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Original Article

The association between neuropsychological impairment, self-perceived cognitive deficit, symptoms, and health related quality of life in newly diagnosed ovarian cancer patients



Liying Wang^{a,b,c}, Yan Ding^{a,d,*}, Yi Zhang^{b,c}, Yaqiong Chen^{b,c}, Mei Xue^{b,c}, Xia Wang^d

^a School of Nursing, Fudan University, Shanghai, China

^b Department of Nursing, Fudan University Shanghai Cancer Center, Shanghai, China

^c Department of Oncology, Shanghai Medical College, Fudan University, Shanghai, China

^d Department of Nursing, Obstetrics & Gynecology Hospital of Fudan University, Shanghai, China

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ABSTRACT

Objective: To assess cognitive function in patients newly diagnosed with ovarian cancer (OC) before treatment and explore the relationship between neuropsychological impairment, self-perceived cognitive deficit, symptoms, and health-related quality of life in them.

Methods: From May 2021 to February 2022, 105 women newly diagnosed with OC were enrolled in the Cancer Center of Fudan University, Shanghai, China. Objective and subjective cognitive functions were assessed using the Montreal Cognitive Assessment (MoCA) scale and Perceptual Deficits Questionnaire (PDQ). Symptoms and quality of life were evaluated using the Memorial Symptom Assessment Scale (MSAS) and Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O), respectively.

Results: This study included 105 newly diagnosed OC patients, with an average age of 49.73 (\pm 8.48) years. Of these, 72.38% had impaired neuropsychological test scores, especially in delayed recall, abstraction, and visuo-spatial/executive function. Retrospective, and prospective memory were the most serious perceived deficits. The results of the MoCA test were not associated with PDQ ($R_s = -0.180$, P = 0.067) and significantly correlated with the distress index, physiological and total scores of the MSAS, and emotional well- being of the FACT-O. The PDQ positively correlated with all MSAS dimensions but not with the FACT-O.

Conclusion: The incidence of neuropsychological impairment in patients newly diagnosed with OC was high, with no association with self-perceived cognitive deficits. It is recommended that healthcare providers include cognitive impairment in symptom management in this population, who may benefit from early assessment, prevention, and intervention.

Introduction

The incidence and mortality of ovarian cancer (OC) are at the forefront of malignant tumors in females. According to global cancer statistics, in 2020, there were approximately 310,000 new cases and 200,000 deaths, which accounted for 2.1% of all cancer-related deaths.¹ Its incidence is increasing rapidly in China owing to reproductive status, hormone levels, and lifestyle changes.^{2,3} Cancer-related cognitive impairment (CRCI) is a common and persistent cancer-related symptom in patients with OC. Studies showed that 17% to 80% of patients reported cognitive dysfunction.⁴ Two years after treatment, the proportion was as high as 70%, with 18% indicating that the symptoms

(specifically, learning and memory) were severe.^{5,6} CRCI severely disturbs patients' daily lives and interpersonal relationships and also reduces their participation in medical decision-making and compliance with treatment.⁷ According to Correa's report, several studies have documented declines in self-reported cognitive function among OC patients, which may have an impact on their quality of life (QOL). However, the findings across these studies were inconsistent, particularly regarding the relationship between neurocognitive changes and QOL.⁸ A previous study suggests that disease-related and treatment-related factors may contribute to the development of neurocognitive changes among OC patients.^{9,10} Studies conducted on patients with other noncentral nervous system malignancies (such as

* Corresponding author. E-mail address: ding_yan@fudan.edu.cn (Y. Ding).

