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[Soo Hyun Kim](#)^{*} and Ha Yeon Jo

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Article

Factors Associated with Poor Quality of Life in Breast Cancer Survivors: A 3-Year Follow-Up Study

Soo Hyun Kim^{1,*} and Ha Yeon Jo²

¹ Department of Nursing, Inha University, Incheon 22212, Republic of Korea; soohyun@inha.ac.kr

² Department of Nursing, Inha University, Incheon 22212, Republic of Korea; dddus92@gmail.com

* Correspondence: soohyun@inha.ac.kr; Tel.: +82-32-860-8213

Simple Summary: Although the quality of life (QOL) improves over time for most breast cancer survivors (BCS), specific subgroup of BCS may show persistently low or deteriorated QOL even after their treatment ends. Early identification of high-risk groups for QOL deterioration is crucial for quality cancer care. This study was conducted to identify subgroups of QOL change among 101 Korean BCS and to examine factors associated with subgroups that show poor QOL. During a 3-year observation, 22.6% of the participants showed consistently low or deteriorated QOL. Persistent symptoms of insomnia, fatigue, anxiety, depression, and comorbidity were found to be significant risk factors of poor QOL in BCS. These findings are helpful to identify high-risk group for QOL deterioration among BCS.

Abstract: The purpose of this study was to identify subgroups of quality of life (QOL) changes in breast cancer survivors (BCS) and to determine factors associated with subgroups of consistently low or deteriorated QOL. We enrolled 101 women recently diagnosed with breast cancer in South Korea and asked them to complete a questionnaire at baseline (within 1 month of diagnosis), 1 year later (Year 1), 2 years later (Year 2), and 3 years later (Year 3). We assessed QOL using the global QOL subscale from the EORTC QLQ-C30. We defined low QOL as a global QOL score 10 points below the mean score of the general population. Based on low QOL as defined in this study, we identified subgroups of QOL changes over 3 years. We identified four subgroups of QOL changes: improved (47.4%), stable (30%), continuously low (8.8%), and deteriorated (13.8%) and considered the last two categories (22.6%) as poor QOL. Logistic regression analyses demonstrated that significant determinants of poor QOL were insomnia at Year 1, fatigue and anxiety at Year 2, and fatigue, depression, and comorbidity at Year 3. In conclusion, persistent symptoms of insomnia, fatigue, anxiety, depression, and comorbidity are potential risk factors for poor QOL in BCS.

Keywords: breast cancer; depression; fatigue; insomnia; quality of life

1. Introduction

Breast cancer is the most common female cancer in South Korea, as it is worldwide [1]. Due to advances in early detection and treatment, the relative 5-year survival rate for breast cancer survivors (BCS) in high-income countries exceeds 90% [2], resulting in a constantly growing number of long-term survivors. As the number of BCS has increased, quality of life (QOL) issues have become a vital consideration for care in this population.

Previous studies reveal that a substantial portion of BCS suffer from long-term or late effects of cancer treatment, including pain, fatigue, insomnia, and lymphedema [3,4], ultimately decreasing their QOL [4]. In several large population-based studies, the QOL in post-treatment BCS was significantly lower than that in the general population [5-7]. Longitudinal studies on QOL among BCS indicate that overall, QOL tends to deteriorate during the first year post-diagnosis and improve in the long term [8-14].

The QOL of many BCS recover to that of the general population between 1- and 3-year post-diagnosis [11,15], however, specific groups continue to have a low or deteriorated QOL [16-18]. Di

Meglio et al. [18] characterized long-term QOL trajectories in a large sample (n = 4,131) of BCS. During 4 years of follow-up, 10% of participants (n = 413) showed a deteriorated QOL, and 6.6% (n = 272) showed a consistently low QOL. Similarly, Goyal et al. [17] reported that 14.2% (93/653) of a BCS cohort showed a consistently low QOL 18 months after a breast cancer diagnosis. In a study of Korean BCS (n = 126) [16], 58.9% had a consistently low QOL from pre-chemotherapy to 6 and 12 months after chemotherapy completion. Such subgroups that show consistently low or deteriorated QOL should be a prioritized target for survivorship care. Thus, identification of characteristics associated with this subgroup (hereafter defined as poor QOL group) is crucial.

