ACCSCIENCE PUBLISHING

Eurasian Journal of Medicine and Oncology

ORIGINAL RESEARCH ARTICLE

Influencing factors of chemotherapy-related cognitive impairment in patients with breast cancer

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Abstract

Introduction: The chemotherapy-related cognitive impairment is common, but the influencing factors and effective intervention measures are not well known.

Objective: To investigate the changes of cognitive function in breast cancer patients before and after chemotherapy, identify the influencing factors of cognitive function in chemotherapy patients, and investigate whether there is a mediating effect among multiple factors. Finally, an intervention was implemented for patients experiencing cognitive dysfunction to evaluate its effects on cognitive function.

Methods: Using the convenience sampling method, we recruited 380 breast cancer chemotherapy patients at three tertiary hospitals in Xi'an from October 2018 to May 2019. The Chinese version of the Functional Assessment of Cancer Therapy-Cognitive Function scale, the Hamilton Anxiety Scale, the Hamilton Depression Scale, and the social support rating scale were used to evaluate the cognitive function of breast cancer patients during chemotherapy, and analyze the influencing factors of cognitive function.

Results: The incidence of chemotherapy-related cognitive dysfunction in breast cancer patients was 19.74% (75/380). The results of the univariate analysis showed that the education level, medical expense payment method, family history of breast cancer, disease stage, and presence of comorbidities could impact cognitive functioning in breast cancer patients receiving chemotherapy ($p<0.05$). Correlation analysis revealed that there was a negative correlation among cognitive function and anxiety and depression ($p<0.01$), while a positive correlation with social support ($p<0.05$). Furthermore, multivariate stepwise regression analysis showed that the education level, medical expense payment method, disease stage, depression, and social support were independent influencing factors of cognitive function in breast cancer patients receiving chemotherapy and that depressive symptoms had a mediating effect in the relationship between social support and cognitive function. Cognitive has been shown to have a positive impact on cognitive function.

Conclusion: Cognitive dysfunction in breast cancer patients receiving chemotherapy is a multifactorial condition that requires rigorous educational and social support interventions for improvements of patient outcomes.

Keywords: Breast cancer; Chemotherapy; Chemotherapy-related cognitive impairment

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Citation: Zhang Y, Wu S, Ma Y, *et al.* Influencing factors of chemotherapy-related cognitive impairment in patients with breast cancer. *Eurasian J Med Oncol.* 2025;9(3):133-146.
doi: 10.36922/EJMO025130073

Received: March 27, 2025

Revised: April 26, 2025

Accepted: May 8, 2025

Published online: June 3, 2025

1. Introduction

Breast cancer is among the most prevalent malignant tumors affecting women globally, significantly impacting women's health and quality of life.[1] Chemotherapy constitutes an essential component of systemic treatment for breast cancer, both in pre-operative and post-operative settings, playing a critical role in patient management. With advancements in adjuvant intensive and metronomic chemotherapy, a variety of long-term oral chemotherapy regimens have emerged. As a cytotoxic anti-tumor agent, chemotherapy can induce a range of adverse reactions, including gastrointestinal disturbances (such as nausea, vomiting, diarrhea, and constipation), myelosuppression (manifested as leukopenia and thrombocytopenia), alopecia, hepatic and renal impairment, and vascular damage.[2] These side effects have garnered considerable attention and are well-managed in clinical practice. However, it is important to highlight that chemotherapy-related cognitive dysfunction remains an underexplored issue in cancer treatment and management.[3] This challenge is closely associated with the absence of standardized evaluation criteria and routine intervention protocols.

Chemotherapy-related cognitive impairment (CRCI) is characterized by a decline in cognitive function observed in cancer patients during or following chemotherapy, primarily manifesting as memory loss and diminished concentration.[4] According to the American Cancer Society, CRCI encompasses difficulties in thinking, concentrating, recalling details, and managing multiple tasks simultaneously, as well as challenges with word recall and decreased task efficiency.[5] Research indicates that 16 – 75% of breast cancer patients undergoing chemotherapy experience moderate-to-severe cognitive impairment during treatment, with 35 – 45% continuing to exhibit symptoms post-treatment.[6,7] CRCI adversely affects self-esteem, impedes interpersonal communication, and hinders individuals' ability to reintegrate into society.[8] Consequently, CRCI in cancer patients has emerged as a critical issue warranting increased attention and emphasis.

