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ORIGINAL ARTICLE

Does Chemotherapy Really Affect the Quality of Life of Women with Breast Cancer?

Sook Yeon Hwang, Sun Ju Chang[1], Byeong-Woo Park[2]

Department of Social Welfare, Duksung Women's University College of Social Sciences, Seoul; [1]Gachon University College of Nursing, Incheon; [2]Department of Surgery, Yonsei University Health System, Yonsei University College of Medicine, Seoul, Korea

Purpose: The aims of this cross-sectional study were to explore and evaluate the impact of adjuvant chemotherapy on quality of life in breast cancer patients according to the survival time from surgery. **Methods:** Completed questionnaires were collected from 534 women with breast cancer. Clinical and sociodemographic characteristics were reviewed and Functional Assessment of Cancer Therapy-Breast cancer instrument, global quality of life, Beck Depression Inventory, and unmet sexuality needs were administered. Descriptive statistics, t-tests, chi-square tests and multiple analysis of covariance were performed while controlling for confounding variables. **Results:** Statistically significant differences were found between chemotherapy and no chemotherapy group on depression ($p=0.026$), unmet sexuality needs ($p=0.010$), breast cancer specific concerns ($p=0.010$), physical well-being ($p=0.001$), and emotional well-being ($p=0.028$). Chemotherapy effects also varied according to survival time since surgery such as for group 1 (<1 year since surgery), significant differences were found on Beck Depression Inventory ($p=0.042$), unmet sexuality needs ($p=0.016$), breast cancer subscale ($p=0.004$), and physical well-being ($p=0.016$) and for group 3 (>3 years since surgery) on depression ($p=0.019$) and physical well-being ($p=0.028$) respectively; however, there were no significant differences between chemotherapy and no chemotherapy group for group 2 (1-3 years since surgery). **Conclusion:** As expected, breast cancer patients who underwent adjuvant chemotherapy experienced significantly worse quality of life than those who did not receive chemotherapy. Furthermore, the adverse chemotherapy effects on the quality of life appear to vary according to the time since surgery. These results suggest that health care professionals may need to address long-term as well as short-term chemotherapy side-effects and intervene accordingly to enhance quality of life of breast cancer patients.

Key Words: *Adjuvant chemotherapy, Breast neoplasms, Quality of life, Survivors*

INTRODUCTION

Early detection and novel systemic adjuvant therapy strategies have considerably improved the survival of breast cancer patients [1,2]. As chemotherapy in the adjuvant setting known to contribute to significant progress in the management of breast cancer [1], it is imperative to examine the possible impact of chemotherapy on the quality of life (QOL) of breast cancer patients and provide information about adverse effects of chemotherapy from the acute phase of treatment to ongoing survivorship.

Correspondence to: **Byeong-Woo Park**
Department of Surgery, Yonsei University Health System, Yonsei University College of Medicine, 50 Yonsei-ro, Seodaemun-gu, Seoul 120-752, Korea
Tel: +82-2-2228-2100, Fax: +82-2-313-8289
E-mail: bwpark@yuhs.ac

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Many studies have been conducted on the impact of surgery method on QOL and psychological distress of women with breast cancer; however, few have investigated the impact of adjuvant chemotherapy on overall QOL of women with breast cancer. Previous research indicated that QOL variables including emotional functioning, anxiety, and depression, mood, well-being, and distress have not differed by surgery method with the exception of daily disruption [2-8].

Adjuvant chemotherapy is reported to partially influence QOL during or after the treatment period [9-11]. However, earlier studies on the impact of chemotherapy are controversial based on the survival time, as some studies reported that chemotherapy was not a significant predictor of QOL during the first year after diagnosis [8,12,13], while the statistically significant negative association of past chemotherapy with current QOL was found in long-term survivors at least 5 years since diagnosis not only in sexual functioning but in other

general QOL aspects including physical and social functioning as well as general health [2]. Contrary to this, Joly et al. [11] did not find any evidence of adjuvant chemotherapy impairing long-term QOL or social life in women with premenopausal node-negative women with breast cancer.

