Original Article

Symptom clusters using the Brief Pain Inventory in patients with breast cancer

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Background: The purpose of this study was to assess symptom clusters in functional interference using the brief pain inventory (BPI) in patients with non-metastatic breast cancer (BC) during and after chemotherapy.

Methods: A principal component analysis with varimax rotation was conducted on data from 228 patients to identify two clusters at baseline and two intervals following treatment.

Results: Physical (general activity, normal work, walking ability) and psychosocial (mood, relationships, sleep, enjoyment of life) interference clusters were present at baseline. Clusters were observed at 1-month (cluster 1: general activity, normal work, enjoyment of life; cluster 2: relationships, sleep) and 3-month (cluster 1: general activity, normal work, relationships; cluster 2: sleep, enjoyment of life) post-treatment.

Conclusions: Results from our study suggest dynamic symptom clusters in this patient population, and encourage continued symptom management following completion of treatment.

Keywords: Quality of life; chemotherapy; pain; functional interference

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Introduction

Patients with cancer often experience several disease- and treatment- related symptoms, highlighting the importance of sensitivity and responsiveness to symptom identification and control in their care. Symptom clusters are groups of a minimum of two symptoms that co-occur in patients. Due to their implications on management of patient quality of life, they are of great clinical interest (1). Although symptom cluster research was recently named a priority in oncology nursing, there is limited data regarding symptom clusters in patients undergoing chemotherapy (2).

The majority of research conducted on symptom management in patients with breast cancer (BC) is focused on isolated symptoms, with the most prevalent being fatigue, pain, anxiety and depression (3). A literature review conducted by Nguyen *et al.* amalgamated results from five relevant studies published from 2005 to 2009 on symptom clusters in BC patients (4). However, these studies differed in terms of the number of clusters and the composition of items across clusters.

With great inter- and intra- patient variability cited in BC patients undergoing adjuvant chemotherapy, there are several challenges associated with the management of quality of life in these patients (5). Although currently limited, research on symptom cluster in women with BC undergoing chemotherapy may better illustrate the experiences of this patient population, and facilitate improved symptom identification and management. The aim of the present study is to investigate symptom clusters in patients with non-metastatic BC during and after chemotherapy.

Methods

This is a secondary analysis of a prospective study on docetaxel-associated pain syndrome, which accrued patients with non-metastatic BC commencing taxane chemotherapy at the Sunnybrook Odette Cancer Centre and North York General Hospital (6). Ethical approval for the study was obtained at the respective institutions, and all patients provided informed consent. Patients were followed for the first three consecutive cycles of docetaxel, paclitaxel or nab-paclitaxel chemotherapy.

The brief pain inventory (BPI) is a multiple-item measure of pain used extensively in the cancer patient population (7). The sensory component measures intensity of pain on 4 different scales (worst, least, average, and current pain) wherein higher scores are indicative of worse pain. The affective component of the BPI assesses the effect of pain on 7 functional items at baseline: general activity, normal work, walking ability, mood, sleep, relationships and enjoyment of life. The BPI utilizes an 11-point scale, wherein higher scores are indicative of greater functional interference.

In the present study, patients completed the BPI at baseline, throughout days 1–21 during all three cycles (acute phase), and again at 1, 3, 6, 9, and 12 months post-treatment (delayed phase). During the delayed phase, mood and walking ability were not assessed. Average BPI scores were calculated for cycles 1–3 and used in the analysis. Consent was provided by all patients. Ethical approval was obtained from the hospital research ethics board.

