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유방암 환자의 항우울제 처방 현황 및 영향요인 연구

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Prescribing Patterns of Antidepressants and Their Associated Factors in Breast Cancer Patients

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Purpose: The aim of this study was to investigate the current state of antidepressant prescriptions in breast cancer patients and factors affecting the prescription of antidepressants. **Methods:** This study targeted female breast cancer patients who were prescribed antidepressants by a psychiatrist at least once between August 2010 and July 2011 at the Asan Medical Center in Seoul. The prescription history of each study subject was investigated to analyze the current state of antidepressant prescriptions in breast cancer patients. **Results:** The analysis of the prescription histories of 136 subjects in the antidepressant group determined that escitalopram, mirtazapine, and trazodone were the three most commonly prescribed medications with an average of 1.54 antidepressants prescribed per patient. A logistic regression analysis showed a statistically significant increase in antidepressant prescriptions in patients who were divorced or widowed, had sleep disturbances, or had undergone oncologic surgery for the breast cancer ($p<0.050$). In contrast, the prescription rate was lower for patients with tumour sizes greater than 50 mm ($p<0.050$). **Conclusion:** The sociodemographic factor of marital status, clinical factors of sleep disorders and tumour size, and a treatment-specific factor of the use of surgical therapy were identified as affecting the prescription of antidepressants in female breast cancer patients.

□ Key words - Antidepressive agents, Breast cancer, Depression, Prescribing pattern, Risk factors

INTRODUCTION

Breast cancer is one of the most common cancer worldwide and is the leading cause of cancer-related death in women.[1)] The incidence of breast cancer increased significantly until the early 2000s, and this trend has been suggested to be related to an increased exposure to estrogen due to both late marriages and decreased birth rates,[2)] to westernized diets and changes in nutritional status, as well as to an increased rate of early diagnosis due to the broad implementation of mammography.[3,4)] Early diagnosis has improved the survival for breast cancer patients, thereby highlighting the importance of considering quality of life improvements in addition to the prolongation of survival in the treatment of breast cancer.

There are many factors that affect the quality of life in cancer patients, but depression is a particularly important one. Many prior studies determined that there is an increased frequency of anxiety or depression symptoms in breast cancer patients relative to other patients.[5)] Cancer is a serious illness on its own, and depression may worsen the prognosis in cancer patients and lead to decreased adherence to treatment-related drugs, ultimately resulting in increased mortality.[6-8)]

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It has been suggested that both the rate of diagnosis of depression requiring pharmacotherapy and the rate of those receiving treatment is low among cancer patients.[9-11] It is important to identify risk factors related to the onset of depression to appropriately diagnose the condition that can influence both the treatment results and quality of life. Many previous studies have sought to understand the risk factors related to depression.[11-16]

Several treatment-specific factors, such as surgical therapy,[16-20] and clinical factors, such as comorbidity,[11,15,16] insomnia,[12,13] pain,[13] and fatigue,[12] have been identified as being associated with the onset of depression. The level of education and total household income showed a correlation, although there was no correlation with age.[11,15,16] In summary, earlier studies do not show consistency in objective risk factors for depression, and due to the nature of psychiatric disorders, the living environment of the patient and social factors may also be related to disease onset.

Research by Suppli *et al.*[21] demonstrated that the use of antidepressants in patients without a history of antidepressant usage occurred more frequently in those with newly diagnosed primary breast cancer compared to those without the diagnosis with a hazard ratio (HR) of 3.34 (95% confidence interval (CI)=1.50-7.76). The HR for antidepressant use in patients with recurrent breast cancer compared to those without recurrent disease was 2.56 (95% CI 1.86-3.52). Unemployed subjects were more likely to use antidepressants compared to those that were employed (HR=1.56, 95% CI=1.16-2.10), and those who do not live with their children, have low income, or have multiple invaded lymph nodes displayed a lower correlation compared to those without these characteristics. Therefore, the risk of antidepressant drug use was affected more by sociodemographic factors than by disease- or treatment-specific factors.

