Symptom Clusters and Quality of Life in Women with Breast Cancer Receiving Adjuvant Chemotherapy

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Abstract: This prospective longitudinal study explored symptom clusters and influences on quality of life among women with stage I-IIIA breast cancer who received treatment with chemotherapy. A sample of 112 women receiving adjuvant chemotherapy for breast cancer at a university hospital in Bangkok were recruited to this study using convenience sampling. Data were collected three times: before chemotherapy (Time 1); before receiving the second cycle of chemotherapy (Time 2), and 1-month after completion of chemotherapy (Time 3). Instruments used were a Demographic and Medical Record Form; the Modified Memorial Symptom Assessment Scale; and the Functional Assessment of Cancer Therapy-Breast. Factor analysis and multiple regression were used to identify symptom clusters and their influences on quality of life.

The results revealed that the participants with breast cancer experienced multiple symptoms concurrently. There were five symptom clusters existing at each time point: menopausal, psychologically-related self-image, and gastrointestinal-related fatigue symptom clusters tended to be stable across all three stages of data collection. "I don't look like myself", worrying, and feeling drowsy were found to be the strongest predictors of quality of life across all data collection phases. Issues regarding instability of symptoms within a cluster across phases were discussed.

Knowledge obtained from this study can be beneficial for nurses and other health care providers to better understand and care for multiple symptom experiences in women with breast cancer. It will also help such women to plan ahead for them to manage concurrent symptoms to promote their quality of life. However, future research is recommended to clarify the stability and extent of symptoms within various symptom clusters in women receiving chemotherapy for breast cancer.

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Introduction

Breast cancer is one of the leading causes of cancer death among women worldwide. The World Health Organization (WHO) surveyed specific causes of deaths among 194 countries in the year of 2008, and cancer was the second leading cause of death among Thai adult age-standardized 30-70 years.[1] In Thailand, breast cancer is the most frequently diagnosed cancer in women. Data from the National Cancer Institute also showed that the incidence rate

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of breast cancer becomes the largest proportion of cancer among Thai females since 2003. Particularly, the trend of incidence rate is still increasing each year. In addition, it ranks as one of the fatal diseases that affect Thai women resulting in their premature death.[2] Postoperative adjuvant chemotherapy is a well-established and routine part of treatment for breast cancer women. Although, adjuvant chemotherapy has been shown to significantly decrease mortality and increase disease-free survival, most of its side effects and late toxicities are threats to a patient's life. Moreover, unrelieved symptoms may cause long-term quality of life (QOL) impairments for women with breast cancer receiving chemotherapy.[3] Apparently, the occurrence of multiple symptoms caused by breast cancer or treatments may reduce females' abilities to perform work, to bath and dress, to concentrate, enjoy life, sexual functioning, and to affect mood in breast cancer women receiving chemotherapy.[4] Persistent multiple symptoms can affect QOL and functional status.[6-10] Nonetheless, little is known about multiple symptoms that concurrently occur across treatment trajectory and their influence on QOL.[5-9] Most studies have used cross-sectional designs,[10,11] heterogeneous patient samples, and relatively short follow-up.[5,6,8,9] Other limitations of current research about symptom clusters of Thai women with breast cancer receiving chemotherapy included cross-sectional study design[10]and one longitudinal study[12] to explore pattern of symptom clusters over time in breast cancer women receiving chemotherapy. The researchers selected some certain symptoms (i.e., nausea/vomiting, fatigue, and sleep alterations) which were identified from a previous study as most-common or highly prevalent symptoms during treatment.[12] From previous western studies,[5,6,11,16-20] the researchers selected some symptoms (i.e., pain, fatigue, sleep alterations, and depression) which were identified as most-common or highly prevalent symptoms during treatment. The researchers also assumed that these most-common symptoms could be grouped together as a cluster.

Knowledge from this current study would be a useful basis for planning intervention studies to manage multiple concurrent symptoms associated with chemotherapy across treatment phases[13,14] and may lead to the development of effective management strategies with the goal of improving QOL.

Review of Literature

Research on symptom clusters is still in an early stage and many questions remain unanswered. Symptom cluster has been defined by several investigators: Dodd and colleagues[6] defined this as three or more concurrent symptoms that are related to each other but are not required to share the same etiology. Kim and colleagues[15] defined a symptom cluster as two or more related symptoms or a stable group of symptoms that occur together, relatively independent of other clusters, and may reveal specific underlying dimensions of symptom. Stability of clustering should not change either across subjects or times. In addition, relationships among symptoms within a cluster should be stronger than relationships among symptoms in different clusters and symptoms in a cluster may or may not share the same etiology. In several studies, four selected symptoms (fatigue, pain, sleep alterations, or depression) have been focus of the investigation as a symptom cluster.[5,6,11,16-20] Besides, menopausal symptoms have been associated with fatigue after completion of chemotherapy but they have not been explored as a symptom cluster.[4,21] Nonetheless, there is no general agreement at this time regarding the basis or criteria for selecting symptom to be evaluated for clustering.[22] In addition, there are inconsistent research findings on symptom clusters experienced by individuals with breast cancer, and no evidence existing describing a co-occurring symptom and symptom distress within clusters.[5,6,14,20,21,23,24]

QOL of patients with breast cancer experiencing symptoms is often dynamic. Not all symptoms increase or decrease together. Groups of symptoms or symptom

clusters may have a different temporal pattern in relationship to treatment or disease progression.[25] The impacts of symptoms on QOL have revealed consistent findings. For instance, a high level of psychological symptoms such as anxiety at the start of treatment can negatively affect overall QOL.[24,26,27] Women who have had a mastectomy and received chemotherapy reported substantial decreases in physical and emotional well-being, and sexual functioning at the end of treatment.[28] Moreover, the symptom experience is dynamic and therefore will trigger different symptoms to cluster over time.[29] Women undergoing treatment for breast cancer are logically expected to experience a decline in their perceived QOL during treatment, but whether this impact is transitory or long-term is not known yet. Therefore, longitudinal studies are needed to fully understand the experience of women with breast cancer.

The two aims of this study were to identify the existence of symptom clusters; and examine the influences of distressing symptoms on QOL in women with breast cancer at before, during, and 1-month after completion of adjuvant chemotherapy.