Previous studies revealed that younger age, low economic status, excess body weight, comorbidity, endocrine therapy, current smoking, insufficient physical activity, and depression have been associated with long-term poor QOL [16-18]. Psychological factors, including low social support, passive coping, and less optimism have been associated [17]. Few studies, however, have examined the association of long-term BCS symptoms with poor QOL.

We have reported our longitudinal observation of coping style and QOL—and their association from diagnosis to 3 years post-diagnosis—among 101 BCS [19]. Using those cohort data, we conducted a second analysis to better understand QOL changes and their correlates. The purpose of the current study was to identify subgroups of QOL changes in BCS over 3 years after diagnosis and determine factors associated with poor QOL group, including sociodemographic, clinical, lifestyle, and symptom variables.

2. Materials and Methods

2.1. Study Design and Participants

This is a secondary analysis of a longitudinal study [19] that examined the association between coping style at diagnosis and subsequent QOL for 3 years among BCS. Included were women aged ≥ 19 years who had received a first-time diagnosis of breast cancer within 1 month, had a plan for cancer treatment, and were able to read and write Korean. Women were excluded if they had other cancer(s), had cognitive impairment, or were already undergoing cancer treatment. We screened 165 women and enrolled 101. The retention rate was 82.2% (n = 83) 1 year after enrollment ('Year 1'), 85.1% (n = 86) 2 years after enrolment ('Year 2'), and 79.2% (n = 80) 3 years after enrolment ('Year 3'). Detailed participant flow is described elsewhere [19].

2.2. Data Collection

Between 2010 and 2011, after approval from the Institutional Review Board of Inha University Hospital in South Korea, participants were recruited within 1 month of breast cancer diagnosis. Physicians screened subjects for their interest in participating in this study, which a research nurse explained in face-to-face interviews. Women who agreed to participate were provided with an informed consent form followed by a questionnaire. Data collection was conducted 1, 2, and 3 years after enrolment. Follow-up questionnaires were mailed to participants to complete and return to the research team. Clinical information was obtained through electronic medical records after completion of primary treatment. Participants were followed until 2015.

2.3. Measures

We measured physical symptoms and financial impact using the symptom subscales and items from the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC QLQ-C30), including fatigue (3 items), nausea/vomiting (2 items), pain (2 items), dyspnea (1 item), insomnia (1 item), appetite loss (1 item), constipation (1 item), diarrhea (1 item), and financial difficulties (1 item). The scoring principle and imputation of missing values follow the EORTC scoring manual [20]. Scores range from 0 to 100, with higher scores representing more severe symptom. The Korean version of the EORTC QLQ-C30 has been validated [21]. In this study, the Cronbach's alpha of the three subscales ranged from 0.62 to 0.72. In order to analyze symptom variables as binary variables, we dichotomized them using the thresholds for clinical

importance (TCIs) developed by Giesinger [22]. The TCIs for the symptom variables were fatigue (39), nausea/vomiting (8), pain (25), dyspnea (17), insomnia (50), appetite loss (50), constipation (50), diarrhea (17), and financial difficulties (17). These TCIs were used in a previous BCS study [18].

We measured psychological symptoms using the Korean version of the Hospital Anxiety and Depression Scale (HADS) [23]. The HADS consists of two subscales with anxiety (7 items) and depression (7 items), each on a 4-point Likert scale (0–3). The score is obtained by summing the scores within each subscale, which ranged from 0 to 21. A higher score denotes more severe symptoms. In this study, the Cronbach's alpha was 0.86 for the anxiety subscale and 0.80 for the depression subscale. In order to analyze symptom variables as binary variables, we used a cut-off score of ≥ 8 for each subscale, as in a previously validated study [24].

We measured QOL using the global QOL subscale (2 items) from the Korean version of EORTC QLQ-C30 [21]. The scoring principle and imputation of missing values are followed by the EORTC scoring manual [20]. The score ranges from 0 to 100, with a higher score representing a better QOL. In this study, the Cronbach alpha of the global QOL subscale was 0.85. To analyze the QOL as a binary variable, we dichotomized it using normative reference data. We based our binary QOL variable on whether the global QOL score had fallen more than the minimal clinically important difference (MCID) below the Korean female general population mean of 67.7 [25]. The MCID of the EORTC QLQ-C30 used was 10 points, in keeping with previous studies [26, 27] and resulting in a score of 57.7 for the study cut-off. Thus, a low QOL was defined as a global QOL score of < 57.7 .