At present, there is a notable paucity of research specifically addressing CRCI, its influencing factors, and the interconnections between these factors in cancer patients. The potential mechanisms underlying CRCI primarily involve organic changes in the brain and psychosocial factors. Chemotherapy agents are known to adversely affect the nervous system by inducing localized inflammatory responses and causing global alterations in hormonal and metabolic levels. Research by Yao *et al.*[9] has demonstrated significant anatomical reshaping of the prefrontal lobe in patients undergoing chemotherapy, which may serve as the physiological basis for cognitive dysfunction. Several factors are recognized as influencing the cognitive function of cancer patients receiving chemotherapy, including hemoglobin levels, social support, and emotional state. Hemoglobin is a critical indicator of anemia, and its decline following chemotherapy can lead to cerebral hypoxia, disrupt cellular enzyme activity, impair brain metabolism, and consequently damage cognitive function.[10] Conversely, social support can provide mental stimulation to synapses and neurons, thereby playing a compensatory role in maintaining normal cognitive function. According to the study by McHugh Power *et al.*,[11] social support is significantly associated with cognitive function to a certain degree during follow-up periods. Moreover, anxiety and depression emerge as key predictors among the factors affecting sleep quality. Cancer patients exhibiting higher levels of depressive tendencies are consistently associated with cognitive dysfunction persisting for 6 months or more following chemotherapy. This may be attributed to the depressive state disrupting the balance of the hypothalamic-pituitary-adrenal cortex axis, potentially causing damage to neurons and the central nervous system, thereby impairing memory and executive function.[12]

Recent research indicates that CRCI encompasses cognitive domains such as memory, language ability, and executive function,[13] aligning with observed deficits in memory, diminished attention, and reduced processing speed.[14] Nevertheless, the prevalence and determinants of chemotherapy-induced cognitive dysfunction in breast cancer patients remain inadequately understood. This study employed the Functional Assessment of Cancer Therapy-Cognitive Function (FACT-Cog) scale, as part of the American Chronic Disease Management System, to assess cognitive function levels in breast cancer patients undergoing chemotherapy. The aim was to gain a comprehensive understanding of their cognitive function status and to investigate the sociopsychological factors influencing cognitive function during chemotherapy. In addition, the study explored potential mediating effects and interactions among various factors. Subsequently, we implemented cognitive behavioral therapy to address cognitive dysfunction in patients following chemotherapy. This study aimed to preliminarily investigate the intervention's efficacy in ameliorating cognitive dysfunction, with the goal of offering an effective and feasible rehabilitation nursing strategy for breast cancer patients. The findings aim to inform the development of evidence-based interventions to enhance the cognitive function of breast cancer patients receiving chemotherapy.

2. Materials and methods

2.1. Study design and participants

Between October 2018 and May 2019, a cohort of patients diagnosed with breast cancer was selected through convenience sampling. All participants were exclusively undergoing chemotherapy, which included neoadjuvant chemotherapy before surgery and adjuvant chemotherapy following surgery, with a minimum of three chemotherapy cycles. The inclusion criteria are as follows: (i) patients diagnosed with primary breast cancer confirmed by biopsy or post-operative pathology; (ii) patients who received no more than three cycles of chemotherapy; and (iii) patients possessing effective communication skills, which enable them to make informed consent. The exclusion criteria include: (i) patients with brain metastases; (ii) patients with other significant diseases; (iii) patients with malignant tumors in other anatomical locations; and (iv) patients who received alternative treatments, such as targeted therapy, radiotherapy, or immunotherapy. This study received ethical approval from the Ethics Committee of the Shaanxi Provincial People's Hospital, Xi'an (approval number: 2021071609). Based on the sample size estimation formula commonly employed in medical research,[15] the incidence rate of cognitive impairment among patients undergoing chemotherapy for breast cancer ranges from 16% to 75%. Consequently, the minimum required sample size for this study was determined to be 196 participants. Ultimately, the study encompassed a total of 380 breast cancer patients.

2.2. Data collection instruments

2.2.1. General information questionnaire

A custom-designed questionnaire was employed to collect demographic and sociological data, including variables such as age, gender, body mass index (BMI), educational attainment, marital status, and occupation. Furthermore, clinical disease data encompass various parameters, including the stage of the disease, family medical history, the presence of complications, and the existence of comorbid conditions such as diabetes, among other factors.

2.2.2. Cognitive function assessment

The cognitive function of the patients was assessed utilizing the Chinese version of the Functional Assessment of Cancer Therapy–Cognitive Function (FACT-Cog) Scale. This scale was originally developed by Wagner *et al.*[16] and subsequently translated into Chinese by Cheung's team in Singapore,[17] in accordance with the guidelines established by the Functional Assessment of Chronic Illness Therapy (FACIT) and the International Society for Pharmacoeconomics and Outcomes Research. The scale comprises 37 items distributed across four dimensions: perceived cognitive impairment (20 items), comments from others (4 items), perceived cognitive abilities (9 items), and impact on quality of life (4 items). Each item is rated on a 5-point Likert scale ranging from 0 to 4, with higher scores indicating better cognitive function. The estimated minimum clinically important difference (MCID) for this scale is between 6.9 and 10.6 points.[18] A difference exceeding this range in pre- and post-study scores for the same subject is considered clinically significant, indicating potential cognitive dysfunction. In this study, the maximum MCID score utilized was 10.6. The Cronbach's alpha coefficient for the scale was 0.96, indicating high internal consistency.