Statistical analysis

Descriptive analyses were performed on demographics and medication taken during treatment cycles, and were summarized as mean, standard deviation (SD), median, inter-quartiles and range for continuous variables, and proportions for categorical variables. BPI items were summarized at baseline, acute phase during treatment and delayed phase post-treatment. Spearman correlation was conducted at baseline, during and post-treatments. A principle component analysis (PCA) with varimax rotation was conducted on the BPI scores to delineate symptom clusters at baseline, at each cycle of the acute phase, and at 1, 3, 6, 9, and 12 months delayed phase. This statistical procedure transforms a number of observed variables into a smaller number of variables or "principal components", wherein the first component accounts for as much variability in the data as possible. The number of significant principal components was selected with an Eigenvalue higher than 0.6 and each component explained more than 10% of the variance. The highest factor loading score predicted the assignment of individual symptoms to an independent factor. Cronbach's alpha values were calculated to estimate the internal consistencies and reliabilities of symptom clusters. The varimax rotation is an orthogonal rotation, meaning that it results in uncorrelated components. Compared to other types of rotations, a varimax rotation tends to maximize the variance of a column of the factor pattern matrix. Robust relationships and correlations among symptoms were displayed with the biplot graphic. The longer the length and closer together the arrows were, the higher the correlation between symptoms. All analyses were conducted using Statistical Analysis Software (SAS version 9.4 for Windows).

Results

A total of 228 patients were accrued to the study. Patient characteristics are found in *Table 1*. The mean age was 52 years, with almost half of patients post-menopausal. Out of the three regimens, docetaxel was administered the most (88%). Most patients were chemotherapy naïve (92%). Medications taken during treatment are listed in *Table 2*. Descriptions of the BPI scores collected at the different phases of the study are provided in *Table 3*.

Significant clusters were observed at baseline and during the delayed phase only.

Baseline

Spearman correlations between all BPI items were significant with P values <0.0001. Using the criterion of minimum eigenvalue of 0.60 and at least 10% of the total variance, the first two components accounted for 77% and 10% of the total variance respectively (*Table 4*). Cumulatively, 87% of the variance was accounted for.

Cluster 1 was composed of mood, relationships, sleep and enjoyment of life. Cluster 2 consisted of general activity, walking ability and normal work. Final communality is the proportion of variance in an observed variable that is accounted for by the retained clusters. Values in this study showed that all variables were well accounted for by the two clusters, with final communalities ranging from 0.77 (sleep)

Table 1 Patient characteristics

Characteristic	Non-metastatic patients (N=228)
Age (year)	
N	228
Mean ± SD	52.0±11.0
Median [Inter-quartiles]	52 [44,60]
Range	27–86
BMI	
N	228
Mean ± SD	26.35±4.85
Median (Inter-quartiles)	25.5 (22.8–28.5)
Range	17.5–45.0
Treatment intent	
Adjuvant	198 (86.88%)
Neoadjuvant	30 (13.16%)
Menopausal status	
Premenopausal	80 (35.09%)
Early perimenopausal	18 (7.89%)
Late perimenopausal	17 (7.46%)
Postmenopausal	113 (49.56%)
Co-morbidities	152 (66.67%)

SD, standard deviation; BMI, Body Mass Index.

Table 2 Medication taken during treatment cycles

Medication	Non-metastatic patients (N=228)
Dexamethasone	
Standard	19 (86.64%)
IV	30 (13.16%)
GCSF	81 (35.53%)
NSAIDS	155 (67.99%)
Opioids	54 (23.68%)
Gabapentin	3 (1.32%)

GCSF, granulocyte colony-stimulating factor; NSAIDS, non-steroidal anti-inflammatory drugs.

to 0.92 (general activity) (*Table 5*). Cronbach's alpha values demonstrated good internal consistency with values of 0.93 and 0.94 for the two clusters respectively. The two clusters can also be observed in the biplot (*Figure 1*).

Delayed phase

In delayed phase, clusters were identified at 1 and 3 months post-treatment. BPI scores for mood and walking ability were not collected during delayed phase. Spearman correlations at months 1 and 3 between the remaining 5 BPI items were all significant, with P values <0.0001.

At 1 month post-treatment, 2 clusters were identified, respectively accounting for 75% and 12% of the total variance (*Table 6*). Cumulatively, the clusters explained 87% of the variance. Cluster 1 was composed of general activity, normal work and enjoyment of life. Cluster 2 was composed of relationships and sleep. Final communality values ranged from 0.79 (relationships) to 0.93 (normal work) (*Table 7*). Cronbach's alpha values for the two clusters were 0.94 and 0.79 respectively, indicating good internal consistencies.