Conceptual Framework

The mid-range Theory of Unpleasant Symptoms (TOUS)[30] was used as the framework to guide the study. This Theory provides a structure for beginning to determine the extent of overlapping among symptoms, and also the dimensions of symptoms or the characteristics of the symptoms in the TOUS (timing, severity, distress, and quality). Each symptom can vary in duration, intensity, quality, and distress, and multiple symptoms can occur together as a result of a single event, or one symptom can precede another. Further, the nature of the relationships among symptoms has been described as multiplicative rather than additive. Likewise, two or more concurrent symptoms are likely to catalyze each other. For instance, lack of energy seems considerably worse when both difficulty sleeping and lack of appetite are experienced concurrently during chemotherapy. TOUS appears to be a good fit to describe symptom experience, as well as to examine the relationships among symptom and symptom clusters in women with breast cancer. QOL was used as an outcome or effect of these symptoms experiences in this study.

METHODS

Design

A prospective longitudinal study design was used to obtain data before, during, and 1-month after completion of chemotherapy among Thai women with stages I-IIIA of breast cancer.

Ethical considerations

This study was approved by the Institutional Review Board of Siriraj Hospital, Faculty of Medicine, Mahidol University which was used as a study site. Each potential subject was informed about the purpose of the study, reassurance about confidentiality and anonymity, and that they had the right to withdraw at any point in the study with no effect on their treatment or hospital services.

Sample

The sample size calculation was based on power analysis with a desired power of 0.80, significance level of 0.05, and effect size of 0.50 plus an additional 10 % for attrition, which resulted in the need for at least 97 participants to be included in the study. Symptom clusters were identified using factor analysis and Pearson correlation.

1) The researchers wanted to explore the relationships among symptoms in each cluster. The correlation coefficients between symptoms in each cluster from a previous study[10] ranged from 0.30 to 0.50. To achieve a power of 0.80 with an α of 0.05, the sample size needed in the study would lie between 88 (for an effect size of 0.30) and 32 (for

an effect size of 0.50).[31] Since the attrition rate for longitudinal study from a previous study[32] was expected to be 10%, the sample size of this study should be at least 97 participants (for an effect size of 0.30).

2) Symptom clusters were identified using factor analysis. In general, a ratio at least 10:1 is the common rule regarding number of participants and number of independent variables. However, the minimum ratio of at least five participants per variables were acceptable.[33] The numbers of symptoms being explored in the study were 20 distressing symptoms. Therefore, at least 100 participants were enough for purposes of the study. In the study, a sample size of 112 was judged adequate for using factor analysis.[33]

Participants were selected from the population of women with stage I-IIIA breast cancer who were receiving adjuvant chemotherapy at the university hospital. Inclusion criteria were that participants were: women diagnosed with non-metastatic breast cancer after breast surgery; aged at least 18 years; receiving chemotherapy for the first time; and willing to participate in the study.

In the case of participants' ≥60 years, the degree of cognitive function was assessed using the Thai Short Portable Mental Status Questionnaire by Yamwong[34] to screen if they had some degree of cognitive impairment. It was a 10-item questionnaire using to assess short and long term memory, orientation to surroundings, knowledge of current events, and ability to perform mathematical tasks. The scores of 8 or over refer to the normal cognitive functioning. If participants had cognitive impairment, they were excluded from the study. Moreover, potential participants were excluded if they had documented psychiatric illness; or were physically ill to the degree that would preclude an individual from being interviewed or filling out the questionnaires.

Instruments

Three instruments were used to collect data:

1. Demographic and Medical Record Form (DMRF) was developed by the first researcher and team to collect demographic characteristics and medical history of participants. This included age, educational level, marital status, religion, number of family members living at home, employment status, average monthly family income, cancer diagnosis, stage of disease, cancer treatment, and any co-morbid conditions.

2. The Modified Memorial Symptom Assessment Scale (Modified MSAS)[35] was used to evaluate 39 physical and psychological symptoms that are associated with cancer. Participants were asked to rate whether or not they had experienced each symptom in the past week. If a symptom occurred, they were asked to rate its frequency, intensity, and the level of any distress. The MSAS Thai version was translated by Suwisith[10] and the tool was modified to use in this study by the investigator with permission from the original English developer[35] by adding seven new items: hot flashes, night sweats, vaginal discharge, vaginal itching/irritation, vaginal dryness, mood swings, and joint pain, all of which can be menopausal symptoms[21,36-39] These items were validated for content and language appropriateness by five experts in various areas of oncology which comprised one medical oncologist, two oncology nurse specialists in medical and surgical oncology, and two nurse educators in oncology and women health. The tool was revised according to these expert's recommendations. Symptom frequency was rated using a 4-point Likert scale ranging from 1 (rarely) to 4 (almost constantly). Symptom intensity was rated using a 4-point Likert scale ranging from 1(slight) to 4 (very severe). The scores of symptom distress were rated using a 5-point Likert scale ranging from 0 (not at all) to 4 (very much).The internal consistencies of the symptom frequency, intensity, and distress scale at each time point ranged from 0.68 to 0.77, 0.67 to 0.81, and 0.70 to 0.82, respectively.

3. The Functional Assessment of Cancer Therapy-Breast (FACT-B) version 4,[40] was used to evaluate general QOL(FACT-G) 27 items and additional concerns more specific to women with breast cancer 9 items (BCS subscales), with a 5-point rating scale ranging from 0 (not at all) to 4 (very much). The FACT-B Thai version was translated by Ratanatharathorn and coworkers[41] and permission for its use was obtained prior to use. Higher scores on the FACT-B scales indicate a higher QOL.The internal consistencies of the total FACT-B subscales at each time point were ranging from 0.84 to 0.86.

The reliability of the modified MSAS and the FACT-B were evaluated in a pilot study of 20 Thai women with breast cancer during chemotherapy. The Cronbach's alpha ranged from 0.80 to 0.83 for the modified MSAS and from 0.84 to 0.86 for the FACT-B.

Data collection

All participants who met the inclusion criteria were approached and informed about the study and gave them a chance to ask questions to clarify their doubts. Having obtained written informed consent for participation in the study, the participants were asked to complete three questionnaires including the DMRF, the Modified MSAS, and the FACT-B at three time points: before receiving chemotherapy (Time1), before receiving the second cycle of chemotherapy (Time2), and 1-month after completion of adjuvant chemotherapy (Time3), the researcher attempted to coordinate data collection in person when participants made their clinic visits. If this was not possible, the questionnaires were sent by mail with instructions for return a self-addressed envelope.

Data analysis

All analyses were done using exploratory factor analysis and multiple regression with using SPSS Version 16.0. Prior to the symptom cluster analyses, appropriate descriptive statistics were used to generate information regarding participants' demography, clinical characteristics, and symptom experiences. After all assumptions of the statistic analysis were tested and met, factor analysis was used to determine the number of symptom clusters, and stepwise multiple regression analysis used to determine the predicting ability of symptoms on QOL across the three times of data collection.