2.2.3. Anxiety and depression assessment

The Hamilton Anxiety (HAMA) Scale and the Hamilton Depression (HAMD) Scale were employed to assess anxiety and depression levels following chemotherapy. The HAMA Scale consists of 14 items related to anxiety, each rated on a 4-point scale ranging from "no symptoms" to "extremely severe." A standardized score of ≥7 signifies the presence of anxiety, with severity levels delineated as possible anxiety (7 – 14), anxiety (14 – 21), obvious anxiety (21 – 29), and severe anxiety (≥29). Similarly, the HAMD Scale comprises 17 items pertaining to depressive symptoms, scored in a manner analogous to the HAMA Scale. A standardized score of ≥7 indicates the presence of depression, with severity classified as mild (7 – 17), moderate (17 – 24), or severe (≥24).

2.2.4. Level of social support

The social support rating scale (SSRS), developed by Shuiyuan Xiao,[19] is a widely utilized instrument for assessing varying levels of social support experienced by individuals. The scale comprises 10 items distributed across three dimensions: objective social support, subjective social support, and the utilization of social support. The total SSRS score ranges from 12 to 66, with higher scores indicating greater levels of social support. Specifically, a total SSRS score below 22 signifies a low level of social support, scores between 23 and 44 denote a medium level, and scores above 44 reflect a high level of social support. The Cronbach's alpha coefficients for the overall scale and its three dimensions were 0.896, 0.849, 0.825, and 0.833, respectively, demonstrating good reliability.

2.2.5. Method of intervention

Patients who exhibited cognitive dysfunction in the prior assessment were allocated to the intervention group. The intervention group was provided with cognitive behavioral intervention training in addition to the conventional treatment and health rehabilitation guidance

and education. This training was conducted in a quiet, comfortable, and enclosed setting, occurring twice weekly for sessions lasting 60 minutes each, with the flexibility to adjust based on individual patient needs. The cognitive function changes in the intervention group were assessed using the FACT-Cog scale before the intervention and 3 months post-intervention. The specific components of cognitive behavioral intervention encompass attention enhancement, visuospatial skill development, memory training, orientation exercises, executive function training, and computational ability enhancement.

2.3. Statistical analysis

The data were entered into Epidata 3.0 to construct a database, and statistical analyses were performed using SPSS 26.0 (IBM SPSS 26.0, SPSS Inc.) and AMOS 22.0 software (Amos Development Corporation, Chicago, IL, USA). Descriptive statistics are presented as mean ± standard deviation (SD) for continuous variables and as frequency and percentage for categorical variables. The impact of variables from the general population and disease data on cognitive function was evaluated using one-way analysis of variance. Both unadjusted and multivariable-adjusted logistic regression models were employed to analyze cognitive function. Differences between the two groups were compared using the *t*-test. Explanatory factor analysis was conducted utilizing maximum likelihood estimation with orthogonal rotation, with the scree plot and eigenvalues (≥1) employed to determine the requisite number of factors. Subsequently, confirmatory factor analysis was performed using maximum likelihood estimation methods, and various statistical indices were utilized to assess model fit, including the ratio of the χ^2 to degrees of freedom (CMIN/DF)/Chi-squared statistics, root mean square error of approximation, comparative fit index, standardized root mean square residual, goodness-of-fit index (GFI), adjusted GFI, and Tucker–Lewis index. The ft indices of models were evaluated against the predefined criteria. $p<0.05$ indicated statistically significant difference.

3. Results

3.1. Characteristics of study participants

Table 1 presents the baseline characteristics of the study population. The average age of participants was 63.81 years (SD = 9.01), with a significant proportion (41.05%) being over 41 years of age. The majority of participants were female (99.47%) and married (91.32%). In addition, 61.9% reported no family history of breast cancer, and 73.1% had <12 years of education, with most having completed high school to college education. Furthermore, 36.58% of participants were unemployed, 85.79% had no family history of breast cancer, and 84.47% reported no complications. The predominant living arrangement was with a spouse and children, accounting for 87.89% of the participants. Regarding cancer staging, 24.21% were at stage I, 44.21% at stage II, 21.84% at stage III, and 9.74% at stage IV. Sixty-nine cases (18.16%) had diabetes mellitus, while 311 cases (81.84%) did not. In addition, there were 98 cases (25.79%) with a BMI <18.5 kg/m², 121 cases (31.84%) with a BMI between 18.5 and 24 kg/m², 105 cases (27.63%) with a BMI between 24 and 28 kg/m², and 56 cases (14.74%) with a BMI ≥28 kg/m² (Table 1).