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breast, colorectal, and pancreatic) revealed that approximately 30% to 50% experienced CRCI even before undergoing treatment,¹¹ thus indicating that cancer itself might be responsible for cognitive deficits. Assessing the baseline cognitive function of gynecologic cancer patients prior to treatment initiation holds paramount importance, as those with limited cognitive reserve are more likely to exhibit susceptibility towards.¹² In addition to predicting changes in post-treatment cognitive function, pretreatment CRCI can also exert a direct impact on patients' postoperative quality of life and survival rate through its influence on medication compliance, medical treatment, and health behavior.^{13–15}

Neuropsychological evaluation is regarded as the gold standard for assessing cognitive impairment, and another common method is patient self-reporting.¹⁶ It has been reported that self-reported cognitive impairment is susceptible to the influence of symptoms such as anxiety, depression, and fatigue, whereas neuropsychological tests are less affected by these factors due to their controlled assessment environment. Furthermore, subjective assessments often yield higher incidence rates compared to neuropsychological tests due to the differences in the evaluation of cognitive dimensions.¹⁷ However, the correlation between objective and subjective functions varied due to different populations and assessment tools.¹⁸ Investigating patients' baseline cognitive function prior to treatment and examining the correlation between the two distinct assessment methods and their association with patients' symptoms and quality of life will contribute to a better understanding of the trajectory of CRCI, scientifically interpreting evaluation outcomes, developing more targeted prevention and management strategies, and enhancing patients' quality of life.^{11,16} To the best of our knowledge, limited studies have evaluated objective and subjective cognitive function and explored their relationship in patients newly diagnosed with OC. Therefore, we primarily aimed to investigate cognitive function in newly diagnosed OC patients before treatment and secondarily explore the association between neuropsychological impairment, self-perceived cognitive deficits, symptoms, and health-related quality of life.

Methods

Participants

Participants were purposefully sampled from gynecological oncology wards and the outpatient chemotherapy center at the Shanghai Cancer Center of Fudan University between May 2021 and February 2022. Inclusion criteria encompassed patients aged 18–65 years who were newly diagnosed with OC using noninvasive imaging techniques, had not yet undergone any antitumor treatment, were in a stable condition, and possessed normal Mandarin communication abilities. Exclusion criteria included patients with postoperative pathological diagnoses of benign disease, brain metastases, potential psychiatric disorders, and previous severe cognitive disorders. Ethical approval was obtained from the author's institute.

Instruments

The Montreal Cognitive Assessment Scale

The Montreal Cognitive Assessment (MoCA) scale covers seven cognitive functions: visuospatial/executive, naming, attention, language, abstraction, delayed recall, and orientation. It has been used as a rapid screening tool by neurologists, psychologists, and nurses for mild cognitive impairment (MCI).¹⁹ The scale has been translated and revised into at least 35 languages.²⁰ There were four Chinese versions. The Changsha version by Tu et al. had more cultural revisions and changed the named animals and memory phrases with detailed and scientific instructions. Its Cronbach's α coefficient, retest reliability, and investigator reliability were 0.846, 0.974, and 0.969, respectively. The total score of \geq 27 points was cognitively normal, and 1 point was added if the education years were \leq 6 years. The sensitivity and specificity of the

diagnostic criteria were the best, which were 90.0% and 70.9%, respectively. It was considered suitable for promotion and application among the mainland Chinese population.²¹

Perceived deficit questionnaire

This questionnaire was developed by Sullivan et al. in 1990 for patients with multiple sclerosis and aimed to provide independent reports of cognitive dysfunction from their perspective. It has been widely used in other populations, with good reliability and validity.²² The questionnaire consisted of 20 items, each rated on a 5-point Likert scale from 0 (never) to 4 (almost always), with a higher score indicating more severe subjective cognitive impairment in the past week. The scale assessed four cognitive functions: attention/concentration, retrospective memory, prospective memory, and planning/organization. The Chinese version by Song Zhen had good structural validity and reliability, with structural validity, retest reliability, and internal reliability scores of 0.867, 0.476, and 0.932, respectively.²³

Memorial Symptom Assessment Scale

The memorial symptom assessment scale (MSAS) is a multidimensional symptom assessment scale that includes the physical symptom subscale score (PHYS), psychological symptom subscale score (PSYCH), and Global Distress Index (GDI), with 32 items. Of these, 24 items assessed the frequency, severity, and distress of the symptoms, and the other eight measured severity and distress. A Likert scoring method was used, in which the frequency and severity were graded from 1 to 4 and distress from 1 to 5. The higher the score, the more severe the symptom.²⁴ Cheng Tsing of the Chinese University of Hong Kong Sinicized the MSAS in 2009 through a process of translation and cultural adaptation.²⁵ It has been widely used for the clinical evaluation of cancer and chronic diseases in China.