Sociodemographic variables that we collected included age, marital status, educational level, religion, employment status, monthly income, menopausal status, and comorbidity. Clinical variables included cancer stage at diagnosis, type of surgery, and type of treatments (chemotherapy, radiation therapy, and anti-hormone therapy). Lifestyle variables included regular exercise (yes/no), tobacco use behavior (current, former, never smoking), and alcohol consumption behavior (yes/no).

2.4. Statistical Analysis

In this longitudinal study, we collected data at least three time points (i.e., baseline, Year 1 and/or Year 2, and Year 3) for the analysis. We analyzed data with SPSS 26.0 software (SPSS Inc, Chicago, IL), using standard descriptive measures.

We identified 4 subgroups of QOL changes. For the “improved” group, baseline QOL scores were < 57.7 but increased to ≥ 57.7 at Year 3, regardless of Year 1 or Year 2 scores. For the “stable” group, baseline QOL scores were ≥ 57.7 and maintained until Year 3. For the “continuously low” group, baseline QOL scores were < 57.7 and maintained until Year 3. For the “deteriorated” group, baseline QOL scores were ≥ 57.7 but decreased to < 57.7 at Year 3, regardless of Year 1 or Year 2 scores. In this study, we clustered the “consistently low” and “deteriorated” QOL groups as “poor” QOL group.

We performed univariate logistic regression analyses at three time points (Year 1, Year 2, and Year 3), calculating odds ratio (OR) and corresponding 95% confidence intervals (CIs) to identify potential correlates of poor QOL. Variables with a p value < 0.05 in the univariate analyses at each time point were entered into a corresponding multivariable logistic regression model. We obtained best-fitting multivariable logistic regression models using a forward stepwise elimination procedure. We reported the adjusted OR and 95% CIs for the final models. The significance level was set at $p < 0.05$, and all significance tests were two-sided.

3. Results

3.1. Characteristics of the Participants

Table 1 presents the Year 3 sociodemographic and clinical characteristics of the participants. The mean age of the participants was 54.1 years (SD = 8.9), with most (43.7%) in their 50s. All women received surgery; 73.8% underwent breast-conserving surgery. The majority received chemotherapy (73.8%) or radiation therapy (71.3%).

Table 1. General characteristics of study participants ($n = 80$).

Characteristics	Category	n (%)
Age (years)	< 40	3 (3.8)
	40 – 49	22 (27.5)
	50 – 59	35 (43.7)
	≥ 60	20 (25.0)
Marital status	Married	65 (81.3)
	Single	3 (3.7)
	Divorced/widowed	12 (15.0)
Education (n = 79)	Elementary school	9 (11.3)
	Middle school	17 (21.3)
	High school	42 (52.5)
	College or university	11 (13.8)
Religion	No	32 (40.0)
	Yes	48 (60.0)
Employment status	No	46 (58.2)
	Yes	33 (41.8)
Monthly income (n = 78)	< \$ 2000	28 (35.9)
	≥ \$ 2000	50 (64.1)
Menopause (n = 77)	No	12 (15.6)
	Yes	65 (84.4)
Comorbidity	No	50 (62.5)
	Yes	30 (37.5)
Cancer stage at diagnosis	0	7 (8.7)
	1	29 (36.3)
	2	36 (45.0)
	3	8 (10.0)
Type of surgery	Mastectomy	21 (26.3)
	Breast conserving surgery	59 (73.8)
Chemotherapy	No	22 (27.5)
	Yes	58 (72.5)
Radiation therapy	No	23 (28.7)
	Yes	57 (71.3)
Anti-hormone therapy	No	18 (22.5)
	Yes	62 (77.5)

3.2. Lifestyle and Symptoms Characteristics over Time

Table 2 displays lifestyle and symptom characteristics for 3 years after diagnosis. More than 60% maintained regular exercise across three time points, and the number who smoked decreased remarkably. Alcohol consumption behavior, on the other hand, worsened over time, with the number of drinkers increasing.