3.2. Status of cognition function in breast cancer patients

Following chemotherapy, the FACT-Cog score among the 380 patients in this study was 104.76 ± 22.18 points. Among these patients, 75 exhibited a decrease of ≥10.6 points compared to their pre-chemotherapy scores, indicating a chemotherapy-related cognitive dysfunction incidence rate of 19.74%. The four dimensions assessed were perceived cognitive impairment (58.89 ± 8.19), comments from others (12.95 ± 2.10), perceived cognitive abilities (18.71 ± 7.01), and impact on quality of life (11.68 ± 1.74). A comparison of scores before and after chemotherapy is presented in Table 2.

3.3. Depression, anxiety, social support, and cognitive function in breast cancer patients undergoing chemotherapy

Among 380 breast cancer patients who underwent chemotherapy, 185 individuals (48.68%) exhibited symptoms of anxiety. The prevalence of mild, moderate, and severe anxiety was 30%, 15.79%, and 2.89%, respectively, with an average anxiety score of 16.18 ± 3.77. In addition, 184 patients (48.42%) experienced depressive symptoms, with the incidence rates of mild, moderate, and severe depression being 31.58%, 14.47%, and 2.37%, respectively. The average depression score was 17.39 ± 3.95 (Table 3).

The overall social support scores averaged 38.34 ± 16.31 points, comprising 12.23 ± 16.77 points for objective support, 18.82 ± 3.86 points for subjective support, and 6.61 ± 1.05 points for support utilization. Among the participants, 48 cases (12.63%) exhibited low levels of social support, 201 cases (52.89%) demonstrated medium levels, and 130 cases (34.21%) showed high levels of social support. The *t*-test analyses indicated that both the total and individual dimension scores of social support for patients with breast cancer post-chemotherapy were significantly lower than the normative scores of a healthy domestic population[20] ($p<0.05$), as detailed in Table 4.

Table 1. General data of patients undergoing chemotherapy for breast cancer (*n*=380)

Characteristic	Number (*n*)	Percentage
Age (years)		
≤40	78	20.53
41 – 59	156	41.05
≥60	146	38.42
Gender		
Male	2	0.53
Female	378	99.47
Marital status		
Married	347	91.32
Unmarried	18	4.74
Divorced/widowed	15	3.94
Education level		
Junior middle school and below	87	22.89
Senior high school/technical secondary school	187	49.21
College and above	106	27.90
Occupation		
Farmer	150	39.47
Worker	60	15.79
Cadre	37	9.74
Self-employed	86	22.63
Others	47	12.37
Work status		
Retired	41	89.89
On-the-job	110	28.95
Unemployed	139	36.58
Others	90	23.68
Per-capita monthly household income (RMB)		
<2000	45	11.84
2000 – 2999	73	19.21
3000 – 3999	127	33.42
4000 – 4999	90	23.69
≥5000	45	11.84
Health insurance status		
Provinces and cities medicare	101	26.58
Medical insurance for urban workers	64	16.84
Medical insurance for urban residents	65	17.11
New rural cooperative medical scheme	150	39.47
Family history of breast cancer		
Yes	54	14.21
No	326	85.79

(*Contd*...)

Table 1. (*Continued*)

Characteristic	Number (*n*)	Percentage
TNM stage		
I	92	24.21
II	168	44.21
III	83	21.84
IV	37	9.74
Complication		
Yes	59	15.53
No	321	84.47
Living situation		
Living alone	46	12.11
Not living alone	334	87.89
Diabetes		
Yes	69	18.16
No	311	81.84
BMI (kg/m^2)		
<18.5	98	25.79
18.5 – 24	121	31.84
24 – 28	105	27.63
≥28	56	14.74

Abbreviation: BMI: Body mass index.

Table 2. Comparison of cognitive function scores of breast cancer patients before chemotherapy and 3 months after chemotherapy

Items	Before chemotherapy	Three months after chemotherapy	t	*p*
Perceived cognitive impairment	62.86±8.18	58.89±8.19	−2.365	0.014*
Comments from others	13.07±2.08	12.95±2.10	−0.112	0.901
Perceived cognitive abilities	26.95±6.66	18.71±7.01	−8.235	0.001**
Impact on QoL	11.79±1.85	11.68±1.74	−0.16	0.863
Total FACT-Cog score	116.71±11.78	104.76±22.18	−4.376	0.001**

Notes: *p<0.05, **p<0.01.
Abbreviations: FACT-Cog: Functional Assessment of Cancer Therapy-Cognitive Function scale; QoL: Quality of life.

Table 3. Analysis of anxiety and depression scores in breast cancer patients undergoing chemotherapy

Items	*n* (%)				Mean±SD
	Not present	Mild	Moderate	Severe	
Anxiety	195 (51.32)	114 (30)	60 (15.79)	11 (2.89)	16.18±3.77
Depression	196 (51.58)	120 (31.58)	55 (14.47)	9 (2.37)	17.39±3.95

Abbreviation: SD: Standard deviation.