An exploratory factor analysis (EFA) was performed to identify the number of symptom clusters based on symptom distress ratings. The researcher selected only the 20 most-distressing symptoms which were reported by at least 5% of participants at before receiving chemotherapy, and by at least 30% of participants after receiving chemotherapy in the EFAs.

Exploratory factor analysis with principal components (rotated component matrix with varimax rotation) was used to extract factors using eigenvalues of 1.2 and expressed only factor loadings greater than 0.3. The Kaiser-Meyer-Olkin (KMO) was used to examine sampling adequacy or deciding whether factor analysis is appropriate. The communalities were used to observe the level of shared variance between items. These results met criteria and supported use of factor analysis for this data. Regarding testing of the clustering, all symptoms with factor loadings above 0.30 and loaded on more than one factor were considered and explored through the Pearson's r correlations. The Cronbach's alpha coefficient using to determine the internal consistency and reliability of the clusters was more than 0.60. A Cronbach's alpha coefficient higher than 0.60 indicated the symptoms within a cluster occurred in a homogenous pattern.[33] However, the value of Cronbach's alpha coefficient less than 0.60 was also interpreted with cautions in the study. Cronbach's alpha coefficient, as a measure of internal consistency among factor items, was used for each identified factor at each time point. Otherwise, it was used to test the clustering of symptom clusters which were derived from the factor

analysis. The generally agreed upon lower limit for Cronbach's alpha coefficient is 0.70, although it may decrease to 0.60 in exploratory research.[33] Derived factors were discussed and interpreted between the researchers. Naming and describing the factors extracted were based on the symptoms with higher loadings and correlations among symptoms. In addition, the name of a symptom cluster was based on the most symptoms presented within that cluster, or represented overall by the symptoms inside a cluster.

Results

Participant characteristics

There were 117 participants initially approached to participate in this study. Three (2.6%) participants did not complete the entire course of chemotherapy and subsequently were excluded from the study, and two (1.7%) outlier cases were excluded from the data screening. Finally, 112 participants were included, and thus there was a 4.3% (n = 5) attrition rate. This sample size was judged adequate for using factor analysis.[33]

Participants ranged in age from 19-73 years (mean 49.75, SD 10.70). The majority were married (n=76, 67.9%) and Buddhist (n=107, 95.5%); had completed high school or higher education (n= 79, 70.5%); had an average personal income of 20,000 Bahts per month; perceived themselves as very sufficient financial status (n=94, 83.9%); lived in their home (n=99, 88.4%); had family caregivers (n=110, 98.2%); and had health care costs covered mostly by government welfare (n=63, 56.2%) and some form of universal health care coverage, such as Gold card (n=28, 25%). One-third were diagnosed with stage IIA breast cancer (n=38, 33.9%), and 30.4% (n=34) with stage IIIA breast cancer. All reported having breast surgery; 40.2% (n=45) had a modified radical mastectomy; 47.3% (n=53) received four cycles of doxorubicin and cyclophosphamide; 53.6% (n=60) received hormone therapy; and 60.7% (n=68) received radiation therapy for breast cancer after completion of chemotherapy.

Menstrual status changed in this sample over the course of adjuvant chemotherapy. At Time 1, half of the participants (n=56, 50%) were still having regular menses (being classified as pre-menopausal), 3.6% (n=4) had irregular menstrual cycles (being classified as peri-menopausal), and 46.4% (n=52) had amenorrhea (being classified as post-menopausal). At Time 3, there were some shifts: only 14.3% (n=16) of participants were still having menses or were pre-menopausal, whereas 38.4% (n=43) of participants were becoming peri-menopausal, and the rest of participants (n=53, 47.3%) were post-menopausal.

Symptom experiences

Participants reported the occurrence of 39 different symptoms at each time point. The mean and standard deviation of occurrence at Time 1, Time 2, and Time 3 were 5.12 (SD = 3.11), 16.25 (SD = 5.31), and 14.35 (SD = 5.77), respectively. As shown in **Table 1**, most participants reported "I don't look like myself" as one of the top of five prevalent symptoms across all three time points. The most distressing symptoms differed over the measurement periods. For example, "I don't look like myself" was also rated as one of the top five most- distressing symptoms at Times 1 and 3; and "difficulty sleeping" was rated as one of the top five most distressing symptoms at Times 2 and 3. The level of symptom distress scores ranged from 0.53 to 2.80 (Time 1); 0.80 to 2.86 (Time 2); and 1.12 to 2.09 (Time 3), within a scale of 0-4, respectively.

Table 1 Symptom Occurrence and Distress at Time 1 to Time 3 (N = 112)

