Validation and Clinical Application of the Chinese Version of the M. D. Anderson Symptom Inventory(MDASI-C) in Breast Cancer Patients

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Abstract

Purpose To validate and use the Chinese Version of the M. D. Anderson Symptom Inventory (MDASI-C) to assess the symptom burden of breast cancer patients of China. And to reveal the features of the symptoms and provide a basis for improving their quality of life.

Methods A total of 342 breast cancer patients participated in the study. All patients had pathological diagnosis. They were investigated and evaluated from November 2020 to February 2021 with MDASI-C. The reliability and validity were evaluated respectively. Cluster analysis and correlation analysis were carried out.

Results The Cronbach's alpha coefficient of the symptom and interference items was 0.827 and 0.880, respectively, which meant good reliability. Construct validity revealed a four-factor structure. The Kaiser-Meyer-Olkin (KMO) value was 0.760, which meant good construct validity. The patient's KPS, treatment phase and cancer stage were grouped, and the differences of scores within the groups were significant. The patient's employment status, education level and age had a significant correlation with symptoms. The top three symptoms were disturbed sleep (3.10 ± 2.52), diffificulty remembering (2.54 ± 2.30) and fatigue (2.24 ± 2.13). The higher the patient's education, the lower their symptoms. Patients' Body Mass Index (BMI), hemoglobin (Hb), alkaline phosphatase (ALP), neutral granulocyte lymphocyte ratio (N/L), and serum albumin globulin ratio (A/G) also had an effect on some of the symptoms of patients.

Conclusions MDASI-C is a reliable and effective assessment tool when evaluating patients with breast cancer of China. The symptoms were related to many clinical, biochemical indicators.

Introduction

Recent research data suggests that breast cancer has exceeded lung cancer into the first place in the global cancer incidence[1]. The incidence of breast cancer in China has also increased year by year[2, 3]. The survival time of patients with breast cancer is longer than other cancers, so the quality of life of these patients has become concerned[4, 5]. Modern tumor assessment has developed into comprehensive assessment models based on human science, including tumor size, physical function, psychological, symptoms and social functions of patients[6, 7]. Patients with tumor often suffer from many physical and psychological symptoms such as disturbed sleep, fatigue, pain and distress. These symptoms tend to have a negative impact on the quality of life of patients[8–10]. More seriously, these symptoms greatly affect the function of the patients, and may even lead to patient changes or abandon positive treatment programs[11, 12]. Therefore, it is very urgent to strengthen the symptom management of patients with breast cancer. However, before this, we need to accurately evaluate their symptoms.

It is very important to choose a good assessment tool when evaluating the symptoms of cancer patients, such as M. D. Anderson Symptom Inventory (MDASI)[13–15]. MDASI can almost evaluate all common clinical symptoms related to tumors. Currently, the scale has been translated into different language versions, used to assess multiple symptoms related to tumors themselves in different countries[16–21]. A

systematic review for 57 symptom assessment tools indicate that MDASI is obviously advantageous compared to other assessment tools, both adaptability and specificity[22]. The Chinese version of MDASI (MDASI-C) has also been verified by the confidence and validity. In this study, most solid tumors such as lung cancer, gastrointestinal cancer, breast cancer, head neck cancer were included[15]. However, in our study, we only selected breast cancer patients to assess to determine their reliability and effectiveness. At the same time, various parameters that may affect the severity of the symptoms of breast cancer patients were analyzed.

Materials And Methods

Instrument

The MDASI (19 items, including 13 core items and 6 interference items) has been translated into Chinese by Wang XS et al.in 2004[15], and can be used directly. The MDASI-C questionnaire was explained to patients who participated in the survey until they fully understand the meaning. The 13 symptoms of the metric were expressed as numbers of "0" to "10", representing from "not exist" to " as bad as you can imagine". The 6 Interference items were also expressed as "0" to "10", representing from "no interference" to "complete interference". The symptoms assessed were only included in the past 24 hours.

In addition, patient population features, cancer stage and Karnofsky Performance Status (KPS) were recorded. We also recorded the clinical biochemical indicators of each patient, including: marriage status, working status, education level, age, Body Mass Index (BMI), hemoglobin (Hb), alkaline phosphatase (ALP), neutral granulocyte lymphocyte ratio (N/L), and serum albumin globulin ratio (A/G).

Participants

The inclusion criteria were as follows: inpatients at XXX hospital, with clear pathological diagnosis; aged ≥ 18 years; and could understand and speak Chinese fluently. Exclusion criteria were as follows: impaired ability to listen, read, and understand because of mental disorders and refusal to participate in the research. A total of 348 patients with breast cancer participated in the study and completed the MDASI-C questionnaire. The fifinal valid questionnaire was 342. These patients were investigated and evaluated in the period from November 2020 to February 2021.