3.4. Univariate analysis of factors affecting cognitive function in breast cancer patients

The analysis results suggest several potential factors influencing cognitive function among breast cancer patients. These factors include educational level, method of medical payment, disease stage, and the presence of complications, all of which were statistically significant (p<0.05). For a detailed breakdown, please refer to Table 5.

Table 4. Analysis of social support scores in patients with breast cancer chemotherapy

Items	Breast cancer patients	Domestic norm	*t*	*p*
Objective support	12.23±16.77	12.68±3.47	−3.498	0.001**
Subjective support	18.82±3.86	23.81±4.75	−9.076	0.001**
Support utilization	6.61±1.05	9.38±2.40	−11.201	0.001**
Social support score	38.34±16.31	44.38±8.38	−7.304	0.001**

Notes: *p<0.05, **p<0.01.

3.5. The relationship between anxiety and depression severity, social support levels, and FACT-Cog scores

As illustrated in Table 6, there is a significant relationship between the total FACT-Cog score and perceived cognitive impairment, perceived cognitive abilities, and quality of life among breast cancer patients post-chemotherapy. This score is inversely correlated with anxiety and depression scores (p<0.01). Furthermore, social support exerts a significant influence on the cognitive function of breast cancer patients undergoing chemotherapy. Specifically, the total cognitive function score and its four dimensions exhibit a positive correlation with the total scores of objective support, subjective support, and overall social support (p<0.05), as detailed in Table 6.

3.6. Regression analysis of factors influencing cognitive function in breast cancer patients

The regression analysis, utilizing the bootstrap method with 1,000 iterations, revealed that education level, payment method for medical expenses, disease stage, depression, and level of social support are independent risk factors for cognitive impairment in breast cancer patients (Table 7). In this analysis, the total FACT-Cog score was used as the dependent variable, while the variables showing significant differences in the univariate analysis were included as independent variables. The findings indicate that these factors independently influence cognitive function in breast cancer patients following chemotherapy (p<0.05).

3.7. Path analysis

Figure 1 depicts the sequential mediating roles of social support, depression, and cognitive function. It was found that objective support, subjective support, and support utilization negatively predicted depression, which in turn negatively predicted cognitive function. Through the analysis of mediating effects, it was determined that objective support, subjective support, and support utilization exerted an indirect influence on cognitive function through depression levels. The mediating effects for these identified variables were quantified as 0.031 (95% confidence interval [CI]: 0.005 – 0.065), 0.034 (95% CI: 0.002 – 0.080), and 0.032 (95% CI: 0.007 – 0.065), respectively.

3.8. Effect of the intervention

We administered cognitive behavioral therapy to a cohort of 75 individuals experiencing cognitive dysfunction. The findings indicated that, following a 3-month intervention period, there was a statistically significant improvement in the cognitive function scores of all participants to varying extents. However, these scores did not return to pre-chemotherapy levels. A detailed comparison of cognitive function scores pre- and post-intervention is presented below (Table 8).

4. Discussion

The findings of this study indicate that the FACT-Cog score averaged 104.76 ± 22.18 points, with a clinically significant psychological distress detection rate of 19.74%. This rate aligns with findings from relevant international studies.[14] The cognitive function of perception exhibited the lowest dimension score (18.71 ± 7.01), potentially attributable to the diminished functional connectivity between the hippocampus and the broader brain network post-chemotherapy. Conversely, the highest dimension score, as evaluated by others, was 12.95 ± 2.10 points, corroborating the results of Boscher *et al.*[21] This dimension often manifests as mild and is therefore difficult for patients or their primary caregivers to detect. These findings underscore the necessity for healthcare professionals to recognize and prioritize the cognitive function of patients undergoing chemotherapy, and to develop scientifically informed and appropriate care programs.

In recent years, an increasing number of studies have focused on CRCI in breast cancer patients. Numerous factors contribute to cognitive dysfunction following chemotherapy. This study identified that patients with lower educational levels, those enrolled in the New Rural Cooperative Medical Scheme (NRCMS), those at advanced stages of breast cancer, those with a family history of the disease, and those with additional medical complications are more susceptible to cognitive dysfunction. Educational attainment may serve as an indicator of general intelligence, with higher intelligence levels being associated with a greater density of synapses in the cerebral cortex. This synaptic richness enhances stimulation in cerebral neurons, potentially increasing patients' resilience to cognitive impairment.[22] The increased susceptibility to cognitive dysfunction among NRCMS patients may be attributed to the financial burden that they face compared

Table 5. Analysis of factors influencing cognitive function in breast cancer patients undergoing chemotherapy