At 3 months post-treatment, 2 clusters were identified, respectively accounting for 76% and 12% of the total variance (*Table 8*). Cumulatively, they accounted for 88% of the total variance. Cluster 1 was composed of general activity, normal work and relationships. Cluster 2 was composed of sleep and enjoyment of life. Final communalities ranged from 0.81 (relationships) to 0.95 (sleep) (*Table 9*). Cronbach's alpha values for the two clusters were 0.94 and 0.82 respectively, indicating good internal consistencies.

Discussion

Two functional interference clusters were found in three different stages in the study, at baseline and at 1- and 3-month post-treatment. General activity and normal work consistently clustered together. At baseline, we observed two clusters: physical interference (general working, normal work, walking ability) and psychosocial interference (mood, relationships, sleep and enjoyment of life). These clusters are identical to those observed by Klepstad *et al.* in their study sample of cancer patients (8). Emergence of psychosocial-/mood- and activity-related clusters using the BPI in cancer patients have been noted elsewhere in the literature (9-10). A previous analysis conducted by Chiu *et al.* reported that BPI interference scores correlated best with the average pain scale for patients experiencing taxane-induced arthralgia and myalgia, such as those in the present study sample (11). In contrasting the more stable nature

Table 3 BPI at baseline, acute phase and delayed phase

BPI	Baseline	Acute phase			Delayed phase				
		Cycle 1	Cycle 2	Cycle 3	Month 1	Month 3	Month 6	Month 9	Month 12
General activity	228	208	191	166	158	120	110	102	93
Mean ± SD	0.53±1.82	2.10±2.03	1.66±1.95	1.74±2.16	1.39±2.53	1.32±2.47	0.87±1.94	1.21±2.43	1.17±2.22
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.4 (0.1, 3.3)	1.0 (0.0, 2.8)	0.8 (0.0, 2.8)	0.0 (0.0, 2.0)	0.0 (0.0, 2.0)	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)
Range	0, 10	0, 10	0, 9	0, 10	0, 10	0, 10	0, 8	0, 10	0, 10
Mood	228	208	191	166	NA	NA	NA	NA	NA
Mean ± SD	0.43±1.65	2.00±1.91	1.48±1.81	1.51±1.97					
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.6 (0.2, 3.4)	0.8 (0.0, 2.3)	0.8 (0.0, 2.2)					
Range	0, 9	0, 8	0, 9	0, 10					
Walking ability	228	208	191	166	NA	NA	NA	NA	NA
Mean ± SD	0.46±1.76	1.88±2.02	1.46±1.88	1.60±2.12					
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.3 (0.1, 3.0)	0.7 (0.0, 2.4)	0.7 (0.0, 2.6)					
Range	0, 10	0, 10	0, 9	0, 10					
Normal work	228	208	191	166	158	120	110	102	93
Mean ± SD	0.58±1.98	2.11±2.10	1.67±2.01	1.81±2.25	1.47±2.60	1.35±2.58	1.05±2.26	1.45±2.69	1.23±2.36
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.6 (0.1, 3.3)	0.9 (0.0, 2.8)	0.9 (0.0, 3.0)	0.0 (0.0, 2.0)	0.0 (0.0, 1.5)	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)
Range	0, 10	0, 10	0, 9	0, 10	0, 10	0, 10	0, 10	0, 10	0, 10
Relationships	228	208	191	166	158	120	110	102	93
Mean ± SD	0.41±1.67	1.74±1.89	1.27±1.76	1.37±1.96	0.59±1.67	0.83±2.06	0.60±1.87	0.65±1.93	0.58±1.58
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.1 (0.0, 3.0)	0.4 (0.0, 1.8)	0.4 (0.0, 2.1)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Range	0, 10	0, 9	0, 9	0, 10	0, 10	0, 10	0, 10	0, 10	0, 7
Sleep	228	208	191	166	158	120	110	102	93
Mean ± SD	0.73±2.25	2.12±2.00	1.66±1.99	1.67±2.19	0.97±2.23	1.58±2.89	1.36±2.79	1.62±2.82	1.47±2.76
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.7 (0.2, 3.4)	1.0 (0.0, 2.9)	0.9 (0.0, 2.7)	0.0 (0.0, 0.0)	0.0 (0.0, 2.0)	0.0 (0.0, 0.0)	0.0 (0.0, 2.0)	0.0 (0.0, 2.0)
Range	0, 10	0, 9	0, 9	0, 10	0, 10	0, 10	0, 10	0, 10	0, 10
Enjoyment of life	228	208	191	166	158	120	110	102	93
Mean ± SD	0.55±1.85	2.15±2.07	1.60±1.99	1.67±2.23	1.28±2.52	1.40±2.69	0.95±2.12	1.17±2.40	1.08±2.24
Median (inter-quartiles)	0.0 (0.0, 0.0)	1.7 (0.3, 3.6)	0.9 (0.0, 2.8)	0.8 (0.0, 2.4)	0.0 (0.0, 1.0)	0.0 (0.0, 1.5)	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	0.0 (0.0, 1.0)
Range	0, 9	0, 10	0, 10	0, 10	0, 10	0, 10	0, 9	0, 10	0, 10