Interview

The survey was carried out by three experienced oncologists. They first introduced the purpose and precautions of each participating patient and family, and obtained their consent. The questionnaire was independently completed after the participant was fully understood. Each questionnaire completion time: 15–20 minutes.

Statistical Analyses

The statistics were performed using a 25 version of SPSS statistics software. MDASI-C reliability and validity test method: The reliege test was obtained by calculating the coefficient of cronbach’s alpha, from

0 to 1, higher value represented a smaller measurement error, and prompted to have better reliability. If the value is greater than 0.8, the reliance is good. The construct valid was established by a principal axis factor analysis with direct oblimin rotation. We used oblimin rotation, and determined the final factor number according to their eigenvalues, consistency and clinical significance. Kaiser-Meyer-Olkin (KMO) test confifirmed sample adequacy. If the KMO value is greater than 0.5 indicates that the structure is acceptable. In addition to the main shaft factor analysis, the known-group validation testing also shows whether the construct validity is reasonable. They were analyzed by comparing the patient's different characteristics (KPS, treatment phase, cancer stage, age, education level, working status). Relevance hot maps used Xiantao Academic online(https://www.xiantao.love) analysis tools. Cluster analysis was used to explore clustering relationships between patients with breast cancer.

Results

Patient Characteristics

342 patients who were effectively involved in the study were 50.7 ± 10.1 years old. The proportion of patients aged ≤ 50 years old was 46.8%; the proportion of married patients was 91.8%; the proportion of retirement or unemployed in the work was 83.6%; The proportion of patients with education ≤ 9 years was 55.4%; the ratio of patients in II and III period was 42.7% and 33.3%, respectively; the proportion of patients before, in and after treatment was 64.3%, 32.2% and 3.5%, respectively. the proportion of patients KPS > 70 was 93.6%. (Table 1)

Table 1
Main Demographic and Disease Characteristics (N = 342)

Patient Characteristics	N (%)
Age	
Mean ± SD (yrs)	50.7 ± 10.1
Range (yrs)	27–75
≤ 50 yrs	160 (46.8)
> 50 yrs	182 (53.2)
Marital status	314 (91.8)
Married	
Single (including divorced, widowed)	28 (8.2)
Education level	162 (47.4)
Grade ≤ 9	
Grade > 9	180 (52.6)
Employment status	56 (16.4)
Employed	
Retired or unemployed	286 (83.6)
Cancer stage	62 (18.1)
I	
II	146(42.7)
III	114 (33.3)
IV	20 (5.9)
Treatment phase	
Before treatment	220 (64.3)
In treatment	110 (32.2)
After treatment	12 (3.5)
KPS groop	
Poor ≤ 70	22 (6.4)

SD = standard deviation; KPS(Karnofsky Performance Status). Data are presented as median (range) or absolute frequency (%).

Patient Characteristics	N (%)
Good > 70	320 (93.6)
SD = standard deviation; KPS(Karnofsky Performance Status). Data are presented as median (range) or absolute frequency (%).	

Internal Consistency

Internal consistency was the reliability analysis, which was established using the cronbach's alpha coefficients. Normally, Cronbach's alpha values of > 0.9 are generally rated as excellent, > 0.8 as good, > 0.7 as acceptable, and < 0.6 as doubtful. In MDASI-C, the total cronbach's alpha coefficient of all symptoms items(13) was 0.827, and that of interference items(6) was 0.880. The results show that the scale has a good reliability. (Table 2)

Table 2
Internal Consistency Reliability of MDASI-C

Symptom	Total Cronbach's α	Total Cronbach's α if Item Deleted
Core items (13)	0.827	
Pain		0.899
Fatigue		0.898
Nausea		0.906
Disturbed sleep		0.901
Distress		0.896
Shortness of breath		0.903
Diffificulty remembering		0.904
Lack of appetite		0.900
Drowsiness		0.904
Dry mouth		0.902
Sadness		0.896
Vomiting		0.907
Numbness		0.910
Interference items (6)	0.880	
Activity		0.896
Mood		0.895
Work		0.896
Relations with others		0.897
Walking		0.898
Enjoyment of life		0.897
MDASI-C, Chinese version of M. D. Anderson Symptom Inventory		

Construct Validity

The construct valid was established by a principal axis factor analysis. MDSI-C Symptoms (13) Generate four factors: Factor 1 contains all physical symptoms (disturbed sleep, pain, fatigue, shortness of breath, change in taste, drowsiness, diffificulty remembering,dry mouth); Factor 2 includes gastrointestinal symptoms (vomiting and nausea); Factor 3 represents psychological symptoms (distress and sadness); Factor 4 is related to neural symptoms (numbness). These data were suitable for factor analysis, as the