Symptoms	Time 1			Time 2			Time 3		
	Occurrence (%)	N	Distress (Mean)	Occurrence (%)	N	Distress (Mean)	Occurrence (%)	N	Distress (Mean)
1. Difficulty concentrating	**41.10**[4]	46	1.24	47.30	53	1.66	**69.60**[5]	78	1.55
2. Pain	**61.60**[1]	69	1.54	63.40	71	1.61	67.00	75	1.72
3. Lack of energy	14.30	16	1.50	**86.60**[2]	97	**2.58**[4]	**82.10**[3]	92	1.84
4. Cough	11.60	13	1.66	14.30	16	1.65	11.60	13	**1.91**[5]
5. Feeling nervous	4.50	5	1.12	43.80	49	2.32	10.70	12	1.27
6. Dry mouth	5.40	6	1.20	68.80	77	1.90	61.60	69	1.53
7. Nausea	1.80	2	**2.80**[1]	67.00	75	2.36	9.80	11	1.31
8. Feeling drowsy	6.20	7	1.02	65.20	73	1.85	51.80	58	1.48
9. Numbness/ tingling in hands/ feet	8.00	9	1.33	9.80	11	1.96	49.10	55	1.91
10. Difficulty sleeping	29.50	33	1.92	53.60	60	**2.76**[3]	58.00	65	**2.09**[1]
11. Feeling bloated	4.50	5	1.44	46.40	52	2.37	17.00	19	1.73
12. Problems with urination	2.70	3	1.07	50.00	56	1.70	19.60	22	1.16
13. Vomiting	0.90	1	1.60	31.20	35	2.22	2.70	3	1.60
14. Shortness of breath	6.20	7	1.37	12.50	14	1.60	22.30	25	1.44
15. Diarrhea	0	0	0.00	16.10	18	1.73	4.50	5	1.12
16. Feeling sad	22.30	25	**2.30**[3]	29.50	33	2.26	25.90	29	1.60
17. Sweats	10.70	12	2.00	39.30	44	1.87	49.10	55	1.80
18. Worrying	**58.90**[2]	66	**2.36**[2]	51.80	58	2.00	61.60	69	1.83
19. Problems with sexual interest or activity	0.90	1	0.80	1.80	2	0.80	6.20	7	1.60
20. Itching	8.90	10	1.84	27.70	31	1.91	26.80	30	1.63
21. Lack of appetite	4.50	5	1.44	54.50	61	2.33	41.10	46	1.48
22. Dizziness	9.80	11	1.53	67.00	75	2.28	27.70	31	1.65
23. Difficulty swallowing	0.90	1	0.80	6.20	7	**2.86**[1]	4.50	5	1.60
24. Feeling irritable	**37.50**[5]	42	1.41	47.30	53	2.25	47.30	53	1.63
25. Hot flashes	8.90	10	**2.24**[5]	35.70	40	1.94	45.50	51	1.84
26. Night sweats	7.10	8	1.80	17.00	19	1.47	29.50	33	1.77
27. Vaginal discharge	4.50	5	1.60	7.10	8	1.40	32.10	36	1.51
28. Vaginal itching/ irritation	6.20	7	2.06	11.60	13	1.66	15.20	17	1.55
29. Vaginal dryness	6.20	7	1.26	15.20	17	1.74	37.50	42	1.31
30. Mood swings	12.50	14	2.23	30.40	34	2.26	30.40	34	1.67
31. Joint pain	20.50	23	1.67	21.40	24	1.77	47.30	53	1.75
32. Mouth sores	1.80	2	1.60	54.50	61	2.45	10.70	12	1.73
33. Taste changes	0.90	1	1.60	**77.70**[4]	87	**2.51**[5]	**83.90**[2]	94	1.82
34. Weight loss	21.40	24	0.97	34.80	39	1.27	25.90	29	1.27
35. Hair loss	3.60	4	1.60	**97.30**[1]	109	2.43	40.20	45	**1.92**[4]
36. Constipation	12.50	14	2.00	66.10	74	**2.81**[2]	26.80	30	1.65
37. Swelling of arms/ legs	4.50	5	2.08	3.60	4	1.60	9.80	11	**2.04**[2]
38. "I don't look like myself"	**46.40**[3]	52	**2.27**[4]	**80.40**[3]	90	2.28	**75.90**[4]	85	**2.01**[3]
39. Skin changes	2.70	3	0.53	**71.40**[5]	80	1.40	**96.40**[1]	108	1.52

Note: Top five most-distressing symptoms are **bold**

Symptom clusters

As shown in **Table 2**, in Time 1, five symptoms were loaded on more than one factor with factor loadings above 0.30. Thus, correlations among various symptoms within each cluster were also explored. The correlation between "I don't look like myself" and pain were not significant ($r = 0.167$), so these symptoms did not constitute a cluster. Weight loss was not significantly associated with all symptoms within Factor 4 ($0.146 \leq r \leq 0.149$): even if it had high factor loading, then it was excluded from this factor. Weight loss was loaded on Factor 4 (a fatigue-related symptom cluster consisting lack of energy and difficulty sleeping) with high factor loading (0.740) but it was not significantly associated with all symptoms within a cluster ($0.146 \leq r \leq 0.149$). As a result, weight loss was not classified within this symptom cluster in Factor 4. In addition, lack of energy was significantly correlated with symptoms within Factor 2 (that is, constipation and vaginal itching/ irritation) but lack of energy was not clinically meaningful enough to constitute as a cluster. Thus, lack of energy was identified within Factor 4 instead. As a result, five symptom clusters were identified, with 49.84% of the variance explained: Factor 1 being named "menopausal symptom" (i.e., sweats, night sweats, hot flashes, mood swings, difficulty concentrating, and feeling irritable); Factor 2, "discomfort symptom" (i.e., dizziness, joint pain, vaginal itching/ irritation, and constipation); Factor 3, "post-operative symptom" (coughing, itching, and numbness/tingling in hands and feet); Factor 4,"fatigue symptom" (lack of energy and difficulty sleeping); and Factor 5, "psychological symptom" (feeling sad and worrying). The variance explained in all symptoms of these factors were17.97%, 10.76%, 8.57%, 6.85%, and 6.78%, respectively. Only the menopausal symptom cluster had a Cronbach's alpha coefficient greater than 0.60, which indicated the symptoms within the cluster occurred in a homogenous pattern ($\alpha = 0.773$).

Table 2 Factor Structure at Time 1 (N = 112)

Symptom cluster	Factor loading						h^2
Time 1	Factor1	Factor2	Factor3	Factor4	Factor5	Factor6	
Sweats	**.854**						.799
Night sweats	**.720**						.593
Hot flashes	**.708**						.623
Mood swings	**.685**	.397					.765
Feeling irritable	**.561**	.426	-.413				.710
Dizziness		**.733**					.683
Joint pain		**.639**					.437
Vaginal itching/ irritation		**.607**					.434
Constipation		**.532**					.372
Difficulty concentrating	**.381**	.419					.497
Cough			**.742**				.589
Itching			**.594**				.467
Numbness/ tingling in hands/ feet			**.409**				.399

Table 2 Factor Structure at Time 1 (N = 112) (Continued)

Symptom cluster	Factor loading						h^2
Time 1	**Factor1**	**Factor2**	**Factor3**	**Factor4**	**Factor5**	**Factor6**	
Weight loss				**.740**			.674
Difficulty sleeping				**.528**			.482
Lack of energy		.422		**.515**		.313	.631
Feeling sad					**.737**		.605
Worrying				.327	**.717**		.714
Pain						**.727**	.546
"I don't look like myself"						**.601**	.406
Eigenvalues	3.594	2.152	1.714	1.370	1.355	1.239	
% of variance	17.971	10.758	8.568	6.848	6.776	6.193	
Cronbach's alpha	0.733	0.590	0.348	0.390	0.588		

Note: Symptoms with bolded factor loadings were in the same factor
Factor 1: "Menopausal", Factor 2: "Discomfort", Factor 3: "Post-operative", Factor 4: "Fatigue",
Factor 5: "Psychological", Pain and "I don't look like myself" were excluded (r = 0.167)