Functional Assessment of Cancer Therapy-Ovarian Cancer

This scale is composed of the Functional Assessment of Cancer Therapy-General (FACT-G) generic module and the ovarian cancerspecific module (OCS). The generic module was divided into physiological well-being (PWB), social and family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB). The OCS was composed of 12 items. All items were scored on a five-point scale from 0 to 4, with higher scores indicating a better quality of life. According to the Functional Assessment of Cancer Therapy-Ovarian Cancer (FACT-O) scale scoring standard, an overall score of > 3, 1–3, and < 1 indicated good, medium, and poor quality of life, respectively. In 2013, Chinese scholar Li Wei translated the scale into Chinese, and the FACT-O Chinese version had good content and structural validity.²⁶

Data collection

The principal investigators received cognitive neuropsychology test training organized by the Shanghai Mental Health Center and the official online training of MoCA and passed both assessments. For participant recruitment, patients who initially met the inclusion criteria were explained the purpose and content of the study. Those willing to participate signed an informed consent form and chose the time and place as per their convenience, either in a hospital conference room prepared in advance or at their home. In principle, a relatively comfortable, closed, undisturbed, and quiet environment was selected. Trained investigators conducted one-to-one and face-to-face surveys. Patients completed a general information questionnaire, the MSAS, FACT-O, and perceived deficit questionnaire (PDQ). Subsequently, the investigator conducted an objective cognitive function test strictly in accordance with the MoCA instructions. The entire process took approximately 40–50 min.

Data analysis

SPSS version 24.0 was used. Data were entered independently, crosschecked, and analyzed. For counting data, general data were described using frequency and constituent ratio. For measurement data, mean \pm standard deviation and range were used to describe the data distribution. According to the normal distribution of the variables, Spearman's correlation was used to explore the correlation between the results of the PDQ and MoCA and their relationship with the MSAS and FACT-O. All tests were two-sided, with a test level of $\alpha = 0.05$. In accordance with the journal's guidelines, we will provide our data for independent analysis by a team selected by the editorial team, if requested, for the purposes of additional data analysis or for the reproducibility of this study in other centers.

Results

Sample characteristics

A total of 116 women participated, of whom six did not complete the entire assessment (two had to receive a temporary examination and four declined to continue due to fatigue), and five were diagnosed with benign disease post-surgery. Hence, 105 patients were analyzed. See Table 1 for detailed information.

Neuropsychological impairment

The mean MoCA score was 23.11 (range 9–30; SD, 4.54), with 76 (72.38%) screening positive for cognitive impairment (MoCA scores < 26). Delayed recall, abstraction, and visuospatial/executive functions had the worst average/full scores. Table 2 shows the scores for each function.

Self-perceived cognitive deficit

The mean PDQ score was 17.57 (SD, 8.51). Retrospective memory scored the highest, indicating the most serious cognitive complaints, followed by prospective memory, as shown in Table 3.

Quality of life and perceived symptoms

The mean FACT-O score was 3.26 (SD, 0.37). The EWB and FWB subscales scored the lowest. Anxiety, pain, feeling bloated, difficulty sleeping, and feeling sad and nervous were the top six symptoms regarding incidence, severity, and distress. Of these, the incidence of anxiety had the highest score, and feeling bloated was the most severe and distressing symptom. The PHYS scored the highest.

Correlations between neuropsychological impairment and self-perceived cognitive deficit

The total PDQ score did not significantly correlate with the MoCA test ($r_{\rm s} = -0.180$, P = 0.067); however, it negatively correlated with a specific MoCA score ($r_{\rm s} = -0.244$, P = 0.012). The correlation between the total PDQ score and delayed recall dimension score was statistically significant ($r_{\rm s} = -0.300$, P = 0.002). A comparison of the different dimensions between neuropsychological impairment and self-perceived cognitive deficits is shown in Table 4.