Therefore, this cross-sectional study was conducted with two objectives: to evaluate the impact of adjuvant chemotherapy by comparing QOL between breast cancer patients receiving chemotherapy and those not receiving chemotherapy and to examine the impact of adjuvant chemotherapy according to survival time since surgery.

METHODS

Patients

The subjects were from a consecutive sample of outpatients diagnosed with breast cancer at the Yonsei University Severance Hospital Breast Cancer Clinic [14] and attending regular follow-up appointments postsurgery. The participants were enrolled based on the following inclusion criteria: 1) age between 20 and 80 years, 2) stage I, II, and III cancer, 3) no evidence of systemic metastasis, and 4) no evidence of psychosis, dementia, or suicidal behavior. Among the 1,250 eligible patients who consented to participate in the study, 1,084 returned the survey. In this portion of the study, we retrieved the data of 771 patients who underwent surgery at least 1 month previously and had not received chemotherapy prior to surgery. Also, the data from the participants who did not respond to survey questions more than 10% of the total responses were excluded because missing data more than 10% of the total responses could influence the results of significance tests [15]. Finally, a total of 534 patients were included in the study. The study was approved by the Institutional Review Board of the Yonsei University Severance Hospital (4-2009-0269).

Measures

Sociodemographic and clinical backgrounds

Sociodemographic variables such as age, education, current marital status, employment and economic status were included in the survey. The treatment variables were collected by reviewing the medical records of each patient which include TNM stage, surgery method, hormone therapy, radiation therapy, survival time since surgery. Questions about menstruation status and performance status were also included in the survey. The performance status was measured with the Eastern Cooperative Oncology Group Performance Status (ECOG-PS) scale which assesses the level of functioning based on activity, ambulatory status and need for care ranging from grade 0 (normal activity) to grade 4 (completely bedridden). ECOG-PS is widely used and well validated [16].

Functional Assessment of Cancer Therapy-Breast cancer

Health-related QOL was measured with the Functional Assessment of Cancer Therapy-Breast cancer (FACT-B) version 4 which comprises of 36-items to measure both the 27-item general QOL associated with cancer (FACT-G) and the additional 9-item breast cancer related QOL, breast cancer subscale (BCS). The subscales of FACT-G are physical well-being (PWB), functional well-being (FWB), emotional well-being (EWB), and social/family well-being (SWB). The psychometric properties of the FACT-B are well documented [17] and validated in Korean population [18]. The test was conducted and scored in accordance with the instructions of the version 4 provided by the Functional Assessment of Chronic Illness Therapy (FACIT) Measurement System (www.facit.org). A total FACT-B score is calculated by summing the subscales. The instrument asks respondents to rate how true each statement is for the last 7 days with a response scale ranging from 0 (not at all) to 4 (very much). Cronbach α was 0.79 to 0.90 in the Korean version of FACT-B [18] and Cronbach α in this study was 0.852 for PWB, 0.855 for SWB, 0.808 for EWB, 0.914 for FWB and 0.702 for BCS.

Global QOL

The overall QOL of the patients was assessed using the Ladder of Life, a single-item measure. The respondents are asked to circle the number that represents how they feel at the present time. One represents the worst possible life and 10 represents the best possible life, Ladder of Life is widely used scale and provides a good summary of QOL [19].

The unmet sexuality needs

The unmet sexuality needs of breast cancer patients were assessed with the sexuality needs domain of the supportive care needs survey (SCNS). SCNS was designed to provide direct assessment of cancer patients' perceived needs for help and identify the magnitude of need for help [20]. The participants were asked to indicate their level of the need ranging from 1 'no need (not applicable)' to 5, 'high need' for help over the last month in relation to having cancer and a higher score indicated a higher perceived unmet need. The survey's psychometric properties and the reliability as well as the validity of this measurement have been well documented [20]. In the present study, SCNS-LF59 survey was used in Korean, which had been translated and back-translated by Hwang and Park [21]. The sexuality needs subscale was consisted of 3 items: 1) changes in sexual feelings, 2) changes in sexual relationships,

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and 3) to be given information about sexual relationships. The reliability coefficient of the subscale was found to be 0.913 in this study.