In Time 2, (see **Table 3**), nine symptoms were loaded on more than one factor, with factor loadings above 0.30, thus correlations among symptoms within each factor were examined. The results showed that taste changes loaded on Factor 1 and Factor 5 but the relationships among taste changes with symptoms within Factor 1($0.203 \leq r \leq 0.357$) were higher than Factor 5($0.216 \leq r \leq 0.307$).Thus taste changes was classified as part of Factor 1. Similarly, the correlations among pain with symptoms within Factor 2 ($0.226 \leq r \leq 0.306$) were higher than Factor 1($0.128 \leq r \leq 0.272$), and as a result, pain was classified as part of Factor 2. Furthermore, the problematic symptom for identifying cluster during chemotherapy was skin changes. This showed a high loading on Factor 2 but the relationships of skin changes with symptoms within Factor 2 ($0.129 \leq r \leq 0.351$) were lower than Factor 3 ($0.192 \leq r \leq 0.405$). Thus, skin changes was considered to be part of Factor 3 for the reasons of having higher correlation and clinically meaningful factor. As a result, only five symptom clusters were identified, with 51.51% of the variance explained: Factor 1 was named "gastrointestinal-related fatigue symptom" (that is, lack of energy, nausea, lack of appetite, feeling drowsy, dizziness, and taste changes); Factor 2,"disturbed in mood symptom" (i.e., feeling irritable, feeling nervous, and pain); Factor 3, "psychologically-related self-image symptom" (i.e., "I don't look like myself", worrying, difficulty concentrating, hair loss, and skin changes); Factor 4 "discomfort symptom" (i.e., constipation, problems with urination, difficulty sleeping, and feeling bloated); and Factor 5 "oral symptom" (i.e., mouth sore and dry mouth) symptom clusters. The variance explained in all symptoms of these factors were 19.84%, 9.85%, 8.83%, 6.88%, and 6.11%, respectively. There were two symptom clusters that had a Cronbach's alpha coefficient greater than 0.60, which included gastrointestinal-related fatigue (α = 0.690) and psychologically-related self-image (α = 0.634) symptom clusters.

Table 3 Factor Structure at Time 2 (N = 112)

Symptom cluster	Factor loading					h^2
Time 2	Factor1	Factor2	Factor3	Factor4	Factor5	
Lack of energy	**.753**					.675
Nausea	**.677**					.530
Lack of appetite	**.659**					.522
Skin changes		.684	**.053**			.508
Feeling irritable		**.660**				.532
"I don't look like myself"		.573	**.495**			.593
Worrying		.498	**.369**			.420
Pain	.308	**.431**				.293
Feeling nervous		**.375**	.359			.407
Difficulty concentrating			**.671**			.487
Feeling drowsy	**.442**		.585			.589
Hair loss			**.539**			.466
Constipation				**.655**	.383	.578
Problems with urination				**.609**		.524
Difficulty sleeping		.422		**.568**		.510
Feeling bloated				**.536**		.408
Dizziness	**.447**			.512		.533
Mouth sores					**.803**	.670
Dry mouth					**.744**	.592
Taste changes	**.394**				.422	.464
Eigenvalues	3.967	1.970	1.766	1.376	1.222	
% of variance	19.837	9.848	8.828	6.882	6.112	
Cronbach's alpha	0.690	0.571	0.634	0.513	0.576	

Note: Symptoms with bolded factor loadings were in the same factor
Factor 1: "GI-related fatigue", Factor 2: "Disturbed in mood",
Factor 3: "Psychologically-related self-image", Factor 4: "Discomfort", Factor 5: "Oral"

At Time3, as shown in **Table 4**, seven symptoms loaded on more than one factors. The findings revealed that the correlations among difficulty sleeping and difficulty concentrating with all symptoms within Factor 1 ($0.174 \leq r \leq 0.293$ and $0.100 \leq r \leq 0.206$, respectively) were lower than with symptoms within Factor 2 ($0.190 \leq r \leq 0.343$ and $0.124 \leq r \leq 0.300$, respectively). Thus, these symptoms were considered to be part of Factor 2. Similarly, joint pain was classified in Factor 3 and skin changes was classified in Factor 5 due to the fact they had higher correlations with symptoms within these factors than other factors. In addition, worrying was classified in Factor 2 because it had significantly correlated with symptoms within the cluster (except for sweats), while it only significantly correlated with dry mouth ($r = 0.408$) in Factor 4. Vaginal dryness was loaded on Factor 4 but it was not significantly associated with any symptom in this factor ($0.022 \leq r \leq 0.155$). Thus, it was not classified as part of the symptom cluster for

Factor 4. As a result, five symptom clusters were identified, with 53.55% of the variance explained: Factor 1 named as "gastrointestinal-related fatigue symptom" (i.e., lack of energy, feeling drowsy, lack of appetite, and taste changes); Factor 2 as "menopausal symptom" (i.e., sweats, hot flashes, night sweats, difficulty concentrating, difficulty sleeping, worrying, and pain); Factor 3 as "disturbed in mood symptom" (i.e., mood swings, feeling irritable, and joint pain); Factor 4 as "discomfort symptom" (i.e., numbness/ tingling in hands/ feet and dry mouth); and finally Factor 5 as "self-image symptom" (i.e., "I don't look like myself", hair loss, and skin changes). The variance explained in all symptoms of these factors were 20.34%, 10.64%, 8.58%, 7.19%, and 6.81%, respectively.There were four symptom clusters that had a Cronbach's alpha coefficient greater than 0.60, which included menopausal (α = 0.721), gastrointestinal-related fatigue (α = 0.678), disturbed in mood (α = 0.671), and self-image (α = 0.603) symptom clusters.

Table 4 Factor Structure at Time 3 (N = 112)

Symptom cluster	**Factor loading**					**h^2**
Time 3	**Factor1**	**Factor2**	**Factor3**	**Factor4**	**Factor5**	
Lack of energy	**.716**					.582
Feeling drowsy	**.668**					. 478
Lack of appetite	**.605**					.433
Taste changes	**.594**					.399
Numbness/ tingling in hands/ feet	.465			**.384**	-.465	.582
Difficulty sleeping	.429	**.401**				.381
Sweats		**.810**				.688
Hot flashes		**.741**				.634
Night sweats		**.698**				.591
Difficulty concentrating	.397	**.465**				.409
Pain		**.450**				.367
Mood swings			**.884**			.816
Feeling irritable			**.862**			.773
Joint pain	.348	.306	**.364**			.350
Dry mouth	.376			**.645**		.574
Vaginal dryness				**.579**		.414
Worrying		**.345**		.577		.489
Skin changes				.546	**.367**	.479
Hair loss					**.764**	.595
"I don't look like myself"					**.734**	.676
Eigenvalues	4.068	2.128	1.716	1.437	1.362	
% of variance	20.338	10.642	8.578	7.185	6.811	
Cronbach's alpha	0.678	0.721	0.671	0.371	0.603	

Note: Symptoms with bolded factor loadings were in the same factor
Factor 1: "GI-related fatigue", Factor 2: "Menopausal" symptom, Factor 3: "Disturbed in mood",
Factor 4: "Discomfort", Factor 5: "Self-image"

Influences of distressing symptoms on QOL in women with breast cancer

The analyses of 20 symptom distress scores were used in the regression analysis instead of the factor scores in each data collection time period. The reason for this was that not all symptoms have statistical significant influence on QOL of the participants ($p < 0.05$). As shown in **Table 5**, worrying was one of the strongest distressing symptoms predicting QOL at Time 1, and it was the strongest distressing symptom predicting QOL at Time2. Lack of appetite and skin changes still persisted as one of the strongest distressing symptoms predicting QOL at Time2 and Time3.