Correlations between cognitive performance, quality of life, and symptoms

There were significant correlations between higher scores on selfperceived cognitive deficits and more serious symptoms in all dimensions. No association was observed between self-perceived cognitive deficits and quality of life. Neuropsychological impairment significantly correlated with the GDI, PHYS, and total symptom distress (TMSAS) in the MSAS and the EWB in the FACT-O (Table 5).

Table 1

Sample characteristics (N = 105).

Characteristics		Mean (SD)	n (%)
Age (years)		49.73 (8.48)	
Education	Primary school or below		32 (30.48)
	Middle school		31 (29.52)
	High school		19 (18.10)
	University or above		23 (21.90)
Marital status	Married		95 (90.48)
	Unmarried		5 (4.76)
	Divorced/separated/widowed		5 (4.76)
Employment status	Employed full time		17 (16.19)
	Employed but on medical leave		16 (15.24)
	Retired		69 (65.71)
	Unemployed/homemaker		3 (2.86)
Living status	With family		99 (94.29)
	Alone		6 (5.71)
Religious belief	None		81 (77.14)
	Buddhism		19 (18.10)
	Christianity		5 (4.76)
Comorbidity	None		74 (70.48)
	One		26 (24.76)
	Two or more		5 (4.76)
Disease stage III or I		90 (85.71)	
Epithelial ovarian tu		86 (81.90)	

FIGO, International Federation of Gynecology and Obstetrics.

Table 2

Neuropsychological test result (N = 105).

Cognitive functions in MoCA	Scoring range	Mean (SD)	
Visuospatial/Executive	0–5	2.97 (1.40)	
Naming	0–3	2.94 (0.34)	
Attention	0–6	5.25 (1.05)	
Language	0–3	1.88 (1.03)	
Abstraction	0–2	1.02 (0.86)	
Delayed recall	0–5	2.84 (1.61)	
Orientation	0–6	5.79 (0.47)	

MoCA, Montreal Cognitive Assessment.

Discussion

Summary of main results

This study showed that up to 72.38% of the women newly diagnosed with OC had neuropsychological impairment, with no association with self-perceived cognitive deficits. Retrospective and prospective memory were the most serious cognitive complaints. Neuropsychological cognition significantly correlated with GDI, PHYS, and TMSAS in symptoms, emotional well-being of quality of life. Subjective cognitive function was significantly correlated with all dimensions of symptoms, with no association with quality of life.

Results in the context of published literature

The data reported in previous similar studies varied greatly. Jung et al. reported that in 95.2% of newly diagnosed female patients with thyroid cancer without any treatment, the score of one or more cognitive function

Table 3

Self-perceived	l cognitive	deficit eva	luation re	esult (N	= 105).
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Cognitive functions in PDQ	Mean (SD)
Attention/Concentration	3.69 (2.56)
Retrospective memory	6.22 (3.05)
Prospective memory	4.21 (2.25)
Planning/Organization	3.48 (2.41)

PQD, Perceived Deficit Questionnaire.

Table 4

Correlations between neuropsychological impairment and self-perceived cognitive deficit.

MoCA	PDQ	PDQ					
	Total score	Attention/Concentration	Retrospective memory	Prospective memory	Planning/Organization		
Visuospatial/Executive	-0.148	-0.194*	-0.129	-0.165	-0.034		
Naming	0.009	0.020	-0.067	-0.065	-0.087		
Attention	-0.179	-0.195*	-0.214*	-0.137	-0.036		
Language	-0.155	-0.256**	-0.100	-0.081	-0.061		
Abstraction	-0.060	-0.136	-0.023	-0.061	-0.024		
Delayed recall	-0.300**	-0.327**	-0.253**	-0.373**	-0.127		
Orientation	0.001	-0.066	0.101	-0.048	-0.038		