The Beck Depression Inventory

The Beck Depression Inventory (BDI) is one of the most commonly used self-rated depression symptom questionnaires in medical settings. BDI is a 21-item inventory that describes symptoms and attitudes. Each item in BDI describes a particular aspect of depression and consists of four self-evaluative statements. The study participants are asked to circle the item that best describes their feelings in the last week. The Korean version of the BDI was standardized [22] and its validity and reliability have been established [23]. The reliability coefficient for BDI was 0.909 in this study.

Statistical analysis

To explore the effects of adjuvant chemotherapy (independent variable) on health related QOL, global QOL, depression and unmet sexuality needs (dependent variables), multiple analysis of covariance (MANCOVA) was performed after controlling confounding variables (covariates). Since dependent variables of the study including health related QOL, global QOL, depression and unmet sexuality needs were significantly correlated with each other, MANCOVA was considered as appropriate for the analysis. First, sociodemographic and clinical variables were analyzed using descriptive statistics including mean, standard deviation, number and percentage. Then, both independent t-tests for continuous variables and chi-square tests for categorical variables were conducted to identify confounding variables between women who had received chemotherapy after surgery and those who had not. Data analyses were performed using SPSS version 20.0 statistical program (IBM, Armonk, USA)

Table 1. Sociodemographic characteristics of the participants (n=534)

Characteristic	Chemotherapy		*p*-value
	Done (n=369) No. (%)	None (n=165) No. (%)	
Age (yr)*	48.2±8.4	48.8±8.9	0.406
Education level			0.193
<High school	49 (13.3)	15 (9.1)	
High school	189 (51.2)	80 (48.5)	
>High school	131 (35.5)	70 (42.4)	
Marital status			0.876
Single/Separated	36 (9.8)	17 (10.3)	
Married/Partnered	333 (90.2)	148 (89.7)	
Employment			0.203
Employed	122 (33.1)	64 (38.7)	
Unemployed	247 (66.9)	101 (61.3)	
Perceived financial status			0.990
High	38 (10.3)	17 (10.3)	
Middle	268 (72.6)	119 (72.1)	
Low	63 (17.1)	29 (17.6)	

*Mean±SD.

RESULTS

Sociodemographic and clinical characteristics of the participants

Sociodemographic and clinical characteristics of the participants are shown in Tables 1 and 2. Among a total of 534 women, about 69% of the participants received chemotherapy after surgery for breast cancer. Participants were classified based on the time since surgery such as <1 year, group 1; 1 to 3 years, group 2; and >3 years, group 3. One hundred seventeen, 108, and 144 participants received chemotherapy after surgery among 198, 152, and 184 participants in group 1, 2, and 3, respectively (data not shown). Homogeneity tests between women receiving chemotherapy and women not receiving chemotherapy showed significant differences in performance status ($p=0.032$), TNM stage ($p<0.001$), hormone therapy

Table 2. Clinical characteristics of the participants (n=534)