A previous study by Bardwell *et al.*[13] ranked and categorized 2,595 female patients diagnosed with early breast cancer into high depression and low depression groups based on severity and then conducted an analysis of cancer-related factors, patient characteristics, the degree of physical activity, and psychosocial factors. Subjective psychosocial variables, rather than objective variables related to the disease, were found to be more influential in the prescription of antidepressants.

Prior research, such as the aforementioned studies, have shown that depression can be an important factor in the treatment results of breast cancer patients. Based on these previous results, the objective of this study is to understand the current state of antidepressant use in breast cancer patients in South Korea and evaluate the risk factors for the prescription of antidepressants.

METHODS

Study subjects

The subjects were recruited from breast cancer patients at the Asan Medical Center in Seoul, South Korea, which is a tertiary care centre with 2,680 beds.

1) Eligibility criteria
   (1) Female breast cancer patients registered with the Asan Medical Center.
   (2) Those who were prescribed antidepressants by a psychiatrist at the Asan Medical Center during the study period (August 2010–July 2011).
2) Exclusion criteria
   (1) Use of the tricyclic antidepressant amitriptylline for the treatment of sensory neuropathy.
   (2) Prior history of psychiatric disorders, including depression, at the time of diagnosis of breast cancer.
   (3) Those who could not be tracked using electronic records or were lost during follow-up.

This investigation was reviewed and approved by the Asan Medical Center Institutional Review Board.

Data collection and methods

To understand the current state of antidepressant prescriptions, the antidepressant group was defined as patients registered at the Asan Medical Center diagnosed with breast cancer who had received antidepressants for the treatment of depression by a psychiatrist at least once during the study period. The control group consisted of female breast cancer patients whose registration numbers immediately preceded those of the sub-

jects who were enrolled in the study group. If the patient having a registration number immediately prior to a subject in the study group was also a study group subject themselves or met the exclusion criteria, the patient with the subsequent registration number was used as a control. This grouping resulted in a 1:1 ratio of study to control patients. Sociodemographic, clinical, and treatment-specific factors were investigated in both groups. For patients in the study group, the generic name of the antidepressant, the total number of antidepressants used, and the duration of the prescription were also investigated. In the analysis of the present state of antidepressant prescriptions, all antidepressants used at least once by eligible subjects during the study period were investigated; multiple antidepressant prescriptions for an individual patient were considered as a multiple response.

Definitions

1) Antidepressants

Antidepressants for the investigation included the following drugs that have prescription codes and are able for prescription at the Asan Medical Center. Tricyclic antidepressants included amitriptylline, clomipramine, imipramine, nortriptyline, and tianeptine. Tetracyclic antidepressants consisted of mirtazapine. Trazodone was an atypical antidepressant used in the study. Selective serotonin reuptake inhibitors (SSRIs) included escitalopram, fluoxetine, fluvoxamine, paroxetine, and setraline. The prescribed serotonin and norepinephrine reuptake inhibitors (SNRIs) included duloxetine, milnacipran, and venlafaxine. Moclobemide was a type of monoamine oxidase used in the study. Although not categorized as antidepressants, aripiprazole and quetiapine are used for the treatment of depression at the Asan Medical Center, and thus were considered to be antidepressants in this study.

2) Sociodemographic factors

The following sociodemographic factors were investigated: current age, highest level of education, employment status, marital status, and the number of children. Age was categorized as less than 40 years old, 40-49, 50-59, and greater than 60. The level of education was divided into elementary school graduate or below, middle school graduate, high school graduate, and university graduate or above. Employment status was categorized as either currently employed or not, with a housewife being considered unemployed and an individual with a self-owned business being considered employed. Marital status was divided into currently married, single, divorced, and widowed. There were three groups for the number of children: no children, one or two children, and three or more children.

