Symptom Clusters in Korean Patients With Metastatic Cancer Undergoing Palliative Chemotherapy

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This study aims to investigate symptom clusters and the physiological, psychological, and situational factors associated with symptom clusters in patients with metastatic cancer undergoing palliative chemotherapy. Also, this research explored how severity of symptom clusters affected physical function. A total of 106 patients with metastatic cancer in South Korea participated. Three symptom clusters were identified: cluster 1 included neuropsychological symptoms (drowsiness, difficulty in remembering, sadness, distress, sleep disturbances, and fatigue), cluster 2 included pain symptoms (shortness of breath, numbness, dry mouth, and pain), and cluster 3 included gastrointestinal symptoms (nausea, vomiting, and poor appetite). Low hemoglobin level (physiological factor) was associated with the pain cluster. High anxiety and low fighting spirit (psychological factors) were associated with 3 clusters, and high depression (psychological factor) was associated with the neuropsychological cluster. Low social support (situational factor) was associated with the gastrointestinal cluster. The participants in the severe subgroups of the 3 symptom clusters experienced low physical function. Palliative nurses should understand the different symptom clusters and their possibly synergistic adverse effects on patient outcomes. Our results provide an important basis for developing palliative strategies to manage concurrent symptoms in patients with metastatic cancer undergoing chemotherapy, with the goal of improving their physical function.

KEY WORDS

cancer, chemotherapy, metastatic, palliative care, symptom cluster

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Cancer is the most frequent cause of death in South Korea. An estimated 224 177 new cases of cancer are expected to be diagnosed each year, and one-third of cancer patients died as a result of their disease in 2012.[1] Patients with metastatic cancer may experience several symptoms, either because of the progress of the disease or as side effects of anticancer treatment. These symptoms include pain, fatigue, anorexia, sleep disturbances, and cognitive impairment. The average number of concurrent symptoms ranges from 4 to as many as 13.[2-4] As the disease progresses, concurrent symptom control becomes an important component of palliative care in patients with metastatic cancer, whose symptoms are frequently complex and for whom symptom palliation is the primary goal of treatment.[4,5]

Palliative chemotherapy treatment to relieve symptoms and improve survival is necessary for patients with metastatic cancer. Yet, it is very common for these patients to experience multiple symptoms during the palliative phase of care related to the adverse effects of treatment.[4] For example, a study demonstrated that the most prevalent symptoms in patients with advanced lung cancer being treated with chemotherapy were pain, fatigue, disturbed sleep, and shortness of breath.[6] If these symptoms are not properly controlled, they impact the patient's functional status and quality of life by decreasing their physical and psychological condition.[4,6] For these reasons, accurate identification of the symptoms that are experienced by metastatic cancer patients is essential.

A symptom cluster (SC) is a group of interrelated symptoms that occur together and that are stable and independent of other symptoms or SCs that may or may not share a common etiology.[7] Investigation of SCs could provide an important scientific foundation for understanding the common mechanism behind multiple symptoms. One study described psychoneurological symptoms as a set of emotional or behavioral symptoms related to psychological or neurologic dysfunction (ie, depressive symptoms, cognitive disturbances, fatigue, sleep disturbances, and pain) that may share a common biological pathway (ie, proinflammatory cytokines and the hypothalamic-pituitary-adrenal axis), which may have an important regulatory role in the development of these symptoms.[8] Another study identified that

pain, depression, and fatigue as an SC might be related to systemic inflammation in advanced cancer patients.[9] These studies highlight the importance of SCs in metastatic cancer patients.

