Response letter

We sincerely thank the reviewers for their thorough examination of our manuscript and for providing very helpful comments to guide our revisions.

Reviewer#1

Point1： In such short section as "Sociodemographic information", please mention "Table 1" only once. I understand you to underline both demographic and disease-related data separately but this can be improved. Consider e.g. changing the beginning of second sentence, or add semicolon to avoid repetition.

Response1：

Thank you very much for your kindness and careful revision on our manuscript.Based on your kindness suggestions, We changed the subheadings to "Sociodemographic information", with demographic and disease-related information separated by semicolons, and cited only one table1.

Point2： In section "Psychosocial Adjustment to Illness Scale-Self Report (PAIS-SR)" there is a mention about total score which is divided to low, moderate and severe. I see that moderate is up to 50, and severe starts with 51. On the contrary, low

is up to 34 but the moderate also starts with 34. Is this intentional or should one number be changed to either 33 or 35?

Response2：

Thank you very much for your careful revision. We are very sorry for making such mistakes. We contacted the original author of the Chinese version and got accurate results for low (0-34), moderate (35-50), and severe (51-138).

Point3： In Table 2 or Figure 1, I would standardize the use of "0" (zero) before dot - most of the time (e.g. Tables 1, 3, 4) it is present but sometimes not (e.g. some examples in Table 2, Figure 1). At first I thought it is left for correlation's r-values but in first row of Table 2 (Sensory neuropathy), "r" is with zeros for Sub1, 2, 4, 5, 6. In Figure 1 it will be also beneficial to spot minus sign when adding zero before dot. Moreover, I am not sure if the minus signs in Figure 1 are actually minuses or hyphens; please double-check it when making corrections.

Response3：

Thank you very much for your careful revision.

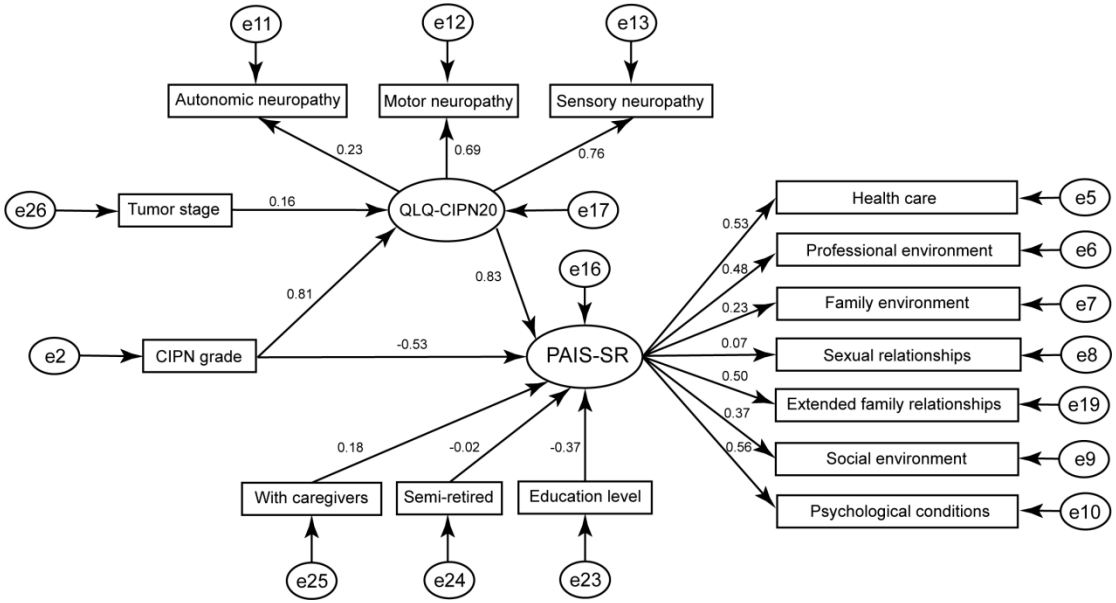
Based on your suggestion, we made a modification as following:We have standardized the format by adding 0 before the decimal point.We standardized the format by adding a "0" before the decimal point in both Table 2 and Figure 1. The "-" in

Figure 1 is a minus sign, which is reflected in Table 4.

