Perceived Cognitive Function and Related Factors in Korean Women With Breast Cancer

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Purpose The aim of this study was to explore perceived cognitive function and its related factors in breast cancer patients that had received or were receiving adjuvant chemotherapy after surgery.
Methods A cross-sectional and correlational design was used in this study. A total of 118 women who had undergone or were undergoing adjuvant chemotherapy after breast cancer surgery recruited from a convenience sample from a university hospital in Korea were included in the study. The attentional function index was used to measure perceived cognitive function while the linear analogue self-assessment scale was used to measure mood disturbance. Hierarchical multiple regression analyses were done to determine possible predictors of perceived cognitive function in patients with breast cancer.
Results Perceived cognitive function and mood disturbance had a mean score of 66.22 ($SD = 13.43$) and 159.78 ($SD = 81.40$), respectively. Mood disturbance was a statistically significant predictor of cognitive function in patients with breast cancer.
Conclusions Breast cancer patients with mood disturbance may experience decrements in perceived cognitive function. Nurses should be aware of mood changes and its influence on perceived cognitive function in breast cancer patients. [*Asian Nursing Research* 2011;5(2):141–150]

Key Words attention, breast neoplasms, cognition

INTRODUCTION

The 5-year survival rate of Korean breast cancer patients is 89.9% (National Cancer Information Center, 2010). However, anticancer therapies, such as chemotherapy, radiation therapy, and hormone therapy, cause physical and psychological side effects that can continue long-term. In order improve and maintain the quality of life of breast cancer survivors, attention should be given not only to the survival rate, but also to the continuing side effects from the treatment. This is especially relevant in Korea where 43% of breast cancer patients are less than 50 years old, and the number of young breast cancer patients is gradually increasing (Health Insurance Review & Assessment Service, 2010). This means that the

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Received: January 10, 2011 **Revised:** June 8, 2011 **Accepted:** June 9, 2011

long-term management of symptoms becomes much more important.

In Korea and other countries, a growing number of studies have documented cancer-related symptoms in patients with breast cancer, and while anticancer treatments have varied, the symptom that researchers have recently been most concerned about is cognitive impairment (Stewart, Bielajew, Collins, Parkinson, & Tomiak, 2006; Wefel, Vardy, Ahles, & Schagen, 2011). The cognitive impairment in cancer patients is not as serious as dementia and is sometimes called mild cognitive impairment (MCI), "chemo-fog," or "chemo-brain." Impairment levels are often described with expressions such as "the memory is cloudy, "mental activity has become slow," and so forth. Cognitive impairment occurs in 16–75% of cancer patients, and attention, concentration, memory, and learning were mainly affected (Falleti, Sanfilippo, Maruff, Weih, & Phillips, 2005; Stewart et al., 2006).

Changes in cognitive function affect the patients' quality of life. The changes may be an indication of central nervous system toxicity and are highly related to functional loss such as a reduction in work performance capacity (Wefel, Lenzi, Theriault, Davis, & Meyers, 2004).

Although the cause of cognitive impairment in cancer patients is not clear, it is thought that the use of neurotoxic anticancer drugs causes various degrees of cognitive impairment due to cerebral shrinkage, cerebral cortex calcification (Verstappen, Heimans, Hoekman, & Postma, 2003), and hypometabolism (Silverman et al., 2007). Genetic diversity, biological properties of tumors, immune responses and so forth may increase a cancer patient's vulnerability to changes in cognitive function from anticancer chemotherapies (Ahles & Saykin, 2007). In addition, anti-estrogen treatments using tamoxifen are related to changes in cognitive function since the estrogen receptor is distributed in the cerebral cortex (Paganini-Hill & Clark, 2000). Of the cognitive, alterations in basic cognitive functions for attention and working memory have been consistently reported in patients with a variety of malignancies and cancer treatment modalities (Cimprich, Visovatti, & Ronis, 2011).

To date, neuropsychological testing has found deficits in a variety of cognitive domains of cancer patients. However, cognitive compromise as assessed by neuropsychological testing appeared to be unrelated to self-reported cognitive dysfunction in many previous studies (Hermelink et al., 2007; Jansen, Cooper, Dood, & Miaskowski, 2010; Mehnert et al., 2007). While the incongruence of subjective and objective assessment has been ascribed to failure of the neuropsychological testing, subjective reports are often considered useful indications of cognitive functioning because patient's self-perceived cognitive dysfunction causes suffering and needs treatment even if it is not based on neuropsychological impairment (Hermelink et al., 2010).