The examination of SCs helps a palliative nurse to gather information about the relationships between multiple symptoms and to understand how mitigating the most influential symptoms may help control other concurrent symptoms. Identification of SCs offers palliative nurses guidance for developing tailored interventions focused on SCs instead of individual symptoms in patients with metastatic cancer.[10] However, each different cluster is composed of 2 to 8 symptoms, and no clusters have consistently been identified across all studies of SCs in patients with metastatic cancer, for whom palliative chemotherapy is necessary and whose goals merit its use.[3]

According to previous studies, cancer patients with anemia report more severe symptoms, such as shortness of breath, dizziness, and fatigue.[11] Also, cancer patients with higher anxiety or depression express a higher intensity of symptoms.[12] A fighting spirit is characterized by a determination to fight the illness and the adoption of an optimistic attitude in the face of a realistic appraisal of one's illness.[13] A fighting spirit is particularly important in adjusting to cancer, and it promotes engagement with other people and enhances social support and positive affect, whereas hopelessness and helplessness are related to less of a fighting spirit in cancer survivors.[14] Meanwhile, a lower level of fighting spirit is correlated with a greater number of symptoms in cancer patients.[12,15] A lower level of social support is correlated with the severity of symptoms in cancer patients.[16] Demographic or clinical variables, such as younger age at diagnosis, being female, advanced disease stage, or chemotherapy treatment are associated with more severe symptoms.[17] It is necessary to examine whether cancer type might be associated with SCs because it is a predictor of SCs in advanced cancer in only 2 of 33 studies examined in a systematic review.[4] Until now, few studies have examined the relationships between these influencing factors and SCs in patients with metastatic cancer undergoing palliative chemotherapy, and the findings from the studies that have been conducted are inconsistent.[15] Thus, it is necessary to identify factors associated with SCs to provide insight into symptom management.

Symptom clusters have a more complicated and synergistic effect on outcomes (ie, functional status) than does a single symptom, as multiple symptoms may exacerbate each other.[4] Clinical subgroups of patients who reported higher symptom severity while receiving treatment experienced the most serious limitations.[18] However, there is little evidence that the severity of SCs affects physical function in patients with metastatic cancer undergoing palliative chemotherapy.

The theory of unpleasant symptoms guided the current study. This theory suggests that multiple symptoms can occur simultaneously and that physiological, psychological, and situational factors may influence these symptoms. This theory also suggests that functional status is a consequence of these symptoms.[19] Therefore, the current aims to (1) identify SCs; (2) explore the physiological (ie, hemoglobin [Hgb] level), psychological (ie, anxiety, depression, and fighting spirit), and situational (ie, social support) factors associated with SCs; and (3) assess the differences in physical function according to SC severity in patients with metastatic cancer undergoing palliative chemotherapy.

METHODS

Participants and Data Collection

A cross-sectional and descriptive design was used for this study. Participants were recruited from the outpatient cancer clinic at a national university hospital in South Korea. A total of 106 participated in the study. Participants were referred by their oncologists and were enrolled according to the following eligibility criteria: (1) older than 30 years, (2) diagnosed with metastatic cancer, (3) currently undergoing palliative chemotherapy, (4) no history of psychiatric disorders, and (5) ability to cognitively and physically respond to questionnaires. The necessary sample size was determined by factor analysis based on the correlation matrix of the items under examination; this analysis indicated that the required sample size must include at least 100 individuals, or 5 times each of the 13 symptoms examined in this study.[20] A total of 106 patients satisfied these requirements. This study was approved by the institutional review board at the hospital where the study was conducted. All patients were informed about the study objectives and then gave written informed consent.

Instruments

Symptoms were measured using subscales of the M.D. Anderson Symptom Inventory.[21] Responses to the 13 items indicate the severity of symptoms over the previous 24 hours and are rated on an 11-point scale, where a higher score represents a higher level of symptom severity. In this study, the Cronbach α was .83.

Anxiety and depression were measured using the Hospital Anxiety and Depression Scale.[22] The Hospital Anxiety and Depression Scale consists of 7 items for anxiety and 7 items for depression, which are rated on a 4-point scale. The total score can range from 0 to 21. A higher score indicates a higher level of anxiety and depression, with scores of 11 or higher representing a probable mood disorder. For this scale, the Cronbach α was .91 for anxiety and .81 for depression.