Table 2. Correlation analysis of CIPN20 dimensions with PAIS-SR scores

		PAIS-SR Total Score	Sub1	Sub2	Sub3	Sub4	Sub5	Sub6	Sub7
Sensory neuropathy	r	0.206	0.124	0.039	0.172	0.075	0.125	0.059	0.183
	p	0.01	0.06	0.56	0.01	0.25	0.06	0.37	0.01
Motor neuropathy	r	0.356	0.150	0.195	0.254	0.109	0.201	0.140	0.299
	p	< 0.01	0.02	0.01	< 0.01	0.10	0.01	0.03	< 0.01
Autonomic neuropathy	r	0.523	0.178	0.142	0.710	0.167	0.216	0.212	0.378
	p	< 0.01	0.01	0.03	< 0.01	0.01	0.01	0.01	< 0.01

Sub1: Health care; Sub2: Professional environment; Sub3: Family environment; Sub4: Sexual environment; Sub5: Extended family relationships; Sub6: Social environment; Sub7: Psychological conditions


e11
e12
e13
Autonomic neuropathy
Motor neuropathy
Sensory neuropathy
0.23
0.69
0.76
e26
Tumor stage
0.16
QLQ-CIPN20
e17
0.83
e16
0.81
e2
CIPN grade
-0.53
PAIS-SR
0.18
-0.02
-0.37
With caregivers
Semi-retired
Education level
e25
e24
e23
0.53
0.48
0.23
0.07
0.50
0.37
0.56
Health care
Professional environment
Family environment
Sexual relationships
Extended family relationships
Social environment
Psychological conditions
e5
e6
e7
e8
e19
e9
e10

Point4： A few circles in Figure 1 could be bigger, I mean some "e-values/numbers" are not well visible when the number is higher. Example is "e26" on the left or all "e" from the top or the bottom. It is also applicable for some in the middle and on the right.

Response4：

Thank you very much for your suggestion.

We have resized all the "e-values/numbers" circles in Figure 1 to a suitable size for easier viewing. See response3.

Reviewer#2

Point： it is well designed and complete study about psychological problems after chemotherapy in patients with cancer.

Response

Thank you very much for your recognition of my manuscript.

Reviewer#3

Point1： The result of this study is the fact that CIPN was an independent factor influencing the PAIS-SR score. The results of this study recognize the importance of therapeutic strategies that aim to improve psychosocial adaptation by preventing or relieving the CIPN through interventions. However, there is no evidence that the psychophysiological approach can improve the PAIS-SR scores worsened by CIPN. Therefore, from the results of this study, it is a logical leap to consider health care

professionals should guide patients and their families to adopt positive coping strategies to avoid the poor adaptation caused by negative coping.

Response1：

Thank you very much for your confirmation of the results of my manuscript.

Point2： PAIS-SR is an excellent questionnaire, but it is old and not a major questionnaire for investigating the quality of life. The authors need to clarify why they used PAIS-SR in this study.

Response2：

Thank you very much for your question.

The PAIS-SR is a scale on the psychosocial adjustment of patients. The study showed that psychosocial adjustment is an independent influencer of quality of life(Zhang Y, Xian H, Yang Y, Zhang X, Wang X. Relationship between psychosocial adaptation and health-related quality of life of patients with stoma: A descriptive, cross-sectional study. J Clin Nurs. 2019 Aug;28(15-16):2880-2888. doi: 10.1111/jocn.14876. Epub 2019 May 5. PMID: 30939212). The scale has been widely used among cancer patients(Zhang Y, Zhu M, Wu X, Meng Y, Pu F, Zhang M. Factors associated with returning to work and work ability of colorectal cancer survivors. Support Care Cancer. 2021 Nov 6. doi: 10.1007/s00520-021-06638-3. Epub ahead of print. PMID: 34743239).

Point3： The discussion of this article consists of merely the citation of the literature. There is a need to shorten the description a little more and add some discussions on how to treat.

Response3：

Thanks greatly for your so much detailed suggestion. This really a great

help for us to improve the quality of our work.The discussion of risk factors has been refined in this paper and may suggest that health care professionals need to focus on.

For the sections where the discussion and conclusions are revised, we will show them in red font.

1. Add the following sentence at the beginning of the third paragraph of the Discussion section.

The results also showed that CIPN is an independent influence on psychosocial adjustment in cancer patients.

