiological variables could be considered. In the future, more latent variables should be further integrated based on a larger sample size to construct a more comprehensive prediction model.

In conclusion, the high prevalence of moderate to severe fatigue in adolescents and young adults with cancer highlights that fatigue is a prevalent and core symptom in this group and needs to be integrated into a systematic assessment and management framework in clinical practice. Notably, fatigue severity increased with age in young adults, suggesting that cumulative treatment toxicity and social role stress may act synergistically to exacerbate the biological and psychosocial burden of fatigue during early adulthood. Further analysis showed that fatigue was significantly correlated with anxiety and sleep quality in both groups, indicating that psychological intervention and sleep management were common intervention targets across age groups. However, age-specific differences were significant: adolescent fatigue was more susceptible to family dysfunction and prolonged hospital stay, reflecting their deep dependence on the family support system and the critical role of adaptability in the medical environment. In young adults, fatigue is associated with the cumulative time of diagnosis and aging, which may be due to the interaction between metabolic disorders and social roles caused by long-term disease burden. Based on this, future interventions need to build a family-centered medical support network for adolescents, design integrated support strategies for young adults, and develop a precise and preventive fatigue management paradigm, to improve the quality of life and smooth treatment.

The results of this study suggest that anxiety, sleep quality, nutritional status, and family function should be comprehensively evaluated when managing fatigue in AYA cancer patients during chemotherapy. Clinical nursing staff should incorporate psychological assessment, nutritional support, and family support into the routine nursing process to provide more comprehensive support for this group. The results suggest that further prospective or intervention studies are needed to explore the causal relationship between various factors and fatigue, especially the intervention effects of anxiety and nutritional status, to develop more accurate intervention strategies for fatigue.

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