KMO value of the sample is 0.760, which is much larger than the acceptable 0.5, prompting good constructure. (Table 3)

Table 3
Construct Validity of the M. D. Anderson Symptom Inventory: Baseline Factor Loadings of the Core Symptom Items (N = 342)

Symptom	Factor 1	Factor 2	Factor 3	Factor 4
Disturbed sleep	**.790**	.054	− .073	− .105
Pain	**.742**	.047	− .012	.144
Fatigue	**.674**	.110	.270	.022
Shortness of breath	**.613**	.041	.187	− .119
Change in taste	**.597**	.420	.089	.311
Drowsiness	**.595**	− .031	.000	− .112
Diffificulty remembering	**.524**	− .141	− .022	.243
Dry mouth	**.443**	− .049	.308	.395
Nausea	.127	**.925**	.088	− .028
Vomiting	.057	**.923**	− .048	− .031
Distress	.440	.022	**.841**	.083
Sadness	.484	.056	**.815**	− .015
Numbness	.128	− .010	.007	**.889**
Kaiser- Meyer-Olkin (KMO) 0.760.				
Values in bold indicate that they belong to the same factor.				

Known-Group Validity

Known-group validity analysis showed that patients with age > 50 years old scores(2.002 ± 2.485) were higher than ≤ 50 years old patients(1.709 ± 2.258). The symptom scores of the education level > 9 years(1.657 ± 2.167) were higher than the level ≤ 9 years(2.093 ± 2.586). Patients with KPS of > 70(1.650 ± 2.191) had signifificantly lower scores than those with KPS of ≤ 70(4.077 ± 3.089). The higher the patient's cancer stage, the higher the scores. The patient's symptom scores of in treatment(2.523 ± 2.512) were higher than those before and after treatment(1.551 ± 2.256). The symptoms of employed patient(1.366 ± 1.927) were lower than those of patients with retirement or unemployed(1.961 ± 2.453). The above difference has significant (P < 0.001). (Fig. 1)

Cluster Analysis

Explored the correlation between symptoms by clustering analysis, and the relative distance between the symptom groups was shown in Fig. 2. The figure showed the result of cluster analysis, which was used to check the similarities of the symptom items. Symptoms that were previously related (left side of the figure) were more relevant than the symptoms that were connected later (right side of the figure). As shown in Fig. 2: nausea and vomiting, sadness and distress, fatigue and drowsiness were highly correlated.

Clinical Application

All symptoms of the MDASI-C scale 0–10 were divided into mild (0–3), moderate (4–6), and severe (7–10). The top three symptom items were disturbed sleep (3.10 ± 2.52), diffificulty remembering (2.54 ± 2.30) and fatigue (2.24 ± 2.13). Among them, the proportion of patients with disturbed sleep (7–10) was 14.6%. The top three interference items were: work (3.95 ± 2.86), enjoyment of life (2.87 ± 2.85) and relations with others (2.16 ± 2.97), and patients with severe score (7–10) were: 19.3%, 14.0% and 12.9%, respectively. (Table 4)

Table 4
Mean and Percentage of Patients With Moderate and/or Severe Scores for Each Item (N = 342)

Symptom	Mean Score ± SD	Score ≤ (3%)	Score > 6 (%)
Severity			
Disturbed sleep	3.10 ± 2.52	62.0	14.6
Diffificulty remembering	2.54 ± 2.30	70.8	6.4
Fatigue	2.24 ± 2.13	76.0	3.5
Dry mouth	1.91 ± 2.06	87.7	4.7
Distress	1.91 ± 2.32	74.3	4.7
Sadness	1.82 ± 2.27	76.6	4.1
Pain	1.76 ± 2.34	83.0	6.4
Lack of appetite	1.74 ± 2.27	80.7	5.3
Drowsiness	1.58 ± 1.86	85.4	1.8
Numbness	1.53 ± 2.18	84.2	4.1
Shortness of breath	0.85 ± 1.57	94.2	1.8
Nausea	0.58 ± 1.22	95.9	0
Vomiting	0.30 ± 0.86	98.8	0
Interference items			
Work	3.95 ± 2.86	48.5	19.3
Enjoyment of life	2.87 ± 2.85	60.8	14.0
Relations with others	2.16 ± 2.97	72.5	12.9
Mood	1.89 ± 2.31	76.6	4.7
Activity	1.34 ± 2.12	88.3	4.1
Walking	1.33 ± 2.25	88.3	4.7

SD = standard deviation. Data are presented as median (range) or absolute frequency (%).