Characteristic	Chemotherapy		*p*-value
	Done (n=369) No. (%)	None (n=165) No. (%)	
Menstruation status			0.622
Absent	246 (66.7)	106 (64.2)	
Present	123 (33.3)	59 (35.8)	
TNM stage			<0.001
0 or I	130 (35.2)	147 (89.1)	
II	197 (53.4)	18 (10.9)	
III	42 (11.4)	0 (0)	
Surgery method			0.264
Total mastectomy	204 (55.3)	80 (48.5)	
Breast-conserving surgery	165 (44.7)	85 (51.5)	
Hormone therapy			0.039
Done	254 (68.8)	128 (77.6)	
None	115 (31.2)	37 (22.4)	
Radiation therapy			0.301
Done	207 (56.1)	84 (50.9)	
None	162 (43.9)	81 (49.1)	
Time since surgery (yr)			<0.001
<1	117 (31.7)	81 (49.1)	
1-3	108 (29.3)	44 (26.7)	
>3	144 (39.0)	40 (24.2)	
ECOG-PS			0.032
0	222 (60.2)	118 (71.5)	
1	132 (35.8)	44 (26.7)	
≥2	15 (4.0)	3 (1.8)	

ECOG-PS=Eastern Cooperative Oncology Group Performance Status.

($p=0.039$), and time since surgery ($p<0.001$).

Effects of chemotherapy on depression, unmet sexuality needs, global QOL, and QOL

The effects of adjuvant chemotherapy on depression, sexuality needs, global QOL and health related QOL among women with breast cancer are shown in Figure 1. Based on the results on descriptive statistics and homogeneity tests, variables including performance scale, hormone therapy, TNM stage, and time since surgery were identified as confounding variables. Hence, MANCOVA with covariates of performance scale, hormone therapy, TNM stage, and time since surgery were conducted. The patients who underwent chemotherapy experienced statistically significant impact on depression (F [1,528] = 4.98, $p=0.026$, partial $\varepsilon^2=0.009$), sexuality needs (F [1,528] = 6.76, $p=0.010$, partial $\varepsilon^2=0.013$), BCS (F [1,528] = 6.60, $p=0.010$, partial $\varepsilon^2=0.012$), PWB (F [1,528] = 10.28, $p=0.001$, partial $\varepsilon^2=0.019$), and EWB (F [1,528] = 4.88, $p=0.028$, partial $\varepsilon^2=0.009$). According to post-hoc analyses, both depression and sexuality needs in the group receiving chemotherapy were statistically higher than those in the group not receiving chemotherapy (Figure 1). The quality of life subscales including breast cancer subscale, physical well-being, and emotional well-being, on the other hand, were statistically higher in the group not receiving chemotherapy than in the group receiving chemotherapy (Figure 1).

The effects of chemotherapy on QOL variables according to time since surgery are summarized in Figure 2. Education, menstruation status, performance scale, hormone therapy, TNM stage, and time since surgery for group 1, TNM stage for group 2, and radiation therapy and TNM stage for group 3 were identified as covariates, and hence, MANCOVA with each set of covariates were conducted. For group 1 (< 1 year), postoperative chemotherapy had a statistically significant effect on depression (F [1,182] = 3.29, $p=0.042$, partial $\varepsilon^2=0.018$), unmet sexuality needs (F [1,182] = 5.91, $p=0.016$, partial $\varepsilon^2=0.031$), BCS (F [1,182] = 8.72, $p=0.004$, partial $\varepsilon^2=0.046$), and PWB (F [1,182] = 5.95, $p=0.016$, partial $\varepsilon^2=0.032$). Post-hoc analyses indicated that both depression and sexuality needs in the group receiving chemotherapy were statistically higher than those in the group not receiving chemotherapy and that both BCS and PWB in women not receiving chemotherapy were statistically higher than those receiving chemotherapy. For group 2 (1-3 years since surgery), chemotherapy did not have a statistically significant effect on any of the measures. However, chemotherapy exhibited a statistically significant effect on depression (F [1,179] = 5.59, $p=0.019$, partial $\varepsilon^2=0.030$) and PWB (F [1,179] = 4.89, $p=0.028$, partial $\varepsilon^2=0.027$) in group 3 (> 3 years since surgery). As in the group 1, depression in women receiving chemotherapy was higher than those not receiving chemotherapy while PWB in women not receiving chemotherapy was higher than those receiving chemotherapy for group 3 (Figure 2).