Characteristic	Cognitive function scores	Statistics	*p*
Age (years)		3.82	0.460
≤40	104.22±13.53		
41 – 59	103.24±12.71		
≥60	102.11±13.09		
Gender		3.87	0.560
Male	98.22±12.09		
Female	99.56±13.01		
Marital status		4.37	0.055
Married	102.22±20.01		
Unmarried	101.24±19.21		
Divorced/widowed	96.25±20.45		
Education level		4.55	0.010*
Junior middle school and below	97.23±20.56		
Senior high school/Technical secondary school	105.12±18.35		
College and above	110.10±21.13		
Occupation		0.89	0.380
Farmer	105.52±20.15		
Worker	105.31±20.21		
Cadre	103.22±19.36		
Self-employed	104.89±19.22		
Others	103.48±18.93		
Work status		0.93	0.450
Retired	103.55±19.16		
On-the-job	104.57±20.39		
Unemployed	103.13±19.47		
Others	104.53±20.26		
Per-capita monthly household income (RMB)		0.88	0.320
<2000	99.25±16.36		
2000 – 2999	101.56±15.45		
3000 – 3999	102.67±13.22		
4000 – 4999	102.58±15.16		
≥5000	103.09±14.14		
Health insurance status		4.51	0.010*
Provinces and cities medicare	114.36±17.64		
Medical insurance for urban workers	105.37±21.28		
Medical insurance for urban residents	99.73±20.15		
New rural cooperative medical scheme	99.16±21.10		
Family history of breast cancer		-4.03	0.001**
Yes	97.25±28.12		
No	109.53±20.88		
TNM stage		-4.87	0.001**
I – II	106.48±19.31		
III – IV	104.22±21.41		

(*Contd...*)

Table 5. (*Continued*)

Characteristic	Cognitive function scores	Statistics	*p*
Complication		-4.26	0.001**
Yes	97.14±26.37		
No	108.41±21.72		
Diabetes		3.43	0.260
Yes	99.16±21.10		
No	101.73±11.10		
BMI (kg/m^2)		1.09	0.130
<18.5	94.36±13.14		
18.5 – 24	93.67±18.23		
24 – 28	99.73±20.15		
≥28	95.16±11.10		

Notes: *p<0.05, **p<0.01.
Abbreviation: BMI: Body mass index.

Table 6. Correlation between cognitive function and anxiety, depression, and social support in breast cancer patients after chemotherapy

Items	Anxiety	Depression	Social support score	Objective support	Subjective support	Support utilization
Total FACT-Cog score	−0.473**	−0.521**	0.507**	0.391**	0.425**	0.510
Perceived cognitive impairment	−0.366**	−0.438**	0.571*	0.156*	0.169*	0.143
Perceived cognitive abilities	−0.411**	−0.453**	0.488**	0.510**	0.651**	0.630
Impact on QOL	−0.373**	−0.412**	0.514**	0.337**	0.332**	0.449
Comments from others	−0.316	−0.408	0.429**	0.318*	0.411*	0.506

Notes: *p<0.05, **p<0.01.
Abbreviations: FACT-Cog: Functional Assessment of Cancer Therapy-Cognitive Function scale; QoL: Quality of life.

Table 7. Multivariate step-by-step regression analysis of cognitive function in breast cancer patients after chemotherapy

Independent variable	Unstandardized regression coefficient	Standard errors	Standard regression coefficient	*T*	*p*
Fixed value	105.063	19.045	—	5.379	0.000
Education level	0.501	0.124	0.236	4.155	0.000
Health insurance status	8.153	1.718	0.134	4.732	0.000
TNM stage	7.147	1.609	0.116	4.643	0.000
Depression total score	−1.082	0.471	-1.142	-2.316	0.020
Social support score	5.031	1.102	0.123	4.201	0.000

Table 8. A comparative analysis of cognitive function scores pre- and post-intervention between the intervention group

Items	Before therapy	Three months after therapy	*t*	*p*
Perceived cognitive impairment	58.89±8.19	60.26±7.91	2.978	0.006**
Comments from others	12.95±2.10	13.59±6.68	−0.701	0.488
Perceived cognitive abilities	18.71±7.01	21.46±2.89	−2.252	0.032*
Impact on QoL	11.68±1.74	11.21±1.87	−1.359	0.184
Total FACT-Cog score	104.76±22.18	108.18±18.27	−3.304	0.002**

Notes: *p<0.05, **p<0.01.
Abbreviations: FACT-Cog: Functional Assessment of Cancer Therapy-Cognitive Function scale; QoL: Quality of life.