As shown in the correlation hotmap of Fig. 3, there was a forward correlation between most symptom items and interference items. We correlated the age with their symptoms. The results showed that except for gastrointestinal symptoms (nausea, vomiting, lack of appetite), psychologyical symptoms (sadness, distress, mood), other symptoms were aggravated as age increased. Symptoms with close relationships with marital status include: fatigue, disturbed sleep, dry mouth, distress, shortness of breath, activity and walking. The correlation analysis of the educational level shown that most of the symptom and

interference items were reduced as the educational level was increased. However, the closer scoring relationship was the patient's KPS, in addition to diffificulty remembering, all other symptom and interference items were reduced as KPS scores increase.

As shown in Fig. 4, we further analyzed the patient biochemical indicators and symptoms. As the patient's BMI increased, the patient's pain, disturbed sleep, and diffificulty remembering would be aggravated, and numbness would alleviate. The items associated with Hb levels were: fatigue, disturbed sleep, dry mouth, sadness, mood, relationships with others and walking. The higher the A/G of the patient, the lower their fatigue, sleep disorder, shortness of breath, appetite, dry mouth, emotions, walking and enjoy the life ratings. Closely related to ALP: shortness of breath, diffificulty remembering, dry mouth, activity, relations with others, walking and enjoyment of life, and they are positively correlated.

Discussion

As our clinical work, many studies have shown that accurate assessments of the symptoms of malignant tumors including breast cancer patients are very important[5, 23–25]. Because only accurate assessments can sufficiently grasp the symptoms of the patient, and thereby discover the features and may perform targeted intervention. In this study, we assessed the effectiveness of MDASI-C in breast cancer. At the same time, we also analyzed factors affecting the symptoms of patients. In this study, 342 patients in group covered almost all types of breast cancer patients, which had good representation.

The reliability test results suggested that cronbach's alpha value was close to 0.9, close to the level of excellent reliability. The KMO value of the construct validity test indicated that the scale had good construct validity. Four factors were obtained by factor analysis, representing four different symptoms. At the same time, we conducted a known-group validity analysis. The results showed that symptoms of patients with age ≥ 50 years were higher. KPS > 70 patient symptom scores were lower. The later the cancer stage, the more serious the patient's symptoms. The symptom score of patients in treatment was higher. This was consistent with the previous research results[26–28]. This is also the case where we are clinically seen. Therefore, age, KPS, cancer stage can distinguish patients, and it is also a commonly used index. Interestingly, we have found that the symptoms of patients with more than 9 years of education are lighter, and the symptoms will alleviate with the increase of education years. We analyzed that patients with high level education can be rationally dealt with their own condition and mentality. Moreover, the correlation hot map shows that the higher the level of education, the earlier the patient's cancer stage. That is to say, the cancer stage of higher level education is earlier. At the same time, the symptom of employed patients was lower than that of patients with retirement or unemployed. This may be because patients in the work will put more time and energy at work, thereby dispersing the attention of their own symptoms.

Previous studies have shown that symptoms of cancer patients often appear with cluster[29, 30]. Our cluster analysis results showed that nausea and vomiting, sadness and distress, fatigue and drowsiness were highly relevant. This is the same as our expectations, and the symptomatic direct correlation is often

accompanied, which is also consistent with the clinical observed situation. In addition, we can see from the related hot maps that there is a forward correlation between most symptom items and the interference items, which further illustrates the aggregation between symptoms.

We made statistics on each item of the patient, according to the ratio of mild (≤ 3) and severe (> 6). We found that patients with severe sleep disorders were 14.6%, meaning that more than 1/7 patient suffered serious sleep problems, which requires us to pay high attention. The severe interference proportional to the work, enjoyment of life and relations with others was 19.3%, 14.0% and 12.9%, respectively. Analysis of the cause may be multifaceted, such as the disease itself and anti-tumor treatment. Of course, it may also be related to changes in work and family after sick. After all, patients under the age of 50 are much more, and these people will have different degrees of impact due to illness, and even lose their jobs. Enjoyment of life and relations with others are an important part of life quality. If you want to increase the quality of life of breast cancer, you must pay attention to them.

As with many articles, our research also shows that the biochemical indicators of patients with breast cancer will affect their symptoms, including: BMI, Hb, A/G, ALP[31–33]. Among them, BMI, Hb, and serum albumin reflect the nutritional status of the patient, and ALP is closely related to cancer load or stage. Therefore, they will affect the symptoms of breast cancer patients.