EORTC QLQ-C30 symptom results showed that fatigue, nausea/vomiting, pain, dyspnea, and insomnia were the most common symptoms across the three time points (range, 17.5% to 35.0%). The prevalence of these symptoms did not decrease; even the prevalence of fatigue, nausea/vomiting, and pain at Year 3 was the same or slightly greater than at Year 1. Financial difficulties were highly reported at all three time points but decreased gradually over time. The prevalence of anxiety ranged from 23.8% to 32.5%, and that of depression ranged from 23.8% to 28.7%. Two psychological morbidities improved slightly at Year 3 compared with Year 1 (Table 2).

Table 2. Lifestyle and symptoms characteristics over time ($n = 80$).

Variables	Year 1	Year 2	Year 3
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	<i>n</i> (%)		
Lifestyle			
Regular exercise	50 (62.5)	51 (63.7)	51 (63.7)
Tobacco use	8 (10.0)	3 (3.8)	1 (1.3)
Alcohol consumption	11 (13.8)	13 (16.3)	16 (20.0)
Symptoms			
EORTC QLQ-C30			
Fatigue	17 (21.3)	23 (28.7)	18 (22.5)
Nausea/vomiting	20 (25.0)	16 (20.0)	20 (25.0)
Pain	26 (32.5)	24 (30.0)	26 (32.5)
Dyspnea	26 (32.5)	28 (35.0)	24 (30.0)
Insomnia	18 (22.5)	16 (20.0)	14 (17.5)
Appetite loss	3 (3.8)	5 (6.3)	4 (5.0)
Constipation	5 (6.3)	8 (10.0)	2 (2.5)
Diarrhea	16 (20.0)	15 (18.8)	16 (20.0)
Financial difficulties	40 (50.0)	38 (47.5)	33 (41.3)
HADS			
Anxiety	26 (32.5)	19 (23.8)	22 (27.5)
Depression	23 (28.7)	22 (27.5)	19 (23.8)

3.3. QOL Change Subgroups

Table 3 shows the frequency of low QOL cases over time and their patterns. At baseline, 56.4% had a low QOL, but the frequency gradually decreased to 33.7% at Year 1, 23.3% at Year 2, and 22.5% at Year 3. Among the QOL change subgroups, 47.4% showed an improved QOL, 30% were stable, 8.8% showed a continuously low QOL, and the QOL of 13.8% deteriorated. Thus, 22.6% of cases showed a poor QOL.

Table 3. Quality of life (QOL) change patterns.

	<i>n</i> (%)
Cases with low QOL	
Baseline (n = 101)	57 (56.4)
Year 1 (n = 83)	28 (33.7)
Year 2 (n = 86)	20 (23.3)
Year 3 (n = 80)	18 (22.6)
QOL change subgroups	
Improved	38 (47.4)
Stable	24 (30.0)
Continuously low	7 (8.8)
Deteriorated	11 (13.8)

3.4. Univariate Logistic Regression Analyses for Poor QOL

Among sociodemographic and clinical factors, only comorbidity was significantly associated with poor QOL. Type of surgery showed borderline significance ($p = 0.052$), while no lifestyle factors showed any association. Among symptom variables, dyspnea, insomnia, and anxiety at Year 1, fatigue, pain, insomnia, anxiety, and depression at Year 2, and all symptoms except for diarrhea at Year 3 were significantly associated with poor QOL (Table 4). Due to their low frequency, smoking and constipation were not available for analysis at Year 3.

Table 4. Univariate logistic regression analyses for poor QOL.