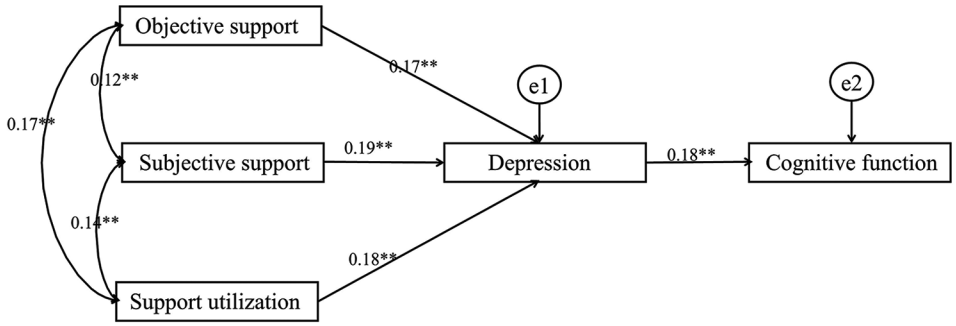

Figure 1. Pathway analysis of social support, depression, and cognitive function. The variables e1 and e2 represent the structure residuals for the depression. Note: $^{**}p<0.01$.

to individuals with other forms of medical insurance. Concerns about family finances, complications, and psychological distress stemming from a family history of breast cancer can elevate psychological stress and negative emotions, thereby exacerbating cognitive impairment. Patients with stage III – IV breast cancer exhibit a higher susceptibility to cognitive impairment compared to those with early-stage disease. This increased vulnerability can be attributed, in part, to the pathophysiological changes induced by the disease itself. In addition, it is associated with the negative emotions experienced by patients in the middle and late stages, who are concerned about the prognosis of their condition. Existing literature has demonstrated a negative correlation between BMI and cognitive function. Individuals with a high BMI, as opposed to those with a low BMI, exhibit poorer performance in language learning and visual modality episodic memory tasks.[23,24] Furthermore, BMI impacts brain volume, with increased BMI being associated with gray matter atrophy in the temporal, frontal, and occipital cortices, as well as in the hippocampus, thalamus, and midbrain, alongside a reduction in white matter integrity throughout the brain.[25] These brain regions are intricately linked to cognitive function, indicating that elevated BMI may be a contributing factor to cognitive impairment. In addition, diabetes emerges as another potential comorbidity influencing cognitive function. Several studies have indicated that type 2 diabetes mellitus can exacerbate age-related cognitive decline.[26,27] Type 2 diabetes mellitus is correlated with deficits in various cognitive domains, including processing speed, attention, spatial working memory, verbal fluency, and executive function.[28] In light of these findings, we examined the BMI levels and diabetes status of the study population to minimize the confounding effects on our research outcomes. Univariate analysis indicated that neither diabetes nor varying BMI levels had a significant impact on the cognitive function of breast cancer patients post-chemotherapy. This result may be influenced by the structural characteristics of the enrolled population and the sample size of the study. Consequently, healthcare professionals can implement tailored cognitive intervention strategies based on the specific characteristics of different patient groups, thereby enhancing the precision and effectiveness of preventing and treating cognitive dysfunction in patients undergoing chemotherapy for breast cancer.

Neuroimaging research has demonstrated a correlation between cognitive function and alterations in neural structures among patients undergoing chemotherapy, with cognitive changes exerting significant effects on neural architecture. In a retrospective study conducted by Kesler *et al.*,[29] it was found that patients treated with anthracyclines exhibited diminished functionality in the left precuneus region of the brain, which was associated with poorer executive and language performance. In addition, an observational study by Piccirillo *et al.*[30] investigated the relationship between self-reported cognitive impairment and structural brain changes. This study revealed significant differences in the connectivity strength within the frontoparietal network between patients with and without cognitive impairment. While the aforementioned studies demonstrated a negative correlation between alterations in brain functional connectivity and perceptual cognitive impairment, they predominantly relied on small sample sizes and retrospective, cross-sectional designs. To address these limitations, we propose conducting larger, prospective studies to investigate the causal mechanisms linking changes in cognitive function and brain structure, as well as the underlying neurobiological trajectories in patients before and after treatment.

Anxiety and depression are prevalent among breast cancer patients following chemotherapy. The apprehension regarding potential adverse reactions to chemotherapy, alterations in body image, and role discrepancies contribute to an increased psychological burden, manifesting as anxiety, depression, and other negative

emotions. Yang *et al.*[31] identified a significant interaction between symptoms of depression and anxiety in this patient population. In the present study, the incidence rates of anxiety and depression post-chemotherapy were 48.68% and 48.42%, respectively. There was a negative correlation between cognitive function scores and scores for anxiety and depression ($p<0.05$, $p<0.01$). Multiple stepwise regression analysis indicated that depression is an independent factor influencing cognitive function, corroborating the findings of Bedillion *et al.*[32] Further studies have demonstrated alterations in frontal lobe function and impaired hormone receptor function in depressed patients, leading to hippocampal neuron death and central nervous system dysfunction, thereby impairing cognitive function.[4] Prolonged exposure to negative emotions has the potential to adversely affect brain structure and result in diminished cognitive function.[33] At present, nursing managers have the capacity to offer psychological counseling to patients, perform emotional assessments, and facilitate the adoption of positive coping strategies through group sandplay therapy.