Fighting spirit was measured using subscales of the Mental Adjustment to Cancer scale, which is used to assess the coping style of patients with cancer.[13] This instrument was designed to measure fighting spirit, anxious preoccupation, helplessness/hopelessness, and fatalism. Fighting spirit was assessed using 16 items on a 4-point scale, with higher scores indicating a greater fighting spirit. The Cronbach α for this scale was .93 in the current study.

Social support was measured using the MOS Social Support Survey.[23] This scale consists of 19 items, and each item uses a 5-point scale. The higher the score, the better the perception of social support. Original scores were translated into a value between 0 and 100 using the MOS Social Support Survey scoring manual. The Cronbach α for social support was .97 in the current study.

Physical function was measured using subscales of the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30.[24] The scale consists of 5 items, and each item uses a 4-point scale. Higher scores indicate greater physical function. Original scores were translated into a value between 0 and 100 using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire C-30 scoring manual. The Cronbach α for physical function was .85.

A blood sample to measure serum Hgb level was drawn from the patients at the time of the survey and processed and analyzed at the clinical area of the cancer center. In this study, anemia was defined as an Hgb level less than 12 g/dL.[25]

Data Analysis

The data were analyzed using SPSS version 21.0. Descriptive statistics were used to summarize demographic and clinical characteristics. To identify the presence of relationships among symptoms and to detect SCs, principal component analysis with varimax rotation was conducted based on the scores of the 13 symptoms. The number of significant principal components was selected based on those with an eigenvalue higher than 1.00. Analysis of communalities was used to observe the level of shared variance between items. The Kaiser-Meyer-Oklin measure was calculated to assess sampling adequacy. Symptoms with salient loading for a factor were considered to be an SC. The internal consistency and reliability of the derived clusters were assessed using Cronbach α.

To determine whether demographic and clinical characteristics had significant relationships with the SCs, an independent t test or a 1-way analysis of variance test was used. To identify the relationships between SCs, Hgb level, anxiety, depression, fighting spirit, and social support, Pearson correlation was used. To identify subgroups based on SC severity, K-means cluster analysis was used. To evaluate the difference in physical function by subgroup based on SC severity, a 1-way analysis of variance test was used. The level of statistical significance was set at $P < .05$.

RESULTS

Participant Characteristics

The total sample consisted of 106 patients with metastatic cancer (65 men, 41 women). Demographic and clinical characteristics are displayed in Table 1. The mean age of participants was 61.79 years. The most frequent type of

cancer was lung cancer (34.9%), and about 78.3% of participants presented with 1 or 2 metastatic sites. Most of the participants were being treated with first- or second-line chemotherapy (74.5%).

Physiological, Psychological, and Situational Factors Associated With SCs

The mean (SD) Hgb level was 11.23 (1.73) g/dL (range, 8.0-15.0 g/dL), and about 70% of participants had anemia. The mean (SD) score for anxiety was 7.73 (4.26) (range, 0-21), and the mean (SD) score for depression was 13.05 (3.86) (range, 0-21), indicating a mild level of anxiety and a moderate level of depression among the study participants. About 29% of the participants were categorized as having an anxiety disorder, and 76% of the participants were categorized as having depression. The mean (SD) score for fighting spirit was 2.90 (0.47) (range, 0-4), indicating a moderate level of fighting spirit. The mean (SD) score for social support was 67.44 (21.37) (range, 0-100), indicating a moderate level of social support. The mean (SD) score for physical function was 57.80 (21.69) (range, 0-100), indicating a moderate level of physical function.