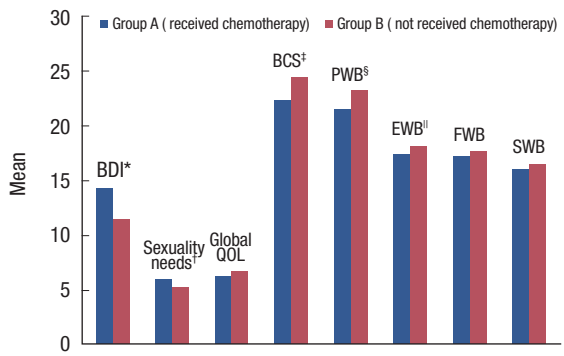

Figure 1. Results of multiple analysis of covariance (MANCOVA) analysis in Beck Depression Inventory (BDI), sexuality needs, global quality of life (QOL), and Functional Assessment Cancer Therapy-Breast (FACT-B). MANCOVA was performed after controlling for variables including performance scale, TNM stage, hormone therapy, and time since surgery groups.
BDI = Beck Depression Inventory; QOL = quality of life; BCS = breast cancer subscale; PWB = physical well-being; EWB = emotional well-being; FWB = functional well-being; SWB = social well-being.
*Group A > Group B ($p=0.026$); †Group A > Group B ($p=0.010$); ‡Group A < Group B ($p=0.010$); §Group A < Group B ($p=0.001$); ‖Group A < Group B ($p=0.028$).

DISCUSSION

In the present investigation, we examined the effects of adjuvant chemotherapy on QOL of women with breast cancer. We observed that women with past chemotherapy reported being more depressed, less satisfied with their life and having higher level of unmet sexuality needs than those without chemotherapy. Furthermore, they experienced significantly poor physical, emotional, social/family, functional well-being and higher breast cancer specific concerns as measured by FACT-B. The results of this study are in corroboration with previous reports [2,9,11], with additional new data on that women with past chemotherapy group suffers more difficulties in such an extensive area of QOL than women without chemotherapy group.

When the impact of adjuvant chemotherapy was analyzed according to survival time since surgery, chemotherapy was associated with poor QOL in group 1 (< 1 year since surgery) and group 3 (> 3 years since surgery). However, no statistical significance was observed in the group 2 (1-3 years since surgery). Also women with past chemotherapy showed higher scores on BDI and unmet sexuality needs and lower scores in