** $P \le 0.01$; * $P \le 0.05$.

MoCA, Montreal Cognitive Assessment; PQD, Perceived Deficit Questionnaire.

dimensions was lower than normal. Furthermore, the incidence of CRCI was 78%.²⁷ However, Araujo et al. reported that only 14.7% of new patients with prostate cancer suffered cognitive impairment. The authors explained that prostate cancer might not cause the same systemic pathophysiological changes as other cancers. In addition, they stressed that inconsistencies in assessment tools and CRCI diagnostic criteria also contributed to the differences.²⁸ In a study by Sayo et al. the incidence of neuropsychological impairment was 20%. Besides the factors mentioned above, this low incidence might be attributed to the Mini-Mental State Examination (MMSE) selected by the researchers.²⁹ In our study, the MoCA, a more sensitive tool to assess mild cognitive impairment, was selected, which may contribute to the high incidence of CRCI. In addition, changes in the human microenvironment caused by tumors are also a widely recognized physiological reason for cancer-related sickness and behavior symptoms, including cognitive dysfunction, which increases proinflammatory factors and acts on the brain through the vagus nerve or across the blood-brain barrier, causing neuroinflammation.³⁰ Psychological factors also play an important role in the development of CRCI. Previous studies confirmed that negative psychological factors, such as anxiety and depression, directly affect the central nervous system and cause changes in brain metabolism and structure.³¹ Simultaneously, they triggered pro-inflammatory cytokines, the hypothalamicpituitary-adrenal axis, monoamine neurotransmission system activation, and changes in the immune system.³⁰ The incidence of negative emotions in patients newly diagnosed with cancer was high, and some developed post-traumatic stress syndrome.³² This study showed that participants' symptoms, namely anxiety, pain, feeling bloated, difficulty sleeping,

Table 5

Correlations	hetween	cognitive	performance	and (JOL	svmi	ntoms
Conciations	Detween	cognitive	periormance	anuv	ŲОL,	5 y 1111	Junio.

	PDQ total score	MoCA total score	The score above normal or not of MoCA
MSAS			
GDI	0.257**	-0.331**	-0.231*
PHYS	0.297**	-0.326**	-0.250*
PSYCH	0.217*	-0.141	-0.084
TMSAS	0.312**	-0.286**	-0.213*
FACT-O			
PWB	-0.179	0.228*	0.147
SWB	0.017	-0.155	-0.071
EWB	-0.152	0.262**	0.264**
FWB	-0.119	0.117	0.094
OCS	-0.117	0.116	0.006
QOL_overall	-0.125	0.146	0.072

** $P \le 0.01$; * $P \le 0.05$.

EWB, emotional well-being; FACT-O, Functional Assessment of Cancer Therapy-Ovarian Cancer; FWB, functional well-being; GDI, Global Distress Index; MoCA, Montreal Cognitive Assessment; MSAS, Memorial Symptom Assessment Scale; OCS, ovarian cancer-specific module; PHYS, physical symptom subscale score; PQD, Perceived Deficit Questionnaire; PSYCH, psychological symptom subscale score; PWB, physiological well-being; QOL, quality of life; SWB, social and family well-being. feeling sad, and nervousness, that mostly belonged to the neuropsychiatric symptom group had high incidence, severity, and distress.

This study confirmed that both subjective and objective cognitive performance were correlated with patient symptom assessment, which was inconsistent with previous studies that reported that neuropsychological tests were not correlated with symptoms. This may be related to Asian patients' attitudes toward cognitive disorders and their tendency to be prone to psychological stress in highly structured assessment environments.³³ Patients are ashamed to talk about cognitive function and impairment.³⁴ Therefore, when being evaluated, patients have to deal with both the psychology of embarrassment and the psychology of gain and loss and feel disdain towards receiving a childish test; however, they also worry about poor results, which may lead to ridicule by others. This complex psychology directly affects patients' performance during neuropsychological evaluations. In this study, some women said that they felt nervous during the test, which negatively affected their performance. This was especially true for patients with low education levels.