TABLE 1	Demographic and Clinical Characteristics of Participants (N = 106)		
Characteristics	**Category**	**n (%)**	**Mean (SD)**
Age, y	<65	56 (52.8)	61.79 (10.86) (range, 31-81)
	≥65	50 (47.2)	
Sex	Male	65 (61.3)	
	Female	41 (38.7)	
Living status	Alone	13 (12.1)	
	With family	93 (86.9)	
Type of cancer	Breast	6 (5.7)	
	Lung	37 (34.9)	
	Colorectal	32 (30.2)	
	Gastric	26 (24.5)	
	Lymphoma	5 (4.7)	
Number of metastatic sites	1-2	83 (78.3)	
	3-4	23 (21.7)	
Chemotherapy line	First-second	79 (74.5)	
	≥Third	27 (25.2)	

Symptom Clusters

Using the principal component analysis method with varimax rotation, 3 factors emerged with eigenvalues greater than 1.00, which together accounted for 54.232% of the total variance. Factor loadings for the 13 symptoms are shown in Table 2. Factor analysis identified 3 SCs: the first cluster (the neuropsychological SC) included drowsiness, difficulty remembering, sadness, distress, sleep disturbances, and fatigue; the second cluster (the pain SC) included shortness of breath, numbness/tingling, dry mouth, and pain; and the third cluster (the gastrointestinal [GI] SC) included nausea, vomiting, and poor appetite (Table 2).

The symptoms within each cluster were all significantly interrelated with one another. The correlation coefficients ranged from 0.225 to 0.733 (all with a $P < .05$).

Demographic and Clinical Characteristics Associated With SCs

Three SCs were associated with chemotherapy line, which meant that participants undergoing treatment with third- or fourth-line chemotherapy experienced more severe symptoms in the neuropsychological SC ($t = -2.680$, $P = .009$), the pain SC ($t = -2.270$, $P = .026$), and the GI SC ($t = -2.276$, $P = .025$) compared with patients undergoing first- or second-line chemotherapy. Other characteristics (age, sex, living status, type of cancer, and number of metastatic sites) were not significantly associated with any of the 3 SCs.

Relationships Among SCs and Physiological, Psychological, and Situational Factors

A lower Hgb level was significantly associated with the pain SC. High anxiety and low fighting spirit were associated with all 3 clusters, and high depression was associated with the neuropsychological cluster. Low social support was associated with the GI cluster (all $P < .05$) (Table 3).

Differences in Physical Function by Subgroups Based on SC Severity

On the basis of the factor scores of the 3 SCs, the 106 participants were divided into 3 subgroups after considering the results of the K-means clustering method. The 3 subgroups

TABLE 2 Symptom Cluster Groups

| Cluster Group | Symptoms | Mean (SD) | Factor Loading | | | Cronbach α |
			Factor 1	Factor 2	Factor 3	
Cluster 1 (neuropsychological)	Drowsiness	3.32 (2.38)	0.771			.77
	Difficulty remembering	2.75 (2.14)	0.681			
	Sadness	1.81 (1.83)	0.669			
	Distress	1.98 (2.00)	0.532			
	Sleep disturbances	3.50 (2.66)	0.498			
	Fatigue	5.18 (2.63)	0.453			
Cluster 2 (pain)	Shortness of breath	2.46 (2.54)		0.773		.63
	Numbness/tingling	4.72 (3.14)		0.609		
	Dry mouth	3.63 (3.05)		0.562		
	Pain	3.21 (2.70)		0.480		
Cluster 3 (gastrointestinal)	Nausea	2.67 (2.56)			0.781	.67
	Vomiting	2.60 (2.00)			0.712	
	Poor appetite	3.59 (2.71)			0.613	
Eigenvalue			4.413	1.405	1.232	
Variance explained, %			33.947	10.807	9.478	
Total variance explained, %			33.947	44.754	54.232	