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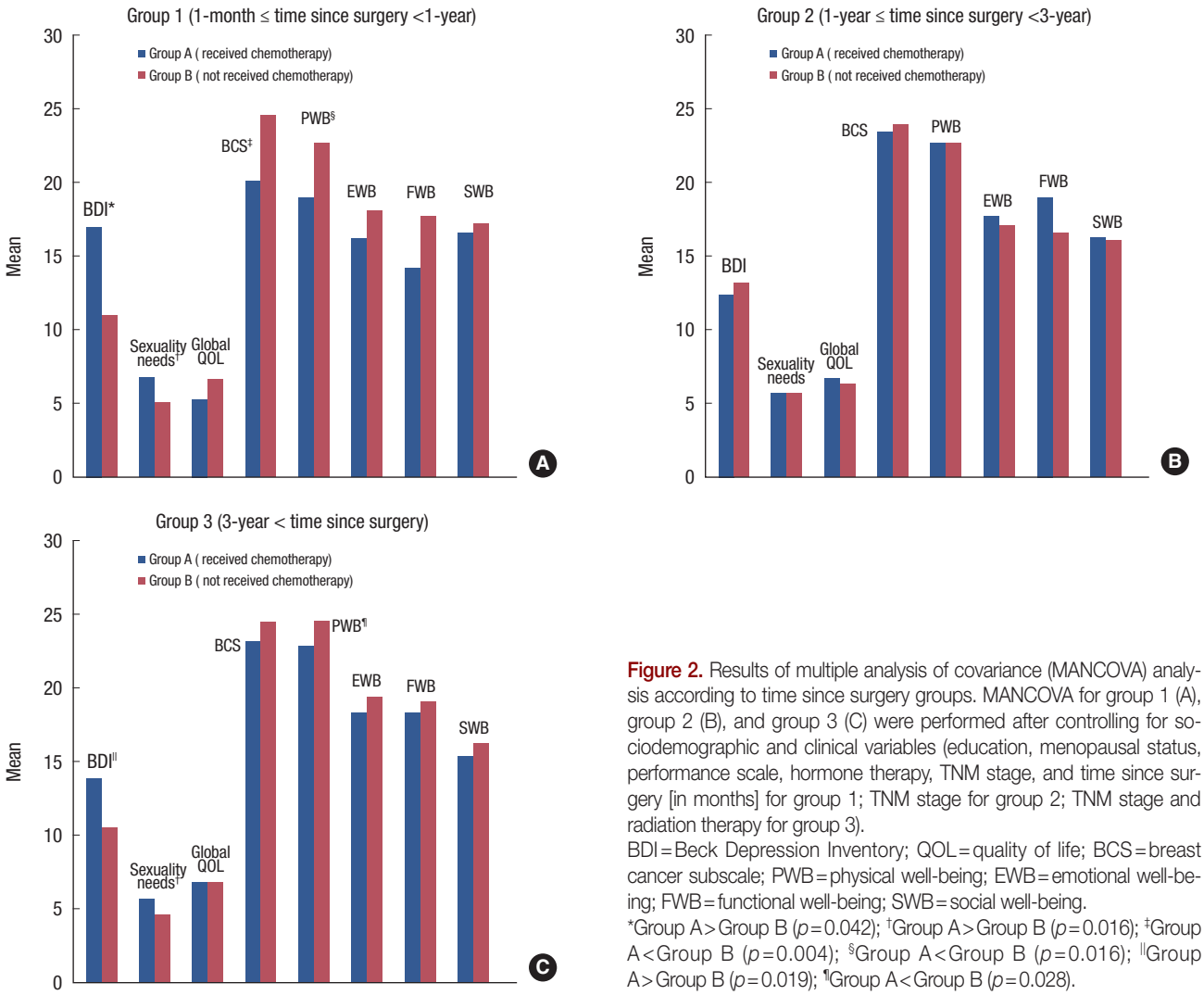

Figure 2. Results of multiple analysis of covariance (MANCOVA) analysis according to time since surgery groups. MANCOVA for group 1 (A), group 2 (B), and group 3 (C) were performed after controlling for sociodemographic and clinical variables (education, menopausal status, performance scale, hormone therapy, TNM stage, and time since surgery [in months] for group 1; TNM stage for group 2; TNM stage and radiation therapy for group 3).
BDI = Beck Depression Inventory; QOL = quality of life; BCS = breast cancer subscale; PWB = physical well-being; EWB = emotional well-being; FWB = functional well-being; SWB = social well-being.
*Group A > Group B (p = 0.042); †Group A > Group B (p = 0.016); ‡Group A < Group B (p = 0.004); §Group A < Group B (p = 0.016); ‖Group A > Group B (p = 0.019); ¶Group A < Group B (p = 0.028).

PWB and BCS than those with no chemotherapy in the group 1 as women in this group possibly suffer short-term adverse effects of chemotherapy more directly. This confirms the previous findings and suggests the end of treatment period, known as 'transition period' and the treatment period itself is quite stressful [24]. While in a study by Ganz et al. [24], women with past chemotherapy at the end of treatment (ranged from 21 to 471 days after surgery) reported worse physical and sexual functioning but no statistically significant differences in mental health functioning including depression, our study participants with past chemotherapy in group 1 (< 1 year) reported being more depressive as well as having worse PWB and higher BCS and sexuality needs. This warrants further investigations focusing on association between chemotherapy and depression. Despite the effects of chemotherapy on sexual functioning is quite inconsistent depending on the tools used [11], it is quite meaningful that women receiving chemotherapy in group 1 expressed significantly higher unmet sexual needs in our study, given the fact that Asian patients are more reluctant to talk about their sexual needs [25]. Oncologists might need to ask patients' sexual functioning and psychological distress related with chemotherapy treatment during their follow-up visits, in addition to their physical well-being.