Related factors of perceived cognitive impairment were mood disturbances or psychological distress. In women with breast cancer, subjective reports of problems with attention and memory were related to psychological distress after chemotherapy (van Dam et al., 1998), and higher mood distress scores in the pretreatment period were related to perceptions of decline in cognitive function (Cimprich, 1999).

Therefore, this study examined the perceived cognitive function and its related factors in patients with breast cancer receiving anticancer chemotherapy or who had already received anticancer chemotherapy. This study will be useful as a guide for developing symptom management and intervention studies regarding perceived cognitive dysfunction in cancer patients.

Aim and objectives

The aim of this study was to explore perceived cognitive function and its related factors among breast cancer patients receiving adjuvant chemotherapy after surgery and who had already received adjuvant chemotherapy. The specific objectives of this study were to determine the differences in perceived cognitive function according to sociodemographic and treatment characteristics, to determine the relationship between perceived cognitive function and mood disturbances, and to determine the predictive factors for perceived cognitive function in patients with breast cancer.

Table 1

Differences in Perceived Cognitive Function According to Demographic and Medical Characteristics (N = 118)

Characteristics	*n* (%)	*M* (*SD*)	*t* or *F*	*p*
Age				
< 50	55 (46.6)	69.04 (13.59)	2.160	.033
≥ 50	63 (53.4)	63.77 (12.90)		
Education				
≤ Middle school	40 (33.9)	62.33 (13.01)	2.301	.023
≥ High school	73 (61.9)	68.34 (13.42)		
Not reported	5 (4.2)			
Marital status				
Married	96 (81.4)	65.93 (13.94)	0.392	.695
Single[a]	18 (15.3)	67.29 (11.05)		
Not reported	4 (3.4)			
Religion				
None	15 (12.7)	66.98 (12.71)	0.258	.797
Yes	99 (83.9)	66.01 (13.66)		
Not reported	4 (3.4)			
Employment status				
Homemaker	95 (80.5)	65.58 (13.81)	0.611	.543
Full or part time	18 (15.3)	67.67 (10.53)		
Not reported	5 (4.2)			
Stage of cancer				
I	27 (22.9)	69.15 (13.15)	1.001	.371
II	64 (54.2)	64.82 (14.58)		
III, IV	27 (22.9)	66.62 (10.50)		
Time since diagnosis (yr)				
< 0.5	27 (22.9)	66.06 (16.58)	0.455	.769
0.5–1	16 (13.6)	66.99 (13.73)		
1–3	40 (33.9)	68.06 (11.24)		
3–5	26 (22.0)	63.80 (12.63)		
5	9 (7.6)	64.20 (15.35)		
Type of surgery				
BCO	54 (45.8)	69.53 (13.05)	2.588	.011
MRM	62 (52.5)	63.24 (13.06)		
Unknown	2 (1.7)			
Current treatment				
Chemo	35 (29.7)	66.25 (13.30)	0.149	.930
Hormone[b]	49 (41.5)	65.55 (12.00)		
Radiation[b]	4 (3.4)	69.75 (13.10)		
Completion of all treatments[b]	30 (25.4)	66.82 (16.18)		

Note. BCO = breast-conserving operation; MRM = modified radical mastectomy.
[a]Single includes widowed, divorced, separated, never married; [b]participants included in these categories already finished chemotherapy.

METHODS

Design

This study used a cross-sectional and correlational design to describe perceived cognitive function and identify factors influencing perceived cognitive function in patients with breast cancer who had received or were undergoing adjuvant chemotherapy after surgery.

Sampling

One hundred and eighteen women that had undergone or were undergoing adjuvant chemotherapy after breast cancer surgery recruited from a convenience sample from Ulsan University Hospital located in Ulsan, South Korea were included in the study. The women ranged from 24 to 70 years in age (M = 49.85 yr, SD = 7.85 yr). The exclusion criteria were as follows: (a) presence of metastatic disease or relapse; (b) a previous or current neurological or psychiatric disorder; (c) use of medication believed to affect current cognitive functioning (i.e., opioid analgesics, anxiolytics, or antidepressants); (d) alcohol and/or drug addiction. The medical records of all patients were checked to assess their eligibility. Of all, 112 had been prescribed cyclophosphamide and doxorubicin, while the others had been prescribed paclitaxel, docetaxel, taxol, and herceptin.

Measurements

Perceived cognitive function

Among cognitive functions, attention is essential for effective cognitive functioning; therefore, understanding problems associated with attention capacity is of key importance in individuals treated for cancer (Cimprich, So, Ronis, & Trask, 2005).