3) Clinical factors

The clinical factors investigated in the study included menopause (pre- or post-menopause), breast cancer stage, tumour size at diagnosis, the number of infiltrated lymph nodes at diagnosis, the presence of pain, the presence of sleep disturbances, and comorbidities. Because it is difficult to achieve an objective evaluation of pain severity, the presence of pain was investigated using the prescription history of analgesics during the study period. The presence of sleep disturbances was investigated based on the prescription history of sedatives used to aid in sleep during the study period. Comorbidities were defined as present when drugs were prescribed for the treatment of comorbid conditions.

4) Treatment-specific factors

Treatment-specific factors investigated in the data collection process were the use of surgical therapy, the type of surgery, and the presence of current treatment. The type of surgery was categorized as those who received a lumpectomy versus a mastectomy. Those patients without surgical treatment were excluded from the statistical analysis of the type of surgery received. Subjects were defined to be in current treatment if they received at least one administration of chemotherapy, hormone therapy, or radiotherapy during the study period.

Statistical analyses

The current state of antidepressant prescriptions was assessed using a frequency analysis and basic statistical analyses. The basic characteristics of the antidepressant

and control groups were expressed as the mean±standard deviation, and a t-test was used to determine the statistical differences between the two groups.

A crosstabulation of the individual factors between the study and control groups was calculated using a chi-square test and Fisher's exact test. In addition, a univariate logistic regression analysis was performed for each factor to obtain the odds ratio (OR), and a multiple logistic regression analysis was performed for variables identified as being statistically significant after univariate logistic regression analysis. SPSS version 12.0 software was used, and a statistical significance was defined as a p-value less than 0.05.

RESULTS

Current state of antidepressant prescriptions

During the study period, there were 156 female breast cancer patients who were prescribed antidepressants by a psychiatrist at the Asan Medical Center in Seoul. Of these patients, a total of 20 patients were excluded from the study (17 with a history of psychiatric disorders prior to the diagnosis of breast cancer, two who could not be accessed through electronic records, and one who was lost during follow-up); therefore, the study group was comprised of a total of 136. An additional 136 patients were chosen as the control group before the analyses were performed.

The analysis of the antidepressant prescriptions in the 136 study group subjects determined that escitalopram, an SSRI, was most widely prescribed (55.1%, 75/136 patients), followed by the tetracyclic antidepressant mirtazapine (26.5%, 36/136), and the atypical antipsychotic trazodone (17.6%, 24/136) (Table 1).

During the one-year study period, patients were prescribed, on average, 1.54 antidepressants. One antidepressant was prescribed in the majority of cases (65.4%, 89/136), whereas 19.9% (27 subjects) and 11.0% (15 subjects) received two or three different antidepressants, respectively.

Results of the crosstabulation of individual variables in the antidepressant and control groups

The average age of the subjects was 51.53 years in the antidepressant group and 50.49 in the control group, which was not statistically significant (p=0.369). In addition, the differences in body mass index (BMI), tumour size, and number of invaded lymph nodes were all statistically insignificant between the two groups (Table 2).

Of the sociodemographic factors, marital status displayed a statistically significant difference between the two groups (p=0.010). Of the analyzed clinical factors, the tumour size (p=0.005) and presence of sleep disturbances (p=0.000) also demonstrated meaningful differences between the two groups. All other clinical factors did not

Table 1. Frequency of antidepressant prescriptions[a] and average prescription duration.

Class	Drug	N[b]	%[c]	Average Prescription (Days)	Min	Max
Tricyclic	Imipramine	1	0.7	14	14	14
	Tianeptine	5	3.7	147.4	10	260
Tetracyclic	Mirtazapine	36	26.5	95.1	1	421
Atypical	Trazodone	24	17.6	112.8	5	364
SSRIs	Escitalopram	75	55.1	145.0	5	393
	Fluvoxamine	2	1.5	263.0	195	331
	Paroxetine	10	7.4	175.2	5	432
	Sertraline	6	4.4	167.2	83	363
SNRIs	Duloxetine	10	7.4	71.2	7	197
	Venlafaxine	16	11.8	135.8	5	355
Antipsychotics	Aripiprazole	2	1.5	37.5	10	65
	Quetiapine fumarate	22	14.0	89.6	2	366

[a]In cases where the same patient received two different drugs during the study period, each drug was considered as one prescription
[b]Total number of patients who were prescribed the corresponding drug
[c]Proportion of patients who received the corresponding drug in the antidepressant group (N=136 patients)

Table 2. Basic characteristics of the antidepressant and control groups.