Variables	OR	95% CI	<i>p</i>
Sociodemographic			

	Age ≥ 50 years	1.263	0.418 – 3.815	0.679
	No spouse	0.968	0.272 – 3.446	0.960
	Education < high school	1.584	0.524 – 4.790	0.415
	No religion	1.062	0.362- 3.111	0.913
	Not employed	1.152	0.399 – 3.327	0.794
	Monthly income < \$2,000	2.065	0.713 – 5.986	0.182
	Menopausal	3.896	0.467 – 32.374	0.209
	Having comorbidity	4.889	1.590 – 15.028	0.006
	Clinical			
	Stage 2-3 (ref. stage 0~1)	1.875	0.625 – 5.629	0.262
	MRM (ref. BCS)	3.015	0.991 – 9.175	0.052
	Chemotherapy	2.209	0.572 – 8.540	0.251
	Radiation therapy	0.547	0.181 – 1.651	0.284
	Anti-hormone therapy	1.021	0.289 – 3.601	0.974
	Lifestyle			
Year 1	Exercises regularly	1.015	0.037 – 3.356	0.980
	Smokes	1.167	0.214 – 6.348	0.858
	Drinks	0.313	0.037 – 2.653	0.287
Year 2	Exercises regularly	1.128	0.372 – 3.425	0.831
	Smokes	7.600	0.645 – 89.574	0.107
	Drinks	0.557	0.111 – 2.782	0.476
Year 3	Exercises regularly	0.871	0.280 – 2.709	0.811
	Drinks	0.677	0.169 – 2.705	0.581
	Symptoms			
Year 1	Fatigue	1.603	0.479 – 5.367	0.444
	Nausea/vomiting	2.399	0.777- 7.409	0.128
	Pain	2.647	0.900 – 7.790	0.077
	Dyspnea	3.594	1.208 – 10.688	0.021
	Insomnia	5.889	1.840 – 18.845	0.003
	Appetite loss	1.765	0.151 – 20.658	0.651
	Diarrhea	1.783	0.526 – 6.040	0.353
	Financial difficulties	1.000	0.350 – 2.586	> 0.999
	Anxiety	3.594	1.208 – 10.688	0.021
	Depression	2.507	0.837 – 7.504	0.100
Year 2	Fatigue	13.520	3.938 – 46.423	< 0.001
	Nausea/vomiting	2.600	0.790 – 8.555	0.116
	Pain	5.923	1.918 – 18.295	0.002
	Dyspnea	2.263	0.776 – 6.599	0.135
	Insomnia	3.747	1.149 – 12.221	0.028
	Appetite loss	6.000	0.919 – 39.185	0.061
	Diarrhea	2.000	0.582 – 6.867	0.271
	Financial difficulties	2.037	0.697 – 5.953	0.193
	Anxiety	7.361	2.290 – 23.664	0.001
	Depression	7.286	2.307 – 23.010	0.001
Year 3	Fatigue	8.281	2.518 – 27.231	0.001
	Nausea/vomiting	4.636	1.497 – 14.361	0.008
	Pain	4.924	1.620 – 14.996	0.005
	Dyspnea	5.923	1.918 – 18.275	0.002
	Insomnia	7.467	2.130 – 26.172	0.002
	Appetite loss	12.200	1.184 – 125.717	0.036
	Diarrhea	1.190	0.332 – 4.271	0.789
	Financial difficulties	2.120	0.732 – 6.136	0.166

Anxiety	3.769	1.245 – 11.414	0.019
Depression	7.361	2.290 – 23.664	0.001

QOL, quality of life, CI = confidence interval, OR = odds ratio, MRM = modified radical mastectomy, BCS = breast conserving surgery.

3.5. Multivariable Logistic Regression Analyses for Poor QOL

Multivariable logistic regression analyses for poor QOL were conducted at three time points. In the model entered by Year 1 variables (type of surgery, dyspnea, insomnia, and anxiety), only insomnia was significantly associated with poor QOL. In the model entered by Year 2 variables (type of surgery, fatigue, pain, insomnia, anxiety, and depression), fatigue and anxiety were significantly associated with poor QOL. In the model entered by Year 3 variables (type of surgery, comorbidity, fatigue, nausea/vomiting, pain, dyspnea, insomnia, appetite loss, anxiety, and depression), comorbidity, fatigue, and depression were significantly associated with poor QOL (Table 5).

Table 5. Multivariable logistic regression analyses for poor QOL.

Time points	Variable	aOR	95% CI	<i>p</i>
Year 1	Insomnia	5.889	1.840 – 18.845	0.003
Year 2	Fatigue	22.783	4.493 – 115.515	< 0.001
	Anxiety	13.985	2.627 – 74.461	0.002
Year 3	Comorbidity	5.056	1.275 – 20.051	0.021
	Fatigue	9.070	2.167 – 37.954	0.003
	Depression	6.540	1.641 – 26.069	0.008

QOL = quality of life, aOR = adjusted odds ratio, CI = confidence interval.