2. Revised at the end of the third paragraph of the Discussion section.

In addition, various behavioral interventions can be evaluated. For example, cognitive-behavioral therapy for insomnia (CBT-I) has been shown to improve insomnia and sleep quality in cancer patients(Aricò D, Raggi A, Ferri R. Cognitive Behavioral Therapy for Insomnia in Breast Cancer Survivors: A Review of the Literature. Front Psychol. 2016 Aug 3;7:1162. doi: 10.3389/fpsyg.2016.01162. PMID: 27536265). Given the uncomfortable response to CIPN, future studies can be extended to CIPN patients, with guidance and self-assessment of the specific effects of the behavioral component.

We have revised the second paragraph of the discussion, lines 4 and 6:The physical, psychological, cognitive, and social functioning of the patient can be affected by neuropathy; lines 12:which indirectly reveals

the complexity of CIPN; lines 14 to 16:Therefore, health care professionals should instruct patients and their families to adopt positive coping strategies to avoid the poor adaptation caused by negative coping.

3. Revise the end of the sixth paragraph of the discussion.

The results demonstrate that the level of psychosocial adjustment of patients with caregivers may be related to patients' personalities, which requires further investigation.

4. We add a sentence to the abstract and to the conclusion at the end of the article： In addition, the intervention strategies can improve the psychosocial adjustment of patients, demonstrating the importance of the strategies.

Response letter

We sincerely thank the reviewers for their thorough examination of our manuscript and for providing very helpful comments to guide our revisions.

Reviewer#1

Point： I wanted you to correct the part on page 7 which is: "The demographic data consisted of 16 items, including gender, age, ethnicity, religiosity, and others. (Table 1). The disease-related data consisted of 14 items, including cancer diagnosis, tumor stage, CIPN grade, and others. (Table 1)." As you can see, there are two mentions of Table 1 in such short sentences and I think the semicolon could be applicable in this part to avoid repetition.

Response

Thank you very much for your suggestion. We have restored the revision of the results section. We have revised it as follows.

Sociodemographic information

The demographic data consisted of 16 items, including gender, age, ethnicity, religiosity, and others; The disease-related data consisted of 14 items, including cancer diagnosis, tumor stage, CIPN grade, and others. (Table 1).

Reviewer #2

Point1： From the results of this study, it seems difficult to consider that

coping by health care professionals induces positive adaptation for CPIN. Please re-consider the conclusion.

Response1：

Thank you very much for your careful revision. Based on your reminder, we have removed this phrase "In addition, the intervention strategies can improve the psychosocial adjustment of patients, demonstrating the importance of the strategies.".

The conclusions of the abstract and text sections are listed below.

Abstract

Patients with CIPN have a poor level of psychosocial adaptation and are affected by a variety of physiological, psychological, and social factors. In the future, patients' adaptive responses should be comprehensively assessed, and targeted interventions should be implemented to improve their psychosocial adaptation level.

Text

This study highlights that the level of adaptation of patients with CIPN is influenced by physical, psychological, and social factors and should be regularly assessed in multiple ways. The findings of this study will help increase knowledge and evidence of CIPN symptom management and the development of individualized interventions. In addition, this study can help patients and their families to recognize their health needs and to improve the quality of life and level of adjustment of patients in the

post-chemotherapy setting.

Point2： There is a duplication in the abstract's conclusion. Please delete it.

Response2：

Thank you very much for your careful examination of our manuscript. We have removed it.

Point3： Please shorten the Discussion to make it easier to read.

Response3：

Thank you very much for your suggestion.

We will revise the discussion section as follows and shorten it appropriately. It mainly includes the discussion of the current status of psychosocial adjustment of CIPN patients and the controlling factors, the effect of CIPN grade on PAIS-SR, the effect of QLQ-CIPN20 on PAIS-SR, and the mediating role of QLQ-CIPN20. The discussion section is as follows:

DISCUSSION

Similar to Winters-Stone et al. [10], the psychosocial adaptation of patients in this study was at a low level, indicating that neurotoxicity leads to a reduced adaptation level in patients. Among all dimensions, the social environment, sexual relationships, and professional environment had higher scores. Consistent with Tanay et al. [19], CIPN symptoms predispose patients to conditions such as abandonment of social activities,

inability to return to work, and unable to perform normal job duties. Sexual dysfunction due to reduced sexual behavior and intimacy can cause psychological distress, which seriously affects the quality of life of patients [20,21]. Tumor stage has an indirect effect on the psychosocial adaptation of patients with CIPN. This result is consistent with the study of Carreira et al. [22], where advanced breast cancer survivors can develop psychological adaptation problems such as cognitive impairment, fatigue, and anxiety during the chemotherapy phase. This study also showed that having caregivers, being semi-retired, and education level all directly affect the level of psychosocial adjustment of CIPN patients. This is consistent with previous studies in which CIPN patients with caregivers experienced psychological distress due to forced caregiving [23], cancer survivors who return to work and reduce overtime hours had improved overall quality of life [24], and patients with higher levels of education are likely to be more understanding and cooperative with treatment [25]. The study showed that multidisciplinary outpatient rehabilitation programmes consisting of exercise intervention, psychotherapy, information support and professional counseling with each other can improve the physical and or psychosocial status of cancer survivors [26]. Our study further demonstrates the psychosocial burden of CIPN patients in the post-chemotherapy setting. Therefore, more high-quality multidisciplinary supportive care needs to be sought to help CIPN

patients cope with post-chemotherapy toxicity.

In addition, the results also showed that CIPN grade was an independent influence on psychosocial adaptation of CIPN patients, with a direct positive effect between the both. Tanay et al. [19] found that ineffective adaptation in patients with moderate to severe CIPN includes anxiety, depression, loss of purpose, sleep disturbance, and unable to perform normal job duties and daily activities, severely affecting patients' family, work, social, and leisure activities. A randomized trial of an automated symptom-monitoring system paired with nurse practitioner follow-up related to chemotherapy neurotoxicity symptom management showed effective improvement in patients' psychological status such as fatigue, anxiety and depression as well as reduction in symptom progression [25].

In addition, cognitive-behavioral therapy for insomnia (CBT-I) has been shown to improve insomnia and sleep quality in cancer patients [27]. Given the uncomfortable response to CIPN, future studies can be extended to CIPN patients, with guidance and self-assessment of the specific effects of the behavioral component. In fact, our findings provide insights for clinical practice. To better improve the level of psychosocial adjustment of patients, interventions developed by health care professionals should include measures that can improve the symptoms of CIPN.

The study showed a significant correlation between QLQ-CIPN20 and PAIS-SR. Sensory, motor and autonomic nerve impairments were all

significant for psychosocial adjustment in CIPN patients. Among them, autonomic nerve impairment had the strongest correlation with patients' psychosocial adjustment. Although these symptoms have been underreported in previous studies [2,4], it has also been shown that autonomic symptoms including dizziness, blurred vision, poor hearing, and sexual dysfunction after chemotherapy affect patients' psychological and emotional state with the expectation of establishing at least a subjective sense of well-being [23]. However, successful adaptation includes: absence of psychological disorders; good functional status; successful mastery of adaptive tasks; low negative and high positive emotions; satisfaction and well-being in multiple life domains [28]. It is evident that symptom burden has an impact on quality of life and consequently on the level of psychosocial adaptation of patients, where increased attention to autonomic impairment is warranted.

The study showed that QLQ-CIPN20 mediates the role between CIPN grade and PAIS-SR. Our study shows that the quality of life of patients becomes worse due to the severity of CIPN, thus decreasing their level of psychosocial adjustment. Childs et al. [29] showed that patients with esophageal cancer suffer from neurotoxic symptoms such as weakness in both lower limbs and dizziness at the chemotherapy stage. These symptoms lead to adverse events such as falls and disruption of daily activities, decreasing the quality of life of patients and creating

psychosocial maladjustment. In addition, other studies have shown that interventions using a biopsychosocial model can significantly improve the quality of life of patients. Biological, psychological and social-environmental factors can improve clinical outcomes, especially for pain management after cancer, and individual factors should not be underestimated [26]. Another study showed that the level of adaptation of CIPN patients influenced individual coping styles and behavioral patterns [30]. The results show that CIPN patients prefer to improve their psychosocial adjustment by improving the impact of their symptoms on their lives. Therefore, health care professionals should focus on reducing the impact of symptoms on life and develop interventions to improve the level of adaptation of CIPN patients by considering the influencing factors such as biological, psychological, social and individual factors.

Reference

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