SD, standard deviation; BPI, brief pain inventory; NA, not available;

Table 4 Eigenvalues and proportions of variance for components at baseline

Component	Eigenvalue	Proportion	Cumulative
1	5.37	0.77	0.77
2	0.66	0.10	0.87
3	0.34	0.05	0.92
4	0.26	0.03	0.95
5	0.15	0.02	0.97
6	0.14	0.02	0.99
7	0.08	0.01	1.00

Table 5 Factor loadings and final communality of BPI items at baseline

BPI items	Component 1	Component 2	Final communality
Mood	0.71	0.57	0.831
Relationship	0.78	0.50	0.852
Sleep	0.81	0.34	0.770
Enjoyment of life	0.89	0.32	0.894
General activity	0.35	0.89	0.918
Walking ability	0.39	0.85	0.880

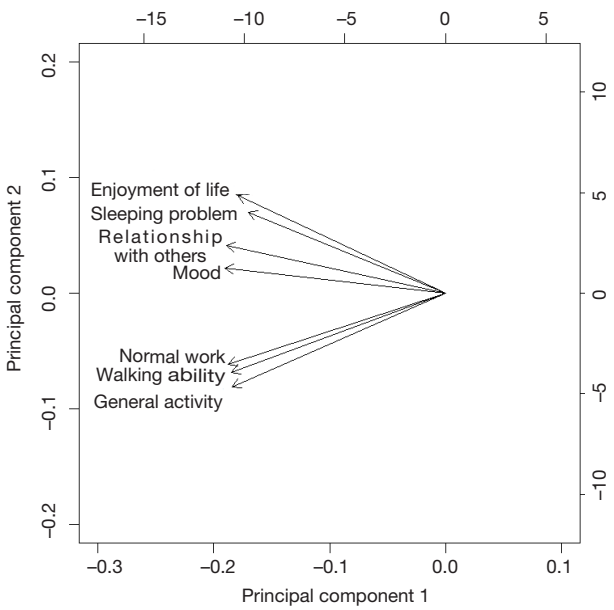

Figure 1 Biplot for clusters at baseline.

Table 6 Eigenvalues and proportions of variance for components at 1 month

Component	Eigenvalue	Proportion	Cumulative
1	3.73	0.75	0.75
2	0.61	0.12	0.87
3	0.34	0.07	0.94
4	0.20	0.04	0.98
5	0.12	0.02	1.00

Table 7 Factor loadings and final communality of BPI items at 1 month

BPI items	Component 1	Component 2	Final communality
General activity	0.87	0.36	0.885
Normal work	0.91	0.30	0.926
Enjoyment of life	0.83	0.43	0.866
Relationship	0.41	0.79	0.793
Sleep	0.29	0.89	0.867
% of variance	75%	12%	
Cronbach's alpha	0.94	0.79	

BPI, brief pain inventory.

of pain of non-metastatic compared to metastatic patients, the authors recommended use of this BPI scale in future evaluations of the symptom in this particular population.