	Antidepressant Group	Control Group	p-value
	N=136	N = 136	
Current age (years)	51.53±9.50	50.49±9.64	0.369
BMI[a] (kg/m^2)	23.07±2.97	23.00±3.02	0.843
Tumour size (mm)	2.19±2.41	2.71±.16	0.066
Tumour-positive axillary lymph nodes	2.43±6.21	2.76±6.56	0.669

Mean±standard deviation, [a]Body mass index

show statistical differences between the two groups. For treatment-specific factors, the history of surgical therapy (p=0.001) and type of surgery (p=0.030) were statistically meaningful between the two groups (Table 3).

Results of univariate logistic regression analysis of the individual variables in the antidepressant and control groups

A univariate logistic regression analysis was performed to analyze the effects of individual factors in the antidepressant group relative to the control group.

Table 3. Comparison of risk factors in the antidepressant and control groups.

Sociodemographic Factors	Antidepressant Group		Control Group		p-value[a]
	N=136	%	N=136	%	
Age (years)					
≤40	18	(13.2)	22	(16.2)	
41-50	44	(32.4)	44	(32.4)	0.664
51-60	48	(35.3)	51	(37.5)	
≥61	26	(19.1)	19	(14.0)	
Level of education					
Elementary	19	(14.0)	14	(10.3)	
Middle school	12	(8.8)	11	(8.1)	0.559
High school	55	(40.4)	66	(48.5)	
College	50	(36.8)	45	(33.1)	
Employment status					
Yes	34	(25.0)	39	(28.7)	0.494
No	102	(75.0)	97	(71.3)	
Religion					
Yes	102	(75.0)	90	(66.2)	0.110
No	34	(25.0)	46	(33.8)	
Marriage					
Married	109	(80.1)	117	(86.0)	0.010
Single	6	(4.4)	12	(8.8)	
Divorced or widowed	21	(15.4)	7	(5.1)	
Children					
0	10	(7.3)	15	(11.0)	0.475
1-2	95	(69.9)	87	(64.0)	
≥3	31	(22.8)	34	(25.0)	
Clinical Factors					
Menopausal status					
Premenopausal	41	(30.1)	32	(23.5)	0.218
Postmenopausal	95	(69.9)	104	(76.5)	
Tumour grade					
Stage I	51	(37.5)	38	(27.9)	
Stage II	62	(45.6)	69	(50.7)	0.318[b]
Stage III	18	(13.2)	25	(18.4)	
Stage IV	5	(3.7)	4	(2.9)	
Tumour size (mm)					
<20	77	(56.6)	56	(41.2)	0.005
≥20 to <50	55	(40.4)	65	(47.8)	
≥50	4	(2.9)	15	(11.0)	
Tumour-positive Axillary lymph nodes					
0	74	(54.4)	60	(44.1)	0.119
1-3	43	(31.6)	54	(39.7)	
4-9	7	(5.1)	14	(10.3)	
≥10	12	(8.8)	8	(5.9)	
Pain					
No analgesic	99	(72.8)	100	(73.5)	0.891
Analgesic	37	(27.2)	36	(26.5)	
Sleep disturbances					
Yes	74	(54.4)	42	(30.9)	0.000
No	62	(45.6)	94	(60.3)	
Comorbidities					
Yes	73	(53.7)	62	(45.6)	0.182
No	63	(46.3)	74	(54.4)	
Treatment-Specific Factors					
Surgery					
OP	135	(99.3)	122	(90.4)	0.001[b]
Non-OP	1	(0.7)	14	(9.6)	
Type of surgery					
Lumpectomy	93	(68.9)	68	(55.7)	0.030
Mastectomy	42	(31.1)	54	(44.3)	
Current treatment					
Yes	93	(68.4)	98	(72.1)	0.507
No	43	(31.6)	38	(27.9)	