As mentioned above, MDASI-C was used to assess the symptoms of Chinese breast cancer patients, which were characterized as follows. First, it provides an objective and effective scale for symptomatic precision assessment of Chinese breast cancer patients. Second, it can be used for monitoring the symptoms of patients with breast cancer, assistance to discovering the changes and providing precision strategies for this purpose. Finally, it provides a standardized form to avoid the subjective judgment between different hospitals or doctors to assess clinical symptoms.

This study also has some limitations. First, our patients come from the same cancer center. Second, we did not add interventions to the research. It is very meaningful to study the symptom change in patients with breast cancer before and after a certain intervention. This will continue to advance in our follow-up research.

Conclusion

Our research shows that MDSI-C is effective and reliable for assessing the symptoms of Chinese breast cancer patients. The patient's age, education level, work and marriage status, KPS status, cancer stage, BMI, A/G, ALP and Hb will affect the patient's symptoms vary from degrees. Using this scale, we can provide more targeted interventions to increase the quality of life of patients with breast cancer while prolonging patient survival.

Declarations

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Conflict of interest

All authors declare that they have no conflict of interest.

Ethical approval

This study was approved by the Ethics in Research Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, China.

Informed consent

Informed consent was obtained from all individual participants included in the study. Participants gave consent for processing their coded responses and merging these with their clinical data.