Abstraction, delayed recall, and visuospatial/executive function decline were the most prominent in patients newly diagnosed with OC. Furthermore, memory was also the most serious in self-perceived cognitive deficits, corresponding to other studies.^{13,17,27} These cognitive dimensions require higher-level functions essential for goal-directed behavior and social functioning, which include learning, decision-making, problem solving, and multi-task execution. Therefore, changes may reduce an individual's effectiveness and ability to interact purposefully.¹⁵ Hence, it is important to understand pretreatment cognitive function changes and their influencing factors, which can provide a reference for formulating individualized symptom management measures.²⁷

In this study, there was no correlation between a normal result on neuropsychological tests and the results of self-perceived cognitive deficit assessment in new patients with OC, which was consistent with previous studies. Based on Amanda et al.'s systematic review, approximately two-thirds of previous studies have reported no significant correlation between the two evaluation results,³⁵ which could be attributed to differences in the nature and content structure of the respective evaluation methods. Patient self-reports comprehensively reflected their experiences of cognitive functions related to recent daily life and were susceptible to fatigue, pain, emotion, treatment expectations, and other factors^{36,37} whereas neuropsychological tests are conducted in a highly structured environment and the cognitions they measure are not closely related to daily life. Thus, objective measurements may not be as sensitive as subjective evaluation methods for slight changes in cognitive function.³⁵ Both assessment methods have advantages and disadvantages; therefore, integrative cognitive assessment needs to be conducted.

Strengths and weaknesses

This study evaluated the cognitive function of patients newly diagnosed with OC before initial treatment, filled the gap in relevant research, and expanded the scope to assess cognitive function before treatment in patients with ovarian cancer. This study was a single-center cross-sectional survey without controls, which limited the generalizability of the findings and conclusions. In addition, there may be some participant bias. Patients willing to participate may have had better physical and mental conditions, treatment effects, and hospital satisfaction. Simultaneously, the factors that influenced cognitive function were not analyzed. Future studies should adopt high-quality cohort studies to explore the changes in cognitive function in new patients with OC along with the course of disease and treatment and analyze their impact on quality of life and survival.

Implications of practice and future research

Given its high incidence, health care providers need to incorporate CRCI into common symptom management to improve the quality of life in new patients with OC. Simultaneously, the influence of this symptom on patients' information understanding, decision-making, and selfmanagement abilities needs to be fully considered, and additional strategies must be adopted to enhance the effect of doctor-patient communication, treatment decision-making, and health education. Meanwhile, the importance of family members' participation during the communication process needs to be considered. Clinicians should also consider the interaction between other symptoms and cognitive function and develop joint management strategies accordingly. It is crucial to conduct a comprehensive assessment, considering clinical feasibility. Efforts can be made to develop a simple and easy evaluation tool that combines subjective and objective forms to facilitate screening and follow-up of cognitive function in patients with cancer.

Conclusions

The incidence of CRCI was high in patients newly diagnosed with OC before treatment, especially regarding abstraction, delayed recall, and visuospatial/executive function, which correlated with other symptoms but not with quality of life. Little correlation was observed between neuropsychological impairment and self-perceived cognitive deficits. It is recommended that health care providers include CRCI in symptom management in new patients with OC who may benefit from early assessment, prevention, and intervention of cognitive function.

CRediT authorship contribution statement

Living Wang: Conceptualization, Methodology, Investigation, Formal analysis, Writing. Yan Ding: Conceptualization, Supervision, Methodology, Writing. Yi Zhang: Resources, Supervision, Writing. Yaqiong Chen: Resources, Supervision, Writing. Mei Xue: Resources, Supervision, Writing. Xia Wang: Methodology. All authors had full access to all the data in the study, and the corresponding author had final responsibility for the decision to submit for publication. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Ethics statement

Ethical approval was obtained from the Shanghai Cancer Center's Ethics Committee (IRB No. 2103232-25). All participants provided written informed consent.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability statement

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

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Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools/services were used during the preparation of this work.

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