The attentional function index (AFI) was used to measure perceived cognitive function (Cimprich, 1992). AFI was developed to assess perceptions of effectiveness in daily life activities that require directed or controlled attention and the higher executive processes served by this basic cognitive system. The AFI consisted of sixteen 100-mm visual analogue scales (VASs) ranging from 0 (*not at all*) to 100 (*extremely well*), on which individuals self-rate how well they are able to perform cognitive activities, such as planning daily activities, getting started on tasks, keeping a train of thought, remembering to do important things, and attending to details. Participants were asked to place a mark through the horizontal line at whatever point best describes how well they are functioning at the time. In this study, the total score on the instrument was computed by obtaining the mean of the 16 VASs, with higher scores indicating a higher level of function. The validity and reliability of the technique have been established in healthy and ill populations (Cimprich, 1992; Cimprich, 1999). Cronbach's alpha for the AFI for Korean gastric cancer patients was .94–.95 (Kim, 2006, unpublished data) and was .88 in this study.

Mood disturbance

The linear analogue self-assessment (LASA) scale (Sutherland, Walker, & Till, 1988) was used to measure mood disturbance. The LASA consisted of six 100-mm linear VASs to measure the following aspects of mood: anxiety, confusion, depression, fatigue, anger, and energy. The total mood disturbance score for the LASA scale was calculated by summing the scores of six items and weighing the energy negatively, and a higher score means a higher level of mood disturbance. Tests of concurrent validity with Profile of Mood Status (POMS) were .79–.83 for the Spearman rank correlation coefficient, and the test-retest reliability coefficient was .80 (Sutherland et al., 1988). Cronbach's alpha for the LASA scale for Korean gastric cancer patients was .85–.95 (Kim, 2006, unpublished data) and was .79 in this study.

Data collection procedures

The institutional review board of Ulsan University Hospital approved this study. Participants were recruited from the outpatient clinic. Each participant signed a written consent form before enrollment, which included research objectives, data collection, and confidentiality. It was explained that the data collection process could be abandoned at any time with no penalty.

A research assistant met the participants one-on-one to collect data. In 2009 from September to December, 125 participants who had regularly visited the clinic or were under active cancer treatment agreed to participate in the study and signed informed consent forms. Of the 125, 7 participants were not used due to missing data in the main variables (perceived cognitive function and mood disturbance), and thus, 118 women participated in this study.

Data analysis

SPSS version 12.0 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. Descriptive statistics were used to characterize the demographic and medical variables of the participants. A *t* test and analysis of variance were used to compare the differences in AFI scores according to demographic and medical characteristics. The Pearson correlation coefficient was used to determine the relationship between perceived cognitive function and mood disturbances.

Hierarchical multiple regression analyses were done to determine possible predictors of perceived cognitive function in participants. A p value of $< .05$ was considered statistically significant. The research hypothesis for hierarchical multiple regression analyses was satisfied with a Durbin-Watson of 1.976, a Tolerance of 0.723–0.961, and a variance inflation factor (VIF) of 1.041–1.383.

RESULTS

Socio-demographic characteristics and perceived cognitive function

Table 1 shows a statistically significant difference in the perceived cognitive function with regard to age and educational level. The AFI score of participants below the age of 50 was 69.06, which was significantly higher than the score of 63.77 for participants above the age of 50 ($t = 2.160$, $p = .033$). Participants with a higher education level had a higher AFI score: with a high school education or higher, the AFI was 68.34, and with a middle school education or lower, it was 62.33 ($t = 2.301$, $p = .023$).

There was no statistically significant difference between the stages of cancer, but the AFI score of stage I cancer participants was 69.15, which was higher than the 64.82 for stage II and 66.62 for stage III or IV. The AFI score for the “time since the diagnosis” for between 1 and 3 years was 68.06, which was higher than the AFI values for shorter or longer times since the diagnosis. The AFI scores in participants with “3 to 5 years” and “over 5 years” since the diagnosis of cancer were 63.80 and 64.20, respectively, and these scores were lower than the 66.06 for “under 0.5 years” and 66.99 for “0.5 to 1 year” since the diagnosis of cancer.

There was a significant difference in AFI scores between surgery types: the score for participants that had breast-conserving operation was higher than in modified radical mastectomy participants (69.53 *vs.* 63.24, respectively; $t = 2.588$, $p = .011$). The AFI score in participants receiving radiation therapy was 69.75, which was higher than in those receiving chemotherapy or hormone therapy, and in those who had finished therapy, but the difference was not significant ($t = 0.149$, $p = .930$).