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Figures

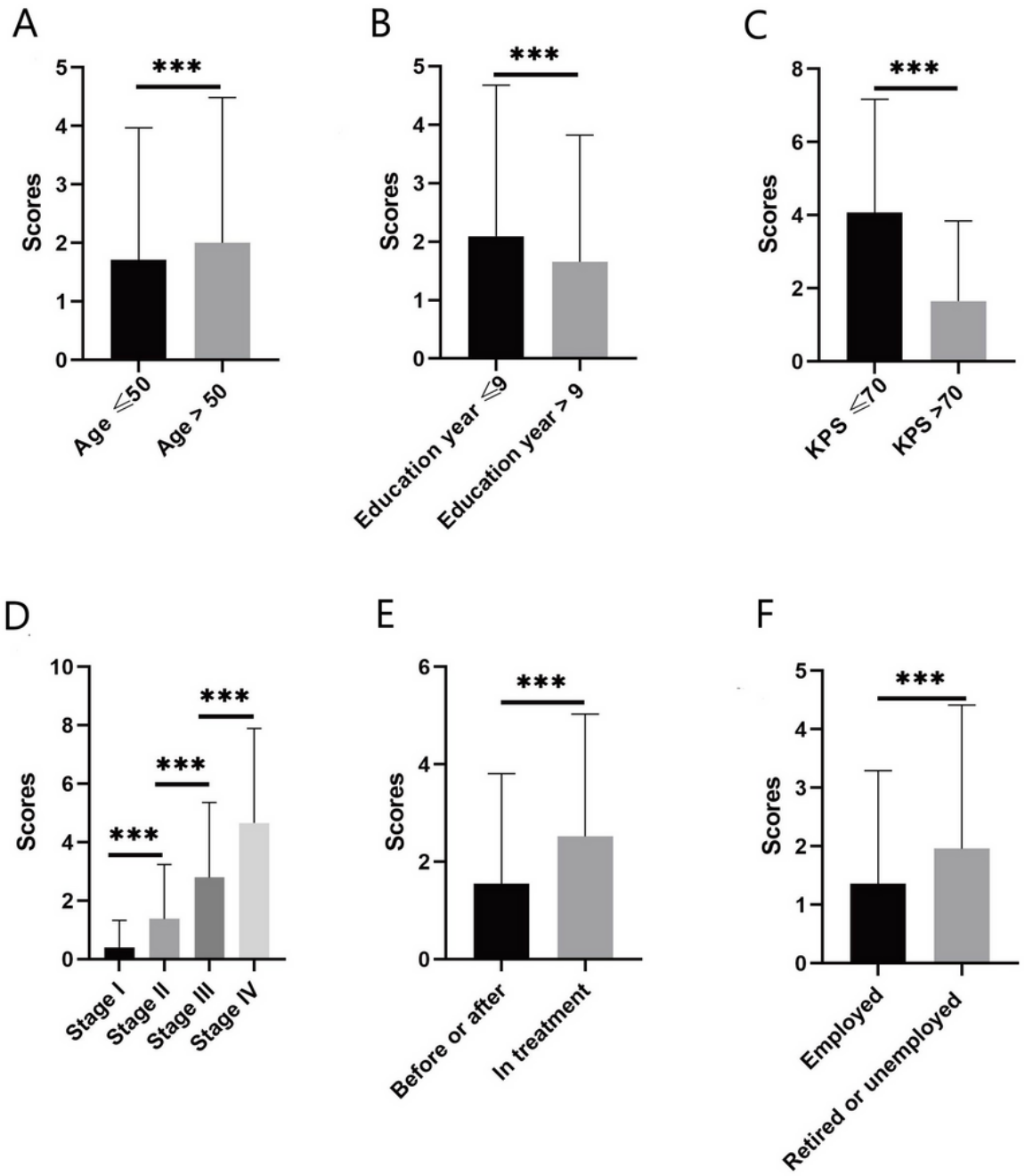

Figure 1

Known-group validity analysis. (A) patients with age > 50 years old scores(2.002±2.485) were higher than ≤50 years old patients(1.709±2.258). (B) patients with the education level > 9 years(1.657±2.167) were higher than the level ≤ 9 years(2.093±2.586). (C) Patients with KPS of >70(1.650±2.191) were lower than those with KPS of ≤ 70(4.077±3.089). (D) The higher the patient's cancer stage, the higher the scores. (E) patients in treatment(2.523±2.512) were higher than those before and after treatment(1.551±2.256). (F)

employed patients(1.366±1.927) were lower than those of patients with retirement or unemployed(1.961±2.453). “* * *” means P <0.001.

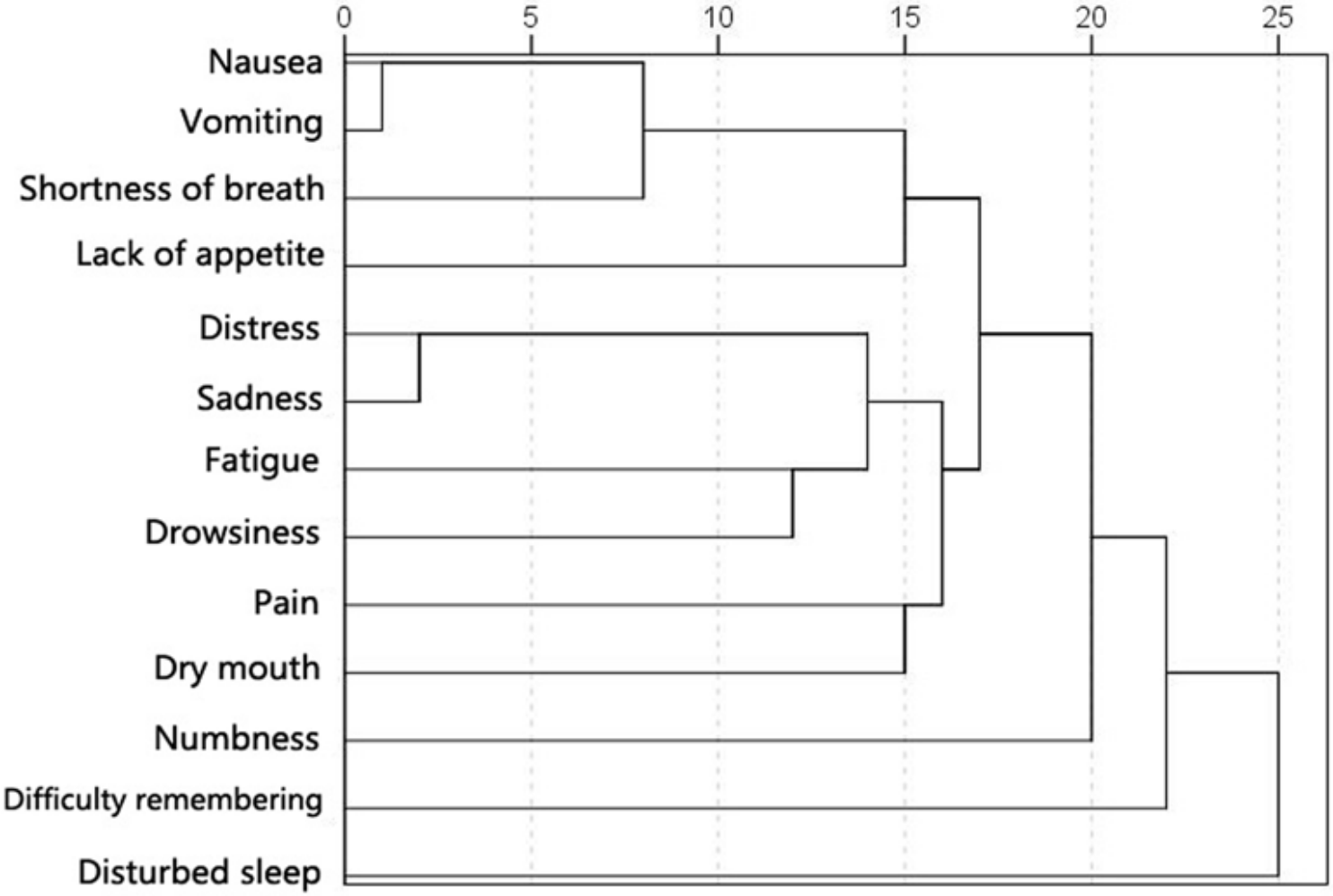

Figure 2

Hierarchical clustering analysis with dendrogram showing relative distances between item clusters. Clusters were formed based on the distance between symptom ratings, which was calculated using squared Euclidian distances. Symptoms that join together earlier (toward the left side of the fifigure) are more similar than symptoms that join together later (toward the right side of the fifigure).