Variables	Cluster 1	Cluster 2	Cluster 3	Hemoglobin	Anxiety	Depression	Fighting Spirit
Cluster 1	1						
Cluster 2	0.544 (<.001)	1					
Cluster 3	0.429 (<.001)	0.421 (<.001)	1				
Hemoglobin	−0.015 (.881)	−0.204 (.036)	−0.172 (.078)	1			
Anxiety	0.492 (<.001)	0.370 (<.001)	0.293 (.002)	0.026 (.792)	1		
Depression	0.354 (<.001)	0.183 (.060)	0.179 (.067)	−0.022 (.823)	0.530 (<.001)	1	
Fighting spirit	−0.338 (<.001)	−0.227 (.019)	−0.255 (.008)	0.016 (.871)	−0.502 (<.001)	−0.507 (<.001)	1
Social support	−0.141 (.150)	−0.112 (.251)	−0.214 (.028)	0.117 (.231)	−0.188 (.054)	−0.203 (.037)	0.397 (<.001)

TABLE 3 Relationships Between Symptom Clusters, Hemoglobin Level, Anxiety, Depression, Fighting Spirit, and Social Support

Data are r (P).

were participants with mild, moderate, and severe symptom severity scores in each of the 3 SCs. In all 3 SCs, physical function was significantly different among the 3 subgroups (all P < .001). The participants in the severe subgroups of all 3 SCs experienced lower physical function (Table 4).

DISCUSSION

Patients with metastatic cancer often experience multiple coexisting symptoms arising from the disease itself or as a side effect of treatment, resulting in different clinical outcomes compared with patients with individual symptoms.[2-5] To the best of our knowledge, this study is the first report that has examined 3 major SCs and their associated physiological (Hgb level), psychological (anxiety, depression, and fighting spirit), and situational (social support) factors and the consequence of SCs (physical function), based on the theory of unpleasant symptoms in metastatic cancer patients undergoing palliative chemotherapy.

Three distinct SCs were identified in this study according to factor analysis. The first cluster (the neuropsychological SC) included drowsiness, difficulty remembering, sadness, distress, sleep disturbances, and fatigue. The second cluster (the pain SC) included shortness of breath, numbness/tingling, dry mouth, and pain. The third cluster (the GI SC) included nausea, vomiting, and poor appetite. However, a systematic review of 32 studies of patients with advanced cancer published between 1950 and 2013 reported 4 main SCs: anxiety-depression, nausea-vomiting, nausea-appetite loss, and fatigue-dyspnea-drowsiness-pain.[4]

The first cluster was named the "neuropsychological" SC because it included neurological, cognitive, or emotional symptoms that occur together or that are interrelated with one another and that could be related to psychological and/or neurologic dysfunction. This cluster contains components that are similar to those of a psychoneurological SC identified in previous studies on cancer patients, including psychosocial and biological characteristics (ie, fatigue, depression, sleep disturbances, cognitive dysfunction, anxiety, or pain).[25] Several studies have provided empirical evidence for a neuropsychological cluster in patients with cancer. For example, in observational studies of patients with all types of cancer, fatigue and sleep disturbances occur in the same cluster, and these symptoms often coexist and have a moderate-to-strong correlation with each other.[9] In studies of metastatic cancer, fatigue and drowsiness were found in the same cluster.[26] Also, sleep disturbances and mood problems were found in the same cluster.[3,18] More recent studies have revealed that sleep disturbances and fatigue form a cluster with other psychoneurolgical symptoms, such as emotional distress and difficulty remembering.[8,18,25] Similar results were found in a study of patients with ovarian cancer who were receiving chemotherapy,[27] which identified fatigue, mood swings, and sleep disturbances as significant predictors of memory problems. Our results show that there are close relationships between neurological symptoms (ie, sleep disturbances), psychological symptoms (ie, sadness or distress), and cognitive dysfunction (ie, difficulty remembering). These are thought to be mediated by proinflammatory cytokines, such as interleukin-1, interleukin-6, and tumor necrosis factor-α. These cytokines might explain the mechanism behind the occurrence of multiple symptoms within the first cluster in metastatic cancer patients undergoing palliative chemotherapy.[18]

TABLE 4 Differences in Physical Function by Subgroup Based on Symptom Cluster Severity