[a]Chi-squared test unless otherwise specified, [b]Fisher's exact test

Results from the analysis of sociodemographic factors determined that those who were divorced or widowed were 3.220-fold more likely to be prescribed antidepressants compared to the currently married subjects (OR=3.220, 95% CI=1.317-7.875, p=0.010). The analysis of clinical variables illustrated that those with tumour sizes larger than 50 mm were 0.194-fold more likely to be prescribed antidepressants compared to those with tumour sizes less than 20 mm (OR=0.194, 95% CI 0.061-0.616, p=0.005). The results of the chi-squared test showed that the number of tumour-positive lymph nodes, which were statistically different between the two groups, did not have a statistically meaningful effect on the likelihood of antidepressant prescription.

Patients with a history of sleep disturbances were 2.671-fold more at risk for antidepressant use (OR=2.671, 95% CI=1.626-4.387, p=0.000). The analysis of treatment-specific factors determined statistically meaningful differences in the history of surgical therapy and type of surgery (p<0.050). For example, the patients who received surgery had a 14.268-fold greater likelihood for antidepressant use (OR=14.268, 95% CI=1.839-110.676, p=0.011). The risk for antidepressant use in subjects with a mastectomy was 0.579-fold higher than in those who received a lumpectomy (OR=0.579, 95% CI=0.348-0.963, p=0.035) (Table 4).

Results of the multivariate logistic regression analysis of the antidepressant and control groups

A multivariate logistic regression analysis was performed for five factors identified as statistically significant according to the univariate logistic regression analysis. These factors included marital status, tumour size, the presence of sleep disturbances, surgical therapy, and the type of surgery. However, because the p-value for surgical therapy was not significant based on the type of surgery, a multivariate logistic regression analysis was performed on the remaining four factors (marital status, tumour size, presence of sleep disturbances, and history of surgical therapy) without considering the type of surgery.

The incidence of antidepressant prescription was 3.241-fold higher in the subjects who were divorced or widowed (OR=3.241, 95% CI=1.389-3.926, p=0.020). Subjects with a tumour size greater than 50 mm had a 0.259-fold greater

Table 4. Results of the univariate logistic regression analysis for risk factors.

Sociodemographic Factors	p-value	OR (95% CI)
Age (years)		
≤40		reference
41-50	0.600	1.222 (0.577-2.588)
51-60	0.710	1.150 (0.550-2.404)
≥61	0.241	1.673 (0.708-3.949)
Level of Education		
College		reference
Elementary	0.624	1.221 (0.549-2.716)
Middle school	0.969	0.982 (0.394-2.444)
High school	0.295	0.750 (0.438-1.285)
Employment Status		
Yes		reference
No	0.494	1.206 (0.705-2.064)
Religion		
Yes		reference
No	0.111	0.652 (0.385-1.104)
Marriage		
Married		reference
Single	0.229	0.537 (0.195-1.480)
Divorced or widowed	0.010	3.220 (1.317-7.875)
Children		
0		reference
1-2	0.256	1.638 (0.699-3.837)
≥3	0.512	1.368 (0.536-3.489)
Clinical Factors		
Menopausal Status		
Pre-menopausal		reference
Post-menopausal	0.219	1.403 (0.818-2.406)
Tumour Grade		
Stage I		reference
Stage II	0.147	0.670 (0.389-1.151)
Stage III	0.098	0.536 (0.257-1.121)
Stage IV	0.920	0.931 (0.234-3.703)
Tumour Size (mm)		
<20		reference
≥20 to <50	0.056	0.615 (0.374-1.012)
≥50	0.005	0.194 (0.061-0.616)
Tumour-positive Axillary lymph nodes		
0		reference
1-3	0.103	0.646 (0.382-1.092)
4-9	0.068	0.405 (0.154-1.068)
≥10	0.689	1.216 (0.467-3.168)
Pain		
No analgesic		reference
Analgesic	0.891	1.038 (0.607-1.775)
Sleep disturbance		
No		reference
Yes	0.000	2.671 (1.626-4.387)
Comorbidity		
No		reference
Yes	0.508	1.192 (0.709-2.007)
Treatment-Specific Factors		
Surgery		
No		reference
Yes	0.011	14.268 (1.839-110.676)
Type of Surgery[a]		
Lumpectomy		reference
Mastectomy	0.035	0.579 (0.348-0.963)
Current Treatment		
Yes		reference
No	0.508	1.192 (0.709-2.007)