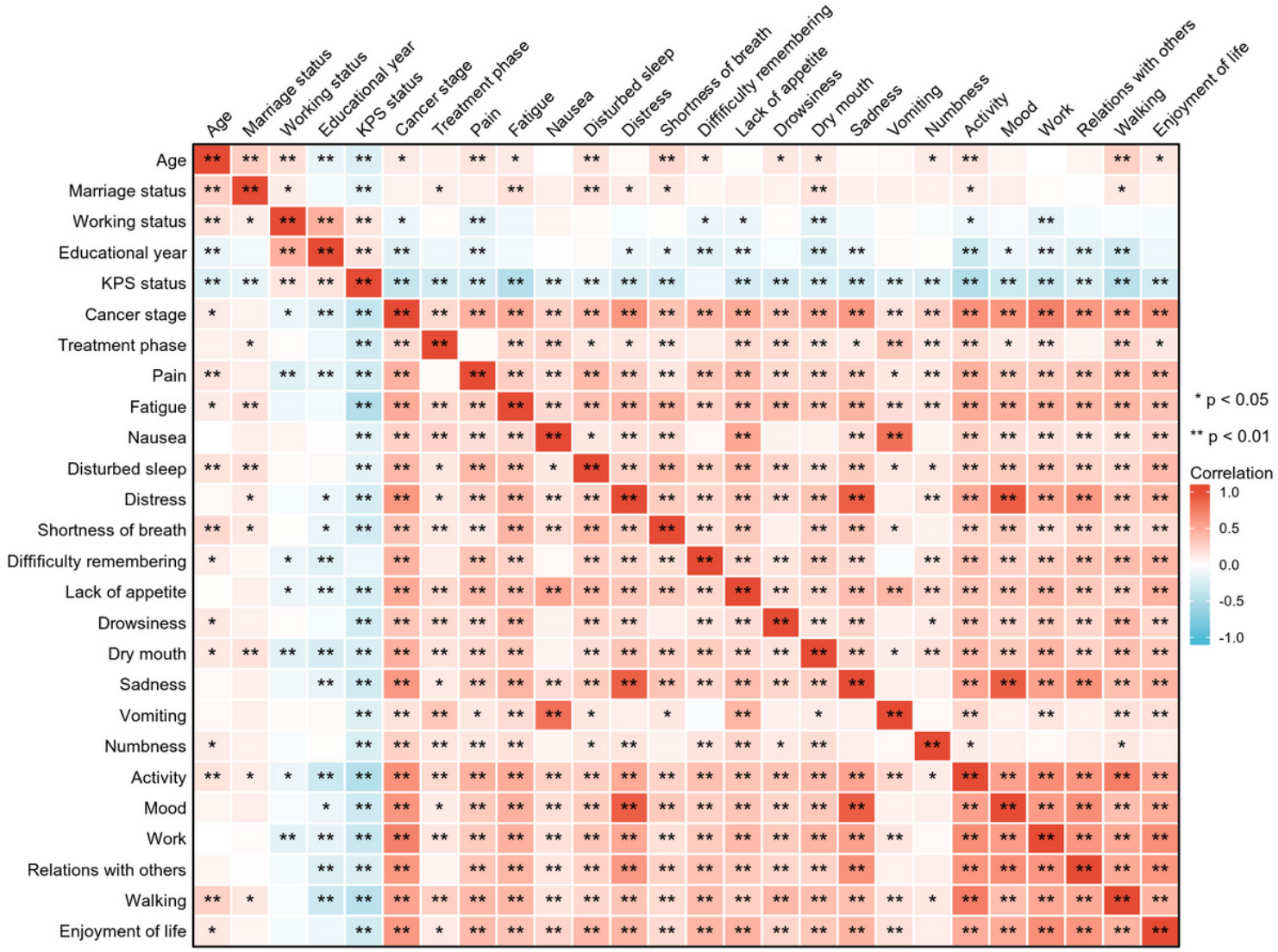

Figure 3

Correlation hotmap of clinical parameters(KPS status, treatment phase, cancer stage, age, marriage status, education level, working status) and symptoms. The figure also showed the degree of correlation between each item and other symptom and interference items. Red represents positive correlation, and blue is negatively correlated. The deeper the color, the more obvious correlation. “ *” means P <0.05. “* *” means P <0.01.