Variable	Cluster 1 (Neuropsychological)					Cluster 2 (Pain)					Cluster 3 (Gastrointestinal)				
	Mild[a] (n = 37) Mean (SD)	Moderate[b] (n = 52) Mean (SD)	Severe[c] (n = 17) Mean (SD)	F	P (Scheff)	Mild[a] (n = 43) Mean (SD)	Moderate[b] (n = 51) Mean (SD)	Severe[c] (n = 12) Mean (SD)	F	P (Scheff)	Mild[a] (n = 58) Mean (SD)	Moderate[b] (n = 32) Mean (SD)	Severe[c] (n = 16) Mean (SD)	F	P (Scheff)
Physical function (range, 0-100)	73.15 (14.18)	51.28 (19.61)	44.31 (23.09)	20.415	<.001 (a > c)	65.74 (18.66)	54.77 (21.84)	42.22 (20.95)	7.240	.001 (a > c)	64.37 (20.20)	47.30 (21.64)	55.00 (19.09)	7.338	.001 (a > b)

The second cluster included shortness of breath, numbness, dry mouth, and pain. This study showed that dyspnea, pain, and numbness are concurrent symptoms, and these findings are in agreement with 2 other studies that showed similar concurrence of these components; the studies grouped these symptoms into (1) pain-numbness-dyspnea,[28] (2) fatigue-shortness of breath-pain,[29] and (3) fatigue-pain-drowsiness-dyspnea.[26] The fact that pain was found to be a part of the second cluster, rather than part of the neuropsychological SC, is a notable difference in our work.[18] The population in this study included patients with metastatic cancer receiving palliative chemotherapy. The symptoms of peripheral neuropathy are pain, sensitivity, numbness, and weakness; these symptoms should be monitored closely to identify nerve damage earlier. In this study, most participants (n = 89, 83.9%) had received or were receiving chemotherapy containing taxanes, vinca-alkaloids, and platinum compounds, which may cause toxic peripheral neuropathy.[30] This might explain why pain occurred together with numbness in the second cluster. Hence, patient and family education should include information about the potential for peripheral neuropathy following chemotherapy for metastatic cancer. In addition, depending upon how severe the symptoms are, the physician may recommend discontinuing chemotherapy or changing or spreading out the dose of the medication.

In the current study, the third cluster included nausea, vomiting, and poor appetite. Previous studies have also reported the concurrence of these 3 symptoms.[2,4,17] Patients with cancer who are receiving chemotherapy may experience as many as 9 different GI symptoms. Therefore, palliative nurses may assume that cancer patients experience many GI problems. The current methods to assess symptoms do not adequately address all of the GI symptoms experienced by patients receiving chemotherapy. Future investigations should include a symptom measurement tool that focuses on a comprehensive list of GI symptoms.

If palliative nurses understand SCs, interrelations of symptoms, and their common mechanisms in metastatic cancer patients receiving palliative chemotherapy, they can more effectively control multiple, concurrent symptoms by executing an accurate symptom assessment and by developing interventions focused on SCs, such as cognitive-behavioral therapy or exercise.[31,32] Also, palliative nurses may be able to predict other symptoms in each SC and the relationship between SCs.

Our results showed that patients who were receiving third- or fourth-line chemotherapy experienced multiple symptoms in all 3 SCs. Hence, nurses should anticipate that such patients will have more severe symptoms. Most patients receiving palliative chemotherapy showed greater impairments and more severe symptoms because of both the progression of their disease and the treatment they were receiving.[17] For this reason, nurses should concentrate

on controlling symptoms regardless of the type of chemotherapy that is being given.

In this study, Hgb level was associated with pain symptoms. Either cancer itself or the treatments for it, including chemotherapy, may cause anemia. [33] As the Hgb level drops, symptoms arise that include fatigue, tachycardia, shortness of breath, trouble breathing, dizziness, chest pain, pale skin, and extreme tiredness.[33] Therefore, health care providers need to monitor Hgb levels to assess whether anemia is a serious threat to the health of patients with metastatic cancer.