[a]Excluding 15 patients who did not receive surgery

Table 5. Results of the multivariate logistic regression analysis.

Factors	p-value	OR (95% CI)
Marriage		
Married		reference
Single	0.650	0.771 (0.251-2.371)
Divorced or widowed	0.020	3.241 (1.208-8.696)
Tumour Size (mm)		
<20		reference
≥20 to <50	0.144	0.676 (0.400-1.143)
≥50	0.032	0.259 (0.076-0.889)
Sleep Disturbances		
No		reference
Yes	0.001	2.335 (1.389-3.926)
Surgery		
No		reference
Yes	0.020	12.221 (1.484-100.617)

likelihood for an antidepressant prescription compared to those with a tumour size less than 20 mm (OR=0.259, 95% CI=0.076-0.889, p=0.032). If sleep disturbances were present, the risk of an antidepressant prescription was 2.336-fold greater than in the control group (OR=2.335, 95% CI=1.389-3.926, p=0.001). Compared to the group without surgical therapy, those who received surgery were 12.221-fold more likely to have an antidepressant prescription (OR=12.221, 95% CI=1.484-100.617, p=0.020) (Table 5).

DISCUSSION

Breast cancer survival has dramatically improved over the past 20 years due to medical advances in early diagnosis, new pharmacological agents, and the development of new cancer therapy methods. This means that breast cancer is no longer considered a fatal disease and is becoming increasingly treatable, thereby implying the need for long-term treatment plans that address the physical, social, and psychological health needs of breast cancer patients rather than simply the improvement of their survival.[22)]

Depression is a type of psychiatric disorder with reports of incidence 2-3 times greater in cancer patients compared to the general population.[23-25)] The development of depression is significant not only for problems related to the disease itself, but depression is also reported to be related to a decreased quality of life, an increased morbidity and mortality of breast cancer, an increased rate of hospital admission,[26,27)] a decreased motivation for cancer treatment, a decreased adherence to therapy,[27)] and an increase in suicide attempts.[28,29)] As the survival period increases due to advances in cancer therapy, treatments to improve the quality of life of patients are becoming more important. Thus, the treatment of depression, which can have a profound effect on quality of life and has a high incidence among cancer patients, is being considered essential for breast cancer patients.

Previous studies regarding clinical depression among cancer patients were led by oncologic specialists who diagnosed and treated depression.[29,30)] However, because oncologists have not received specialized training in the diagnosis and treatment of psychiatric disorders, they may be unsuccessful in diagnosing and treating depression, which requires specialized clinical treatment.[30)] In addition, symptoms of depression, such as fatigue, weight loss, loss of appetite, and sleep disturbances, may be misattributed to malignancy.[31,32)] Therefore, in this study, the antidepressant group was limited to those who were diagnosed with depression and prescribed antidepressants by psychiatrists.

The main antidepressants used for the therapy of depression are SSRIs and SNRIs as well as tricyclic and tetracyclic antidepressants.[5)] Tamoxifen, which is used as an adjuvant therapy after surgery in hormone receptor positive breast cancer, is metabolized by the CYP2D6 enzyme to exert its anti-tumour effect.[33,34)] However, SSRIs and SNRIs act as inhibitors of CYP2D6 in their normal physiologic metabolism. In particular, fluoxetine and paroxetine act as strong CYP2D6 inhibitors, and duloxetine acts as a moderate inhibitor of CYP2D6 acitivity.[35,36)] In contrast, citalopram, escitalopram, fluvoxamine, sertraline, and venlafaxine are weak inhibitors or non-inhibitors of CYP2D6. Therefore, the use of antidepressants that are weak inhibitors or non-inhibitors of CYP2D6 are recommended for most early hormone receptor positive

breast cancer patients taking tamoxifen.[36] The results of this study also confirmed that escitalopram or venlafaxine were used more frequently than fluoxetine or paroxetine.