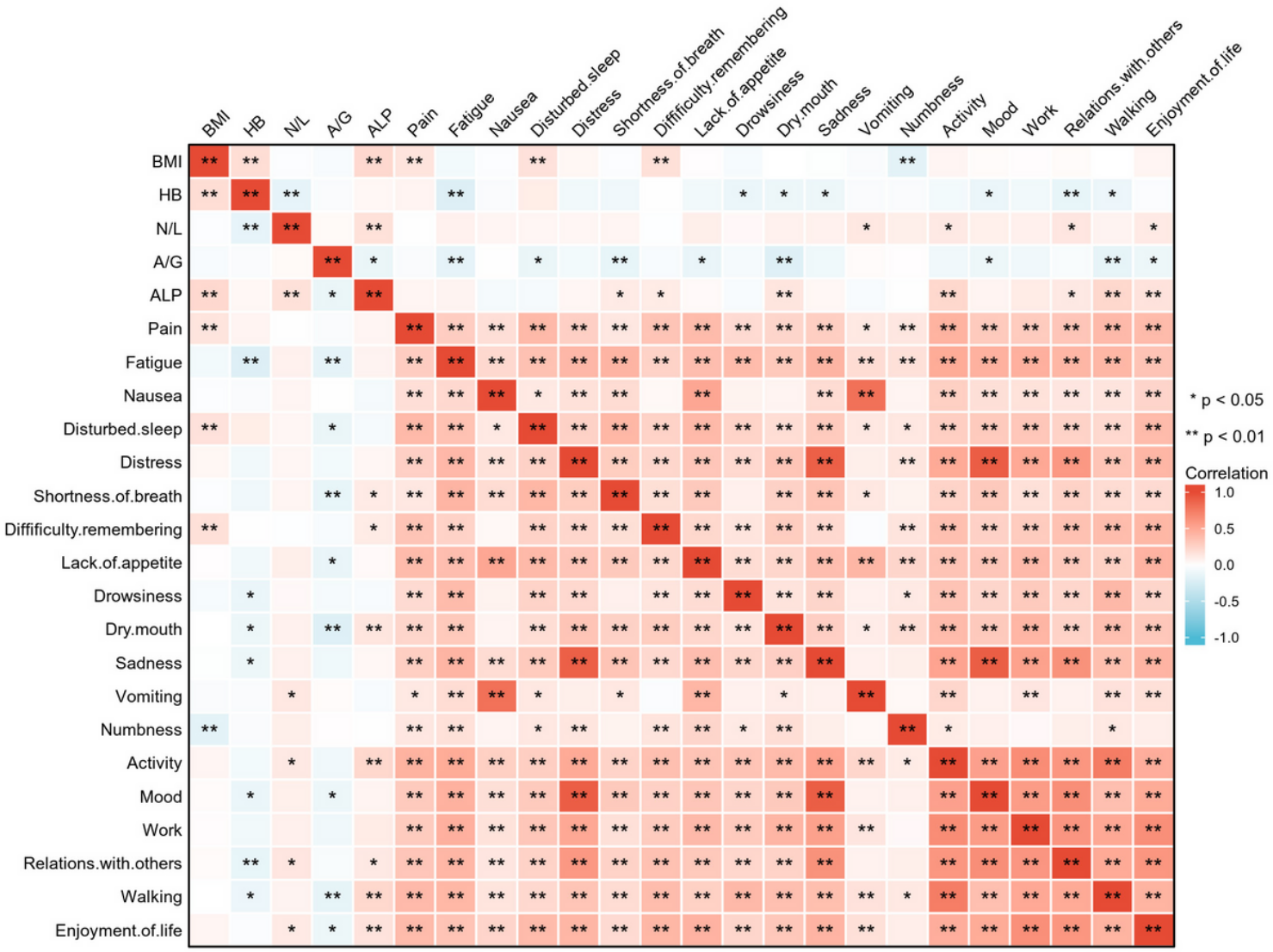

Figure 4

Correlation hotmap of biochemical Indicators (Body Mass Index (BMI), hemoglobin (Hb), alkaline phosphatase (ALP), neutral granulocyte lymphocyte ratio (N/L), and serum albumin globulin ratio (A/G)) and symptoms. The figure also showed the degree of correlation between each item and other symptom and interference items. Red represents positive correlation, and blue is negatively correlated. The deeper the color, the more obvious correlation. “ *” means P <0.05. “* *” means P <0.01.