4. Discussion

Although QOL improves over time for most BCS, some women may have consistently low or deteriorated QOL (defined as 'poor QOL' in this study). We identified subgroups of QOL changes using longitudinal cohort data and sought to examine characteristics that relate to the 'poor QOL' group. We believe that our results provide important evidence for the development of a care program for those survivors who are at risk of a poor QOL during their follow-up period.

The four subgroups of QOL changes that we identified among BCS were characterized by improved (47.4%), stable (30.0%), consistently low (8.8%), and deteriorated (13.8%) QOL. Interestingly, in Di Meglio et al.'s study [18] of 4,131 BCS, the patterns of QOL changes were quite similar to ours although their sample was larger: excellent (51.7%), very good (31.7%), deteriorated (10.0%), and continuously low (6.6%). Goyal et al. [17] identified six subgroups of QOL changes among 653 BCS: consistently high (36.0%), recovery to high (10.3%), consistently medium (26.5%), recovery to medium (13.0%), consistently low (10.3%), and consistently very low (4.0%). Considering our results along with previous studies, approximately 15-20% of BCS may be at risk for poor QOL after cancer treatment. Those women constitute a prioritized target for a survivorship care program.

On the other hand, we found a marked difference in the proportion of survivors in the consistently low group (8.8% vs 58.9%) compared with Park et al.'s study of 126 BCS [16]. This discrepancy might follow from the difference in treatment characteristics of the participants; all Park et al. subjects had received chemotherapy [16], while ours had not. In addition, they tracked QOL after chemotherapy and at 6 and 12 months after its completion, while we followed-up QOL at 1, 2, and 3 years after diagnosis. This means that Park et al.'s [16] sample would have been under a greater impact of treatment than ours, which might have caused their higher proportion of those in the consistently low QOL group.

Early identification of high-risk groups for poor QOL is crucial for prevention of QOL deterioration. From that clinical perspective, our findings provide important results by exploring potential risk factors for poor QOL at each time point. Among Year 1 variables, we found insomnia to significantly increase risk for poor QOL, which was consistent with Lee et al. [8], who also found

that increased insomnia among BCS was significantly associated with deteriorated QOL 1 year after diagnosis. Insomnia is one of the five most burdensome long-term issues in BCS [28]. In the current study, the prevalence of insomnia was highest at Year 1 (22.5%), and persisted. Insomnia is a major side effect of anti-hormone therapy (e.g., tamoxifen). Many BCS initiate this therapy during the first year, and that might cause the insomnia. Natural menopause may also be a cause. In South Korea, the most common age for breast cancer diagnosis is 40-50 years, so menopause might be the cause of insomnia in many. Our results suggest that screening for insomnia and appropriate interventions should be required, particularly in the first year of treatment. Evidence-based guidelines from the National Comprehensive Cancer Network (NCCN) [29] recommend cognitive behavioral treatments (e.g., relaxation therapy, stimulus control, sleep restriction) for insomnia in cancer survivors. Such approaches are preferred over pharmacologic interventions as a first choice [29].

Among Year 2 variables, we found fatigue and anxiety to significantly increase poor QOL risk. Fatigue is one of the most distressing symptoms among all cancer survivors, and approximately one-third of BCS report chronic fatigue [30]. In this study, the prevalence of fatigue was highest at Year 2 (28.7%) and decreased to 22.5% at Year 3, which was slightly higher than at Year 1 (21.3%). Our results support the finding that fatigue persists even after cancer treatment ends. Consistent with our findings, Lee et al. [8] reported that persistent fatigue among BCS was a significant predictor of deteriorated QOL. Currently, fatigue management is well established, and therapies, including physical activity, psychoeducational intervention, mindfulness-based stress reduction (MBSR), and cognitive behavioral therapy [29], need to be applied more actively in clinical practice.