Mood disturbance and perceived cognitive function

Table 2 shows the mean score of the perceived cognitive function and mood disturbance. The mean score of the perceived cognitive function was 66.22 ($SD = 13.43$) and the mean score of the mood

Table 2

Mood Disturbance and Perceived Cognitive Function (N = 118)

Variables	*M* (*SD*)	Min–max	Reference	Correlation coefficient (*p*)
Mood disturbance	159.78 (81.40)	−81 to 347	−100 to 500	−.582 (< .001)
Perceived cognitive function	66.22 (13.43)	22.88–94.06	0–100	

Table 3

Hierarchical Regression Analysis of Perceived Cognitive Function to Identify Predictors (N = 118)

Variables	R^2	F (p)	B	SE	β	t (p)
Age[a] (≥ 50 yr)	.065	3.780 (.026)	–2.464	2.841	–.092	–0.867 (.388)
Education[a]						
(Above high school)			5.587	2.972	.199	1.880 (.063)
Age	.103	4.074 (.009)	–2.663	2.798	–.099	–0.951 (.344)
Education			4.462	2.975	.159	1.500 (.137)
Type of surgery[a]						
(MRM)			–5.277	2.509	–.196	–2.103 (.038)
Age	.375	15.880 (< .001)	–2.330	2.347	–.087	–0.993 (.323)
Education			2.274	2.515	.081	0.904 (.368)
Type of surgery			–3.823	2.115	–.142	–1.808 (.074)
Mood disturbance			–0.088	0.013	–.533	–6.793 (< .001)

Note. MRM = modified radical mastectomy. Adjusted R^2 = .351.
[a]Dummy coded.

disturbance was 159.78 (SD = 81.40). The perceived cognitive function and mood disturbance correlational coefficient was r = –.582 (p < .001).

Predictive factors for perceived cognitive function

Table 3 shows the results of the hierarchical multiple regression analysis. The first step of the hierarchical multiple regression included the age and educational level; the second step included the type of surgery, and the final step included the mood disturbance. The adjusted R-square of the final regression model was 0.351 (F = 15.880, p < .001), and mood disturbance was shown to be a statistically significant explanatory predictor of cognitive function after adjusting for age, educational level, and the type of surgery.

DISCUSSIONS

The cognitive dysfunction induced by chemotherapy was shown to be mild to moderate (Jansen, Miaskowski, Dodd, Dowling, & Kramer, 2005). In this study, the AFI was used to measure perceived effectiveness in cognitive activities. The mean score of perceived cognitive function was 66.22, and this was similar to a score of 65.69 in a previous study (Cimprich et al., 2005). Until now, AFI results have not received much international attention. Therefore, it was very difficult to set up a cutoff point to determine the severity of the perceived cognitive impairment. Further study is needed to determine to what degree changes in the AFI score would indicate perceived cognitive impairment in a clinical setting.

Chemotherapy-related cognitive impairment has been the most widely reported source of cognitive deficit in cancer patients, particularly in breast cancer. Among cognitive function domains, attention domain was the one that showed the significant decrement (Jansen et al., 2010; Quesnel, Savard, & Ivers, 2009; Wefel et al., 2004). While attention is the foundation for cognitive function, decrements of attention will have negative effects on an individual's ability to focus on tasks (Jansen et al., 2010). Recently, physiological evidence showed that chemotherapy seems to affect cerebral white matter integrity and this may reflect mild cognitive impairment (Deprez et al., 2011). However, several studies have not supported the association between chemotherapy and cognitive impairment in breast cancer patients (Debess, Riis, Engebjerg, & Ewertz, 2010; Mehlsen, Pedersen, Jensen, & Zachariae, 2009). The present study did not show that chemotherapy had a negative impact on perceived cognitive function because the AFI score was similar between the participants undergoing chemotherapy and the participants who had completed cancer treatment. Our results are coincident with some longitudinal studies reporting that chemotherapy induced no cognitive impairment in breast cancer patients (Hermelink et al., 2007; Mehlsen et al., 2009). There was also no association between perceived cognitive function and the time since the diagnosis of cancer. The AFI score was actually lower in the 3 or more year-group for the time since the diagnosis than for the 1 or less year-group. This suggests that cognitive function decreases in the long-term and is not an acute side effect of the therapy. In contrast, Jansen et al. (2010) reported that chemotherapy-related cognitive impairment appeared to be more acute than a chronic side effect of the therapy, and a study by Wefel et al. (2004) showed cognitive function improved gradually after completing chemotherapy. There is still no clear correlation among cognitive impairment, chemotherapy, and the time since the diagnosis of cancer (Vearncombe et al., 2009). Recently, studies have found evidence of cognitive impairment prior to the initiation of chemotherapy, that is, being afflicted with breast cancer may be associated with cognitive impairment (Hermelink et al., 2007; Jansen et al., 2010; Wefel et al., 2004).