In this study, anxiety was significantly associated with the severity of symptoms in all 3 clusters, and depression was significantly associated with the severity of symptoms in the first cluster. Many previous studies found that physical symptoms, such as sleep problems, were associated with depression and anxiety,[3,4] thereby suggesting a close relationship between physical and psychosocial symptoms. Other studies have shown that depression is related to pain and fatigue[9] and that sleep disturbance may be influenced by anxiety and depression.[34] Anxiety also contributed significantly to impairments in social functioning as well as nausea and vomiting.[16] Therefore, as anxiety and depression are correlated with SCs, appropriate pharmacological and nonpharmacological approaches to manage psychological distress are likely to improve physical symptoms.

In this study, the severity of symptoms in all 3 clusters showed a significant correlation with a low level of fighting spirit, indicating poor psychological adjustment to cancer. Moreover, lower fighting spirit was related to higher levels of anxiety and depression. This result is similar to the findings of previous studies, which found that less fighting spirit was related to more severe symptom experience and more severe depression in cancer patients.[15,35] It may be that some patients have a low fighting spirit because of a realistic appraisal of their prognosis. Therefore, palliative nurses should focus on developing appropriate interventions to improve fighting spirit in order to control multiple symptoms.

Our results demonstrated that social support was associated with the GI SC. The cancer patients who reported less social support had significantly more occurrences of nausea and vomiting.[16] Personal support from family and friends mediates the effects of symptoms such as insomnia, fatigue, and loss of appetite in breast cancer patients.[36] However, there is no clear evidence as to why this association between social support and GI SCs exists. Therefore, it is necessary to find the mechanism which social support is related to GI symptoms in cancer patients undergoing palliative chemotherapy.

Physical function was negatively correlated with the severity of certain symptoms within the 3 clusters.[4] In particular, greater severity of certain symptoms was associated with lower physical function. Several studies have shown that the coexistence of symptoms contributed to the variance of change in functional status in cancer patients receiving chemotherapy.[37] The level of physical function is an important indicator because it is accepted as a marker for the quality of life, as well as an indicator of the need to change, delay, or discontinue a metastatic cancer treatment.[37]

A few aspects might limit the generalizability of the findings of this study. First, the sample size was small, which may influence the grouping of SC components. Second, this study included patients with various types of cancer and used a cross-sectional design, which might inhibit the ability to make any inferences regarding causality. Therefore, there is a need for future studies that use a longitudinal design to explore changes in SCs over the course of the disease in metastatic cancer patients with a particular type of cancer. Third, the M.D. Anderson Symptom Inventory is a relatively short instrument that assesses only 13 symptoms. Future studies should use more comprehensive tool for symptom assessment.

CONCLUSIONS

This study found that the neuropsychological cluster, the pain cluster, and the GI cluster were associated with Hgb level, anxiety, depression, fighting spirit, and social support. Furthermore, increased symptoms in the 3 SCs had a statistically significant negative impact on physical function in patients with metastatic cancer undergoing palliative chemotherapy. This result is significant because it offers palliative nurses guidance for understanding the mechanisms behind the SCs and developing more optimized management strategies for metastatic cancer patients because treatment of one symptom may be affected by other components in the same cluster. In addition, this study provides palliative nurses initial insights into the effect of a SC on a patient's functional status.

The unpleasant symptom theory proved useful in identifying SCs, associated factors, and the consequences of SCs in metastatic cancer patients undergoing chemotherapy. Hence, our results provide a foundation for the development of interventions to control multiple concurrent symptoms in metastatic cancer patients undergoing palliative care. Palliative nurses need to be aware of the presence and mechanism of SCs and their possibly synergistic adverse effects on patient outcomes. Further research should examine whether symptom management strategies focusing on palliative care are more efficient in controlling SCs. Moreover, it is necessary to develop more palliative interventions to alleviate anxiety and depression, to encourage fighting spirit and increase social support, and to address low Hgb levels, which are associated with SCs in patients with metastatic cancer who are undergoing palliative chemotherapy.

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