Regarding predictability, as shown in **Table 5**, "I don't look like myself", worrying, pain, and constipation, together, accounted for 45.2% of the variance in QOL at Time1; worrying, lack of energy, lack of appetite, feeling irritable, hair loss, and skin changes together accounted for 60.7% of the variance in QOL at Time2; and feeling drowsy, dry mouth, lack of appetite, skin changes, and pain, together, accounted for 39.0% of the variance in QOL at Time3.

Table 5 Summary of Multiple Regression Analysis for Statistically Significant Distressing Symptoms Predicting QOL across Three Time Points (N=112)

Model	B	SE	Beta	t	sig	R^2	Adjust R^2	F Change	P
Time 1									
						.452	.431	22.024	.000
Constant	132.276	2.008		65.879	.000				
"I don't look like myself"	-3.992	.821	-.354	-4.865	.000				
Worrying	-3.694	.811	-.328	-4.557	.000				
Pain	-5.198	1.196	-.318	-4.347	.000				
Constipation	-3.743	1.490	-.181	-2.512	.014				
Time 2									
						.607	.584	27.023	.000
Constant	134.506	2.823		47.643	.000				
Worrying	-4.729	.945	-.327	-5.006	.000				
Lack of energy	-3.549	.931	-.271	-3.814	.000				
Lack of appetite	-2.529	.818	-.210	-3.092	.003				
Feeling irritable	-2.698	.909	-.209	-2.970	.004				
Hair loss	-2.275	.810	-.177	-2.810	.006				
Skin changes	-2.896	1.195	-.161	-2.423	.017				
Time 3									
						.390	.361	13.558	.000
Constant	129.427	2.312		55.971	.000				
Feeling drowsy	-4.019	1.185	-.276	-3.391	.001				
Dry mouth	-3.234	1.135	-.233	-2.850	.005				
Lack of appetite	-2.997	1.180	-.204	-2.541	.012				
Skin changes	-3.086	1.271	-.195	-2.427	.017				
Pain	-2.169	.995	-.170	-2.179	.032				

Discussion

The findings of the study were consistent with previous studies among Thai women with breast cancer and cervical cancer.[10,32,42] The women experienced and weighted their symptoms differently across symptom dimensions and across times of measurement. The most frequently reported symptoms, however, were not the most intense or distressful symptoms reported. In particular, "I don't look like myself" was reported as one of the top five most prevalent symptoms across all three time points.[32] It may be that after initiating chemotherapy and the resulting side effect of chemotherapy affected women's perceptions about themselves. Furthermore, difficulty sleeping was also rated as one of the top five most distressing symptoms that occurred during treatment and still persisted after completion of chemotherapy for one month.[5]

The increasing of prevalent and frequent menopausal symptoms in these women may have been associated with the chemically-induced menopause. Particularly, sweats and vaginal dryness were reported as frequent symptoms approximately in 40-50% of participants after receiving chemotherapy. Consistent with the previous findings,[23,36-38] menopausal symptoms including hot flashes, night sweats, vaginal dryness, sleep alterations, dyspareunia, and weight gain were also often reported by women who received chemotherapy and hormonal therapy. Furthermore, changes in menstrual cycle function occurred in the majority of women. At the beginning of chemotherapy, half of women (n=56, 50%) were still having menses but after completion of chemotherapy for 1 month, only 14.3% (n=16) of women still having regular menses and the majority of women were having irregular menses and amenorrhea after receiving chemotherapy. As time goes on, menopausal symptoms may become more major concerns for some women requiring interventions for symptom management, especially if associated with distress to their roles and daily life.[36-39]

Menopause associated with chemotherapy can be either permanent or reversible. As the result, menopausal symptoms might be only a temporary problem for some of the participants. Consistent with the previous findings,[36,38] not all women have permanent amenorrhea that results from chemotherapy. Knobf[38] also found that hot flashes was reported as mild to extremely distressful and intense at the onset with the varying but gradual improvement in distress overtime. Nevertheless, more than half of participants (n = 60, 53.6%) in the current study received hormonal therapy following a course of chemotherapy. Menopausal symptoms associated with treatment for breast cancer may become major problems that can have a negative impact on QOL in these women with breast cancer.

The symptom experience is dynamic and therefore causes different symptom clustering over time.[29] Nevertheless, there were some specific symptoms within menopausal, psychologically-related self-image, and gastrointestinal-related fatigue symptom clusters that were relatively stable across all times. The first of these included hot flashes, sweats, and night sweats formed a menopausal cluster at Times 1 and 3. At Time2, the participants focused more on their physical and psychological symptoms such as lack of energy, taste changes, constipation, hair loss, difficulty sleeping, 'I don't look like myself' that all resulted from chemotherapy and try to dealing with those side effects. Menopausal symptoms were a lower priority causing concern for the participants. As the results, the participants responded to menopausal symptoms as minimize distressing symptoms. Similarly, Bender and colleagues[13] found that hot flashes and night sweats were highly correlated with each other at pre-post adjuvant chemotherapy. Nevertheless, hot flashes and night sweats were not constituted as a cluster because of the definition of symptom cluster that using in their study was three or more concurrent symptoms. The second relatively stable cluster, "I don't look like myself", hair loss, and skin changes were grouped

together as a psychologically-related self-image symptom after receiving chemotherapy and self-image symptom cluster at Time3. The findings reaffirmed the prior studies in that I don't look like myself", hair loss, and skin changes were formed together as a part of image-related cutaneous symptom cluster,[10] particularly these symptoms were formed together during treatments and still persisted after receiving treatment or 6 months after diagnosis.[29] The third relatively stable cluster, lack of energy, lack of appetite, feeling drowsy, and taste changes were formed together as a gastrointestinal-related fatigue cluster during and after completion of chemotherapy for 1 month. Consistently, Molassiotis and colleagues[29] also found that lack of energy and feeling drowsy frequently occurred together across time at before and during chemotherapy but not evident after 6 months after diagnosis.