This study identified a low overall social support score among breast cancer patients, with a positive correlation between social support and cognitive function following chemotherapy ($p<0.01$). Within the dimensions of social support, subjective support scored the highest, followed by objective support, while support utilization scored the lowest, aligning with the findings of Bailey *et al.*[34] Breast cancer patients express a strong desire for psychological and emotional support from family and friends. Such social support can enhance patients' psychological well-being, stimulate brain synapses and neurons, and consequently play a compensatory role in maintaining normal cognitive function. Gates *et al.*[35] implemented a web-based cognitive rehabilitation intervention for patients experiencing post-chemotherapy cognitive dysfunction, demonstrating significantly greater cognitive recovery in the intervention group compared to the control group. These findings suggest that increased understanding and support from healthcare professionals and family caregivers could be an effective strategy for improving the cognitive status of patients undergoing chemotherapy for breast cancer.

This study conducted an in-depth analysis of the mediating effects among social support, depression, and cognitive function in breast cancer patients post-chemotherapy. The findings revealed that the three dimensions of social support negatively predicted depression, which in turn negatively predicted cognitive function. In addition, depression served as a mediator between the three dimensions of social support and cognitive function. Consequently, enhancing levels of social support may mitigate the decline in emotional well-being and cognitive abilities in breast cancer patients undergoing chemotherapy. Healthcare professionals can facilitate this by encouraging patients to strengthen communication with family and friends, proactively seek assistance, and improve their capacity to confront personal challenges. This approach may help alleviate negative emotions, such as anxiety and depression, thereby reducing or preventing cognitive impairment associated with chemotherapy.

At present, intervention strategies for chemotherapy-induced cognitive impairment can be broadly categorized into pharmacological and non-pharmacological treatments. Pharmacological interventions primarily encompass neuroprotective agents, psychostimulants, and traditional Chinese medicine, among others. Nonetheless, the clinical research in this domain is still in its nascent stages, and the efficacy of these treatments requires further validation. Non-pharmacological interventions include cognitive behavioral training, physical exercise, music therapy, and meditation.[36] Notably, empirical studies suggest that cognitive behavioral therapy is beneficial for enhancing cognitive function and improving quality of life.[37]

The findings of this study indicate that, following a 3-month intervention period, both the overall FACT-Cog score and perceived cognitive abilities were elevated compared to pre-intervention levels, although they did not return to baseline. This suggests that consistent cognitive behavioral intervention training may ameliorate cognitive dysfunction in breast cancer patients post-chemotherapy. The plausible explanation may be attributed to the repeated stimulation of neuronal cells through intervention training, which influences the functions of neurotransmitters and receptors within these cells.[38] Furthermore, several studies have demonstrated that behavioral interventions can modulate synaptic plasticity, enhance synaptic transmission, and consequently facilitate the restoration of memory capabilities.[39]

5. Conclusion

The prevalence of chemotherapy-induced cognitive dysfunction among breast cancer patients in this study was 19.74%. The cognitive function of these patients was influenced by factors such as education level, payment method for medical expenses, family history of breast cancer, disease stage, and the presence of complications. Cognitive function demonstrated a negative correlation with anxiety and depression, while showing a positive correlation with social support. Multiple stepwise regression analysis identified education level, payment method for medical expenses, disease stage, depression, and social support as

independent determinants of cognitive function in breast cancer patients undergoing chemotherapy. Furthermore, depression was found to mediate the relationship between social support and cognitive function. Consequently, the cognitive dysfunction observed in breast cancer patients post-chemotherapy is influenced by a multitude of factors. This necessitates heightened awareness among healthcare professionals, the development of scientifically grounded intervention strategies, the enhancement of social support, and efforts to aid patients in improving their cognitive function. This study proposes that cancer-related cognitive dysfunction can be ameliorated through the implementation of cognitive-enhancing strategies in clinical practice. This includes instructing patients in these strategies, advising them to engage in cognitively demanding tasks during periods of optimal cognitive functioning, and administering cognitive behavioral interventions when deemed necessary. However, we did not investigate the relationship between biochemical parameters and cognitive functioning. Further in-depth observation and analysis in the follow-up study are warranted.

Acknowledgments

None.

Funding

This research was funded by the Beijing Sisco Clinical Oncology Research Fund (grant number Y-L2020-0013), the Shaanxi Clinical Medical Research Center for Breast Diseases (grant number 2024SF-LCZX-08), the Natural Science Basic Research Program of Shaanxi Province (grant number 2023-JC-YB-345), Shaanxi Provincial People's Hospital Elite Talent Project (grant number 2022-JY46), and the Shaanxi Provincial People's Hospital incubation fund project (grant number 2022YJY-57).

Conflict of interest

The authors declare no conflicts of interest.

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Ethics approval and consent to participate

This work received ethical approval from the Shaanxi Provincial People's Hospital Ethics Board (Project number: 2021071609). Written informed consent for participation in the study was obtained from all participants before their involvement.

Consent for publication

Written consent from the patient to report individual data for publication was obtained.

Availability of data

Data are available from the corresponding author on reasonable request.

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