In this study, the type of surgery was not a predictive factor in the detection of cognitive function in the final step of the multiple regression analysis, but cognitive function scores in participants who had a breast-conserving operation were higher in the ANOVA analysis. Mehnert et al. (2007) reported that the modified radical mastectomy group showed worse self-perceived attentional function and more fatigue post-chemotherapy than the breast-conserving operation group. This may be due to the patients' conditional status post-surgery rather than the severity of the disease since there was no significant difference in AFI scores for the stages of cancer. In contrast, Vearncombe et al. (2009) stated that the surgery type was not a clear factor in explaining cognitive function. Therefore, further studies regarding the association between cognitive function and the surgery types are needed.

Studies have evaluated the correlation between chemotherapy-related cognitive impairment and fatigue or mood, especially depression and anxiety. These variables have been linked with subjective cognitive dysfunction when tested by self-report questionnaires. According to a meta-analysis by Anderson-Hanley, Sherman, Riggs, Agocha and Compas (2003), most studies reported that cognitive impairment continued when depression, anxiety, or fatigue were present. Objective neuropsychological tests especially attention and memory tests have shown a relationship to fatigue (Cimprich, 1992; Cimprich, 1993; Mehlsen et al., 2009). This study found that mood disturbances consisting of fatigue, anxiety, and depression were the strongest related factors to perceived cognitive function, and this finding is supported by previous studies. However, Jim et al. (2009) reported that an objective cognitive function analysis showed no significant correlation with psychological factors. More studies are needed to identify the relationship between cognitive impairment and psychological factors.

In terms of sociodemographic variables, age and education level were related to perceived cognitive function in a univariate analysis, but were not significant predictors in multiple regression models. In the cases of perceived cognitive impairment like in the present study, symptom experiences and mood disturbances could be significant predictors of cognitive impairment; however, in the objective cognitive function tests, age and education level could be predictors of decline in attentional function (Cimprich et al., 2005).

Hormone therapy is also known as an important factor associated with cognitive decline. Women with breast cancer who received hormone therapy but had never received chemotherapy showed impaired cognitive function such as verbal memory impairment (Jenkins, Shilling, Fallowfield, Howell, & Hutton, 2004). Even breast cancer survivors who had both chemotherapy and hormone therapy showed a greater degree of cognitive impairment relative to a control group (Castellon et al., 2004). In this study, with the limitation that the influences of hormone therapy could not be determined by itself, no association between perceived cognitive impairment and hormone therapy was found.

The current study has several limitations. First, the nonprobability sampling strategy may have led to selection bias and influenced the study results by limiting generalizability. Second, the study used a cross-sectional design without a control group only capturing patients' perceived cognitive function and related variables at one time point. The effects of mood disturbances during the pre-treatment period on cognitive change need to be assessed longitudinally. Assessing the trends of variables over time, throughout the illness and treatment trajectory, would likely provide valuable data on patterns of cognitive function and on their relationships with other variables.

Third, the perceived cognitive function was conceptualized with the attentional function in this study. Even though AFI can measure higher executive processes served by attention such as memory and planning as well as attention, it's not probably cover all domains of cognitive function. So we need to consider self-perception of the other part of cognition (i.e. language, concept formation, and visuospatial ability) in the future studies.

Fourth, the influence of menopause on cognition was not considered in this study.

Finally, although mood disturbance was a significant predictor of perceived cognitive function, this explained only 37.5% of the perceived cognitive function. More predictive psychosocial factors (e.g., symptom distress, personal traits, social support) need to be studied.

CONCLUSIONS

As evidenced by this study, mood disturbance was the most significant factor in the prediction of perceived cognitive function in Korean breast cancer patients. If patients have a high degree of mood disturbance, they will see their cognitive function as low. Many factors such as operation type and treatment type can affect the mood of the patients so further intensive studies should be done to evaluate all of them.

Nurses play an important role in the assessment and management of cancer-related cognitive impairment. In clinical settings, nurses need to assess cognitive function in the initial phase of treatment regardless of the treatment status, and should carefully take into account the influence mood changes have on cognitive function. Furthermore, as a greater understanding on the mechanisms underlying cognitive function is gained, more potential targets for therapy will emerge. The findings of this study provide fundamental data on the degree of perceived cognitive function and the relationship between perceived cognitive function and mood disturbance in Korean breast cancer patients.

ACKNOWLEDGMENTS

This work was supported by a University of Ulsan Research Grant.

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