Previous studies on depression in breast cancer patients showed mixed results with respect to variables affecting the disorder. Certain studies determined that depression is affected by breast cancer stage [17] or treatment regimen,[18-20] whereas other studies provided evidence that cancer-specific factors do not influence clinical depression in breast cancer patients.[13] Other studies suggested that the frequency or severity of depression in breast cancer patients is affected by comorbidities,[11,15,16] pain,[16] prior history of depression,[21,32] and metabolic diseases.[31] In addition, decreased organ function,[17,19] life stressors, and small changes unrelated to cancer were found to have a profound effect on the psychosocial functioning of the patients who were already weakened by the diagnosis of cancer, and these factors can act as a greater influence over other more objective cancer-specific variables.[13] Thus, this study first determined an antidepressant group (the study group) and a control group and then performed a retrospective investigation of sociodemographic factors, clinical factors, and therapy-specific factors to statistically analyze the effects of individual variables on antidepressant prescription.

This study investigated the differences in marital status, tumour size at diagnosis, the presence of sleep disturbances, history of surgical therapy, and the type of surgery performed between the study and control groups. According to the study by Bardwell *et al*.,[13] patients with early breast cancer, those who are younger, single (marital status), those with a low degree of physical activity, and those with an increased number of vasomotor or GI symptoms were all shown to be more likely to have severe symptoms according to a binary logistic regression when psychosocial variables were not considered in the analysis. However, the aforementioned variables all appeared to be statistically insignificant after psychosocial variables were included in the analysis. In contrast, psychosocial variables such as life events, sleep disturbances, and social pressure, were determined to influence symptoms of depression in a statistically significant manner. Our study also demonstrated the high risk for antidepressant prescription in those with sleep disturbances based on both univariate and multivariate logistic regression analyses, which is consistent with the results from previous studies. A divorced or widowed status was associated with a higher risk of antidepressant prescription compared to patients who were currently married. Because the divorce or death of a spouse can be considered part of the 'life events' variable, these results can be considered consistent with those of Bardwell *et al*.

In this study, the calculated risks of antidepressant use relative to tumour size and type of surgery performed were different from those of previous studies. Suppli *et al*.[21] calculated an increase in the HR of 1.01 (95% CI=0.95-1.07) for every 1 cm increase in tumour size; however, in our study, subjects with tumours greater than 50 mm had a reduced risk for antidepressant prescription compared to those with tumour size less than 20 mm. Previous studies found that patients who had a lumpectomy had a relatively high HR (0.92; 95% CI=0.74-1.14) compared to those receiving a mastectomy,[21] whereas our study determined that there was a lower rate of antidepressant prescription in mastectomy patients. This difference is thought to be due to the fact that Suppli *et al*. targeted newly diagnosed breast cancer patients during their study period and analyzed all antidepressants prescribed to eligible subjects. In contrast, our study targeted all patients diagnosed with breast cancer during the study period and only included antidepressants, as well as the inclusion of antipsychotics used for the treatment of depression, prescribed by a psychiatrist.

The limitations of this study include the small sample size in addition to the geographical limitation to one specific tertiary care hospital in a specific location. Pain-related issues or the economic status of the patients, which were found to be meaningful variables in prior studies, were not properly analyzed in this study, and therefore, can also be considered a limitation here. Further research,

including additional variables such as economic status and physical symptoms in a larger number of patients, should be pursued in the future.

The results of this study illustrate that not only cancer-specific factors, such as tumour size and the presence of surgical intervention, but also psychosocial variables unrelated to breast cancer, such as marital status and sleep disturbances, have a significant impact on the prescription of antidepressants in breast cancer patients.

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