In contrary to above findings, the impact of chemotherapy was not found in group 2 (1-3 years since surgery). Patient in this group did not show any significant difference in QOL, global QOL, depression or unmet sexuality needs. It is reasonable to assume that after 1 year of surgery, women receiving chemotherapy might be relatively relieved that not only chemotherapy had been completed but the side effects of chemotherapy were significantly reduced, indicating their level of functioning have been quite recovered. Therefore, women with chemotherapy might have relatively good QOL during this time period, which can contribute to no QOL difference

between chemotherapy group and no chemotherapy group.

It is interesting to note that the difference of QOL, especially in terms of physical well-being and depression reappear in the group 3 (>3 years since surgery). Since the previous long-term follow-up studies on the late effect of adjuvant chemotherapy are quite conflicting, one study suggested chemotherapy was associated with poorer physical, social and sexual functioning in the long term follow-up [2], contrary to this, an another study showed that past chemotherapy did not impair QOL [11]. However, our data confirms that the adverse effects of adjuvant chemotherapy on physical health and depression may persist or worsen 3 years after surgery. Given that women treated with chemotherapy might have worse prognosis than those with no chemotherapy, they may experience increased fear of recurrence as they realize still having chemotherapy related problems, and this might be reflected on significantly higher scores on the BDI. In addition to this, the results may also be related with the early menopausal symptoms. It is noteworthy to mention that the mean age of breast cancer patients in Korea is much younger than Western counterparts, with the prevalence being the highest in 40s (39.7%), followed by 50s (24.98%), and 30s (14.80%) [26]. Considering high proportion of premenopausal patients (the mean age in this study is 48.2±8.4 years in women receiving chemotherapy), the chemotherapy induced menopausal symptoms still persist even years after treatment reflecting in lower physical functioning and higher level of depression.

Women who persistently depressed may be at risk of poor QOL and also vulnerable to premature death [27], which needs prompt professional psychological assessment and support. A long-term follow-up study suggested that the persistent fatigue was also associated with depression [28]. Physical activity intervention may be an efficient intervention strategy [29,30] in addition to psychological intervention, which needs to be confirmed in future studies.

It is important to recognize differences of QOL based on the various phases of survival time since surgery among chemotherapy group as chemotherapy-related side effects may appear differently depending on time since surgery. Our results stress the need of health care professionals to monitor not only short-term adverse effects but also the long term effects of chemotherapy.

The present study has several limitations. First, the impact of the adjuvant chemotherapy according to time since surgery can only be determined indirectly because of the cross-sectional design. Second, the unmet sexuality needs measure evaluated only the needs not resolved without asking sexual functioning with partner directly, hence this study results cannot be compared with those of other studies in terms of the chemotherapy effect on sexual functioning. Finally, the study participants were recruited from a single urban university hospital so the study results may not be generalized to all breast cancer patients in Korea.

In conclusion, adjuvant chemotherapy for breast cancer significantly affects QOL and the effects of chemotherapy on QOL appear to vary according to time since surgery. Breast cancer patients receiving chemotherapy experience the adverse effects of adjuvant chemotherapy up to 1 year after surgery on overall aspects of QOL and tend to recover later years. However, some negative impacts of chemotherapy on depression and physical well-being seem to reappear many years after surgery. Therefore, if future studies with a prospective design confirm our findings, we recommend that critical intervention strategies should be designed to alleviate long-term as well as short-term chemotherapy side-effects for women with breast cancer.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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