Studies conducted in BC patients during and after treatment have used other symptom assessment tools. Implementing four different questionnaires across the span of chemotherapy and radiotherapy, Kim *et al.* observed a psychoneurological cluster in BC patients composed of cognitive disturbances, depressed mood, fatigue, insomnia and pain (12). This remained stable throughout treatment, with the exception of hot flashes appearing and disappearing after the initiation of treatment. Using the Profile of Mood States, EORTC-QLQ-C30 and -BR23, Evangelista and Santos observed physical (dyspnea, pain, arm symptoms, insomnia) and psychoemotional (depression, confusion, anger, tension, fatigue, breast symptoms) symptom clusters in their study of 138 BC patients following completion of adjuvant chemotherapy with curative intent (13). Bender *et al.* conducted a pooled analysis of results from three independent studies with women at different phases of

Table 8 Eigenvalues and proportions of variance for components at 3 months

Component	Eigenvalue	Proportion	Cumulative
1	3.81	0.76	0.76
2	0.62	0.12	0.88
3	0.28	0.06	0.94
4	0.20	0.04	0.98
5	0.09	0.02	1.00

Table 9 Factor loadings and final communality of BPI items at 3 months

BPI items	Component 1	Component 2	Final communality
General activity	0.92	0.26	0.917
Normal work	0.91	0.32	0.931
Relationship	0.82	0.37	0.805
Sleep	0.25	0.94	0.954
Enjoyment of life	0.62	0.66	0.825
% of variance	76	12	
Cronbach's alpha	0.94	0.82	

BPI, brief pain inventory.

BC, following primary resection, adjuvant chemotherapy and metastatic development. Their analysis identified 3 symptom clusters corresponding to different phases, composed of symptoms relating to fatigue, perceived cognitive impairment and mood (14). So *et al.* investigated the symptoms reported to be the most prevalent in BC patients (fatigue, pain, anxiety and depression) and observed significant correlations between them (15). In addition to confirming the existence of this symptom cluster, the authors remarked on the adverse effect of increased symptomatology in this group on patient quality of life.

Like our present study, an analysis conducted by Albusoul *et al*. used a sample of solely BC patients undergoing adjuvant chemotherapy (16). Their results departed from those of previous studies in this patient population, reporting that clusters were dynamic rather than stable (12,17-19). This was also observed in our study, with no two identical clusters emerging across the span of the study. Albusoul *et al.* reported a treatment-related cluster which at baseline, was composed of anxiety, appearance, concentration and sleep disturbance. At the third cycle of chemotherapy, bowel pattern, fatigue, pain and depression joined the cluster. At the fourth cycle, the cluster contained appetite, depression, fatigue, anxiety, appearance and concentration. At the 1-month mark post-treatment, the cluster divided into two: cluster 1, consisting of fatigue, pain and sleep disturbance; and cluster 2, containing anxiety, appearance and concentration.

There are several limitations to the present study. Since assessment of mood and walking ability were not assessed in the delayed phase in the primary study, the possible inclusion of these items in delayed phase symptom clusters could not be evaluated in this secondary analysis. Another limitation in our study is the low minimum Eigenvalue (0.60) used for cluster inclusion. Using the principal component analysis on average BPI scores, we were unable to identify significant clusters during the acute phase. Therefore, further research is required using the same patient population to assess the validity of the symptom clusters identified.

Conclusions

BC patients may present with symptom clusters in physical and psychological interference. Symptom clusters were identified in the delayed phase and were different at the assessed stages, indicating dynamic behavior. Given the demonstration of clusters and a lack of functional recovery to baseline levels, symptoms should be continuously managed following completion of chemotherapy.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: Ethical approval for the study was obtained at the respective institutions and written informed consent was obtained from all patients.

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