Interestingly, some symptoms emerged as part of a cluster but at the subsequent time they were not maintained within the same cluster that probably was due to the fact that symptoms usually occur after starting treatment and gradually increase to a peak during treatment, and decrease after completion of treatment. Furthermore, clustering of symptoms are dynamic constructs, some symptoms clustering together with moderate coefficients and moderate to high internal consistency but these were only appeared at one time point and not stable across time points. For example, mouth sores and dry mouth formed together as an oral symptom cluster which emerged only Time2 with moderate relationship ($r = 0.404$, $p < 0.01$) but at Time3, dry mouth formed together with numbness/ tingling in hands and feet with moderate relationship ($r = 0.316$, $p < 0.01$). This symptom cluster was more likely a treatment-related symptom cluster because it was not maintained at other time points. It was possible that symptoms of a cluster can also be part of more than one symptom cluster simultaneously.[29]

The stability of symptom clusters still need to be investigated. As a result of few previous findings, symptom clusters were found to be identical overtime. Gift and colleagues[43] found that a single cluster of seven symptoms in lung cancer patients was identified at diagnosis, and this cluster did not change at 3 and 6 months. Kim and colleagues[14] demonstrated that the clustering of symptoms within symptom clusters (i.e., psychoneurological and upper gastrointestinal) was generally stable across the treatment trajectories. Molassiotis and colleagues[29] also found that six clusters were relatively stable over the first 12 months after diagnosis. In contrast with the finding of Kim and colleagues,[23] the specific symptoms within two symptom clusters (i.e., mood-cognitive and sickness-behavior) were not stable overtime at the middle, end, and 1 month after completion of radiation therapy. They suggested that the need for the symptom cluster to remain stable over the course of treatment may not be an essential element of the symptom cluster's definition.

There was a problem in a naming factor as there was no clinical relevance among symptoms even some symptoms within a cluster had moderately correlations (e.g. $r > 0.30$) with each other. For instance, the symptoms of dizziness and joint pain, dizziness and vaginal itching/ irritation ($r = 0.338$, $r = 0.333$, $p < 0.01$, respectively) at Time1, difficulty sleeping and constipation, feeling bloated and constipation ($r = 0.344$, $r = 0.313$, $p < 0.01$, respectively) at Time2, numbness/ tingling in hands/ feet and dry mouth ($r = 0.316$, $p < 0.01$) at Time3. Besides, symptoms within discomfort clusters were relative stability of the clusters across three time points as well as the internal consistency coefficients for discomfort symptom clusters were low to moderate across three time points (Cronbach's alphas ranged from 0.371 to 0.590), however some symptoms changing over time. It was possible that these symptoms related with specific treatments at each

time. Furthermore, the low internal consistency for each symptom cluster indicated the need to be interpreted with cautions.

The clustering of pain with other symptoms was inconclusive when compared to other previous studies. However, the current findings were consistent with a study of Suwisith and colleagues[10] which showed that pain related to discomfort symptoms (i.e., numbness/ tingling, and dry mouth) and emotion symptoms (e.g., feeling irritable, feeling nervous, worrying, and sleeping difficulty). Noticeably, previous studies that selected several most common symptoms in cluster identification, such as pain clustered with fatigue and sleep disturbance,[6] fatigue and depression,[44] fatigue, anxiety, and depression.[20] It is possible that the difference of the analytic methods, time assessments, and the peak level of symptom experience may contribute to the different results and the evaluation of the symptoms experienced by the women. Hence, the clustering of symptoms and the membership of symptoms to clusters should be explored.

Further, the findings revealed that worrying was one of the most distressing symptoms which predicted QOL at Time1 and Time2. In addition, lack of appetite and skin changes still persisted as one of the distressing symptoms predicting QOL at Time2 and Time3. Consistent with prior longitudinal studies, worrying was one of the significant predictor of QOL at before and during chemotherapy, whereas anxiety and depression were negatively associated with QOL at the start of treatment until three months post treatment.[26,27] Lack of energy and decreased energy with feeling drowsy was also persisted at during chemotherapy until after the completion of chemotherapy for 1 month.[5] Interestingly, before initiating chemotherapy. "I don't look like myself" was the strongest symptom predicting QOL in this period followed by worrying. The findings reaffirmed Junda's work[45] concerning the experiences of Thai women diagnosed with breast cancer as they described a diagnosis of breast cancer and its treatment associated with negative attitudes and perception. These women viewed breast cancer as a terrible disease and certain death that made them worried about their breast cancer problems and unpleasant things that might happen over the course of treatment.In addition, the current study indicated that while the prevalent rate and distressful physical symptoms decreased across all times, the distressful psychological symptoms (i.e., "I don't look like myself" and worrying) appeared to increase and still persisted across all times. This finding is needed to further investigation.

The findings obtained from this study support the Theory of Unpleasant Symptoms (TOUS)[30] in that symptom experiences are multidimensional. The participants experienced multiple symptoms rather than a single symptom as well as the participants also rated their symptoms differently across dimensions and across phases. Furthermore, the findings also supported the broad tenets of TOUS[30] in that multiple symptoms and a variety of interactive between various symptoms may have synergistic effects on performance. The findings from this study revealed that symptom clusters changed negatively and accumulated effects on QOL in women with breast cancer undergoing adjuvant chemotherapy.

Some symptoms were classified as a cluster however, these were not clinically meaningful. It is possible that some symptom clusters based on factors or components from statistical procedures might not have a rational explanation. Nevertheless, the current findings revealed that many clinically meaningful symptom clusters including two or more symptoms (i.e., menopausal symptom cluster of sweats, night sweats and hot flashes, psychologically-related self-image symptom cluster of skin changes with not feeling like myself, or gastrointestinal-related fatigue symptom cluster of lack of energy and feeling drowsy), it should be considered when these symptoms clustering only in pairs. This study's findings supported the definition

of the symptom cluster that proposed by Kim *et al.*[15] that "...consists of two or more symptoms that are related to each other and that occur together."(p278)

The results of this study revealed that menopausal symptoms (i.e., sweats, night sweats, hot flashes and mood swings) frequently occurred and clustered with difficulty sleeping, difficulty concentration, and mood symptoms after breast cancer chemotherapy but have not yet to be studied in prior studies as a symptom cluster.[6,10,14,20] Because all of these symptoms were experienced concurrently, and are related, they should be explored as a symptom cluster for further studies.