Many cancer survivors do not have psychiatric clinical diagnoses but still have psychological symptoms such as anxiety and depression that can have a negative impact on QOL. Anxiety or depression affects up to 29% of cancer survivors, and the symptoms do not necessarily resolve with time [29]. At Year 1 in our study, 32.5% of BCS had anxiety and 28.7% had depression. This prevalence did not resolve at Year 3. Anxiety was found to be a risk factor for poor QOL at Year 2, as was depression at Year 3. Those findings were in line with previous longitudinal studies [10,16,17]. In a 14-month longitudinal study on QOL among 83 BCS, Hsiao et al [10] found that increased anxiety and depression predicted worse QOL. Appropriate interventions include a strong recommendation for regular physical activity [29]. In fact, evidence suggests that exercise may be as effective as antidepressants in the treatment of depression [31]. Other alternative treatments include yoga, tai chi, and MBSR [29]. Mindfulness is possibly the best-studied alternative treatment for psychological distress in cancer survivors. For example, in a randomized controlled trial among 322 BCS, Lengacher et al. [32] found that a 6-week MBSR program significantly reduced anxiety and fear of recurrence.

Among Year 3 variables, comorbidity, fatigue, and depression significantly increased risk of poor QOL. Comorbidity is an important issue among cancer survivors because cancer and/or its treatment increases the risk of comorbidities such as cardiovascular disease, diabetes mellitus, and osteoporosis [33]. Several cross-sectional studies of BCS revealed comorbidity severity to be associated with a decrease in QOL [9, 34, 35]. In Schoormans et al.'s study with BCS [35], the negative impact of comorbidity on QOL increased with time after diagnosis. Specifically, cardiovascular disease and depression were the strongest associates. Among longitudinal studies, Di Meglio et al. [18] also found severity of comorbidity to be significantly associated with deteriorated QOL. Longitudinal studies about the impact on QOL of specific types of comorbidities, however, are still lacking. Further research is required.

Unexpectedly, we could not find anything significant regarding lifestyle factors. Di Meglio et al. [18] found that insufficient physical activity and tobacco smoking were significantly associated with deteriorated QOL, suggesting the importance of a healthy lifestyle. The small sample size in our study may have diminished its power to detect significant results. Moreover, the number of smoking women was too small for analysis. Due to these methodological flaws, definite conclusions cannot be drawn.

Our finding of no significant sociodemographic-, disease- or treatment-related factors was unique. Prior longitudinal studies demonstrated that sociodemographic factors such as age [14,16,18,34], education [8,17], economic status [16,18], and employment status [8] were significant

correlates of continuously low or deteriorated QOL. In addition, clinical factors such as chemotherapy [8,17], type of surgery [10], and endocrine therapy [18] were found to be significant QOL correlates. From a clinical perspective, those findings yield a better understanding of where particular attention could be given to specific groups, such as survivors who are younger and/or belong to a low social class. This study's non-significant findings may follow from the small sample size. Further research with larger sample sizes is needed.

4.1. Implications

Our finding of the poor QOL of post-treatment BCS is evident from symptom problems. Since persistent insomnia, fatigue, anxiety, and depression were found to increase the risk of poor QOL, their periodic screening and effective interventions should be incorporated into clinical practice. Since comorbidity may also increase poor QOL risk, referrals should be made during the survivorship period. Our results may be valuable for guiding the development of a survivorship care program for post-treatment BCS.

4.2. Limitations

This study had several limitations. First, the study sample was enrolled from a single institution in South Korea, which limits its generalizability. Second, our sample size was relatively small, so it may have not detected low frequency subgroups of QOL changes, increasing the likelihood of a Type II error. Future studies from other institutions and larger sample sizes are required. Third, given its secondary analysis nature, this study did not include other psychological factors (e.g., coping, social support, self-efficacy) likely to affect QOL change.

5. Conclusions

This study identified subgroups of QOL changes in BCS for 3 years after diagnosis. Most BCS maintained or recovered their QOL over time, but 22.6% showed continuously low or deteriorated QOL. Persistent symptoms, such as insomnia, fatigue, anxiety, and depression, as well as comorbidity, were found to be potential risk factors for continuously low or deteriorated QOL. The findings offer clinically important insight for the development of interventions to preserve QOL in post-treatment BCS, including periodic symptom assessment and management, as well as timely referral for comorbidity management.

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