Conclusions and recommendations

The results of the study showed that three symptom clusters tended to be stable in the treatment trajectory were menopausal cluster, psychologically-related self-image cluster, and gastrointestinal-related fatigue cluster. Particularly, menopausal cluster was a relatively stable cluster at the beginning and the end of chemotherapy for 1 month, whereas psychologically-related self-image cluster and gastrointestinal-related fatigue cluster were relatively stable clusters after receiving chemotherapy and after completion of chemotherapy for 1 month. Interestingly, women in the current study experienced menopausal symptoms which were significantly more frequent as the resulting from adjuvant chemotherapy. Thus, women need to be informed of these possible symptoms associated with hormone therapy because women diagnosed with early stage breast cancer will be asked to undergo longer term hormone therapy. QOL studies should be continued and extended where appropriate for the benefit of women starting such hormone therapy in the future.

Based on this study's findings, recommendations have been made for nursing practice and research. Firstly, nurses need to assess symptoms among women with breast cancer receiving chemotherapy across the treatment trajectory. In addition, information regarding symptoms that may occur at different stages of chemotherapy need to be provided to women to help them plan ahead in managing their symptoms effectively during and after chemotherapy treatment. This may help the women cope effectively with the symptoms during chemotherapy. It is expected that women will experience fewer symptoms during treatment, if specific interventions targeting a cluster of symptoms are given before starting adjuvant chemotherapy.

Further research is needed in nursing practice to: determine the stability of symptom clusters over time in women with breast cancer; the investigation of symptom experiences of women with breast cancer receiving adjuvant chemotherapy in this current study was not examined in specific regimen of chemotherapy, therefore, future studies on specific regimens are recommended. As the women diagnosed with early stage breast cancer will be continued hormone therapy after receiving adjuvant chemotherapy. Future research on the late QOL effects of breast cancer who received hormone therapy is also recommended.

Limitations

Some limitations of this study need to be mentioned. First, the sample size was not large enough for factor analysis in 39 symptoms. In addition, the symptoms that entered into the factor analysis in each time were different because the prevalence, frequency, and distress of these various symptoms changed overtime. Nevertheless, considering the 20 most-distressing symptoms in each period for symptom clustering may better represent symptom clusters that need to be managed in women with breast cancer receiving adjuvant chemotherapy. Moreover, this study was specifically conducted in women with breast cancer receiving adjuvant chemotherapy in one university hospital. Thus, generalizability to patients with other types of cancers and settings is limited.

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กลุ่มอาการและคุณภาพชีวิตของสตรีที่เป็นมะเร็งเต้านมที่ได้รับการรักษาเสริมด้วยเคมีบำบัด

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บทคัดย่อ: การศึกษาติดตามไปข้างหน้าครั้งนี้มีวัตถุประสงค์เพื่อศึกษากลุ่มอาการและอิทธิพลต่อคุณภาพชีวิตของผู้ป่วยมะเร็งเต้านมระยะที่ I-IIIA ที่ได้รับเคมีบำบัดในระยะก่อน ระหว่างการรักษา และภายหลังได้รับยาเคมีบำบัดครบ 1 เดือน กลุ่มตัวอย่างเป็นผู้ป่วยสตรีมะเร็งเต้านมระยะที่ I-IIIA จำนวน 112 คนที่มารับยาเคมีบำบัดที่โรงพยาบาลมหาวิทยาลัยแห่งหนึ่งในกรุงเทพมหานครโดยใช้การคัดเลือกกลุ่มตัวอย่างแบบสะดวกทำการเก็บรวบรวมข้อมูล 3 ครั้งในระยะก่อน ระหว่างรับยาเคมีบำบัด (ก่อนได้รับยาเคมีบำบัดวงรอบที่ 2) และภายหลังได้รับยาเคมีบำบัดครบ 1 เดือน เครื่องมือที่ใช้ในการวิจัยได้แก่ แบบบันทึกข้อมูลส่วนบุคคล โรคและการรักษา แบบประเมินอาการจากโรคและการรักษา และแบบสอบถามเพื่อประเมินคุณภาพชีวิตวิเคราะห์ข้อมูลโดยการวิเคราะห์ปัจจัยในการศึกษาองค์ประกอบของกลุ่มอาการ และการวิเคราะห์ความถดถอยเชิงพหุในการศึกษาอำนาจการทำนายของอาการต่อคุณภาพชีวิต

ผลการศึกษาพบว่าผู้ป่วยมะเร็งเต้านมเผชิญกับประสบการณ์การมีอาการหลายอาการร่วมกัน ในการวิเคราะห์การจัดกลุ่มอาการ สามารถจำแนกกลุ่มอาการได้ 5 กลุ่มในแต่ละระยะของการประเมิน กลุ่มอาการที่มีแนวโน้มเกิดทั้ง 3 ระยะ คือ กลุ่มอาการหมดประจำเดือน กลุ่มอาการด้านจิตใจและภาพลักษณ์ และกลุ่มอาการทางเดินอาหารและเหนื่อยล้า นอกจากนี้พบว่าอาการมองตนเองไม่เหมือนเดิมหรือเปลี่ยนแปลงไป ความกลุ้มใจ อาการง่วงนอน/ เซื่องซึม เป็นอาการที่ทำนายคุณภาพชีวิตของผู้ป่วยที่มีน้ำหนักมากที่สุดในทั้ง 3 ระยะ ประเด็นอาการที่เกิดร่วมกันในแต่ละกลุ่มอาการของแต่ละระยะการประเมินซึ่งมีความไม่คงที่ ได้รับการอภิปรายผล

ความรู้จากการศึกษานี้อาจเป็นประโยชน์สำหรับพยาบาล และบุคลากรทีมสุขภาพอื่นๆ ให้มีความเข้าใจกลุ่มอาการที่เกิดขึ้นร่วมกันในผู้ป่วยมะเร็งเต้านมในระหว่างการรักษาดีขึ้น และนำไปใช้วางแผนล่วงหน้าสำหรับผู้ป่วยเพื่อจัดการกับอาการหลายอาการที่เกิดขึ้นพร้อมกัน เพื่อส่งเสริมคุณภาพชีวิตของผู้ป่วยต่อไป ข้อเสนอแนะงานวิจัยในอนาคต ควรศึกษาในประเด็นความไม่คงที่ของอาการที่พบร่วมกันในแต่ละกลุ่มอาการเมื่อเวลาเปลี่ยนแปลงไป

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