

Symptom Clusters in Cancer Survivors

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Conflict of Interest

The authors have no conflicts of interest to report.



Background: Survivors & Symptoms

- **Over 16.9 million cancer survivors are living in the United States in 2019**
 - **5.0% of the population**
- **21.7 million survivors by 2029**
- **26.1 million survivors by 2040**
- **Report co-occurring symptoms after completion of treatment**



Background: Survivors & Symptom Clusters

- **Symptom Cluster**
 - **Two or more symptoms that co-occur and are inter-related**
 - **Etiology, mechanism, variance, outcome**
- **Literature Limitations:**
 - **Variability in type of clusters found**
 - **Most done during treatment**
 - **Most done in breast cancer survivors**
- **Little is known about how symptoms cluster together in cancer survivors**

Purposes of Study

Study purposes were to:

- **Evaluate for differences in number and types of symptom clusters using ratings of occurrence, severity, and distress**
- **Evaluate for differences in symptom cluster severity scores using a number of phenotypic characteristics**



Design and Methods

- **Cross-sectional study**
- **Parent study designed to evaluate survivors with and without CIPN**
- **Patients were recruited from throughout the San Francisco Bay area**
- **Inclusion criteria:**
 - **18 years of age**
 - **Had received a platinum +/- taxane compound**
 - **Completed chemotherapy and primary cancer treatment**
 - **English**

Study Procedures

- **Written informed consent was obtained from all survivors**
- **Survivors were sent self-report questionnaires to complete in their home**
- **Medical records were reviewed for disease and treatment information**



Instruments

- **Demographic questionnaire**
- **Karnofsky Performance Status scale**
- **Self Administered Co-morbidity Questionnaire**
- **Memorial Symptom Assessment Scale**
 - **32 symptoms**
 - **Occurrence: Y/N**
 - **Severity: 0 (none) to 10 (intolerable)**
 - **Distress: 0 (not at all distressing) to 10 (most distressing)**

Data Analysis

- **Descriptive statistics**
 - **Demographic and clinical characteristics**
- **Exploratory Factor Analysis (EFA)**
 - **Unobserved, latent variables = clusters**
 - **EFA across three dimensions**
 - **occurrence, severity, distress**
- **Bootstrapped linear regression**
 - **Symptom severity score and phenotypic characteristics**



Demographic Characteristics

Characteristic	Mean (SD)
Age (years)	60.1 (11.2)
Education (mean, SD)	16.4 (2.7)
	% (n)
Female	84.7 (527)
Ethnicity	
White	78.8 (491)
Non-white	21.2 (132)
Married/partnered (% yes)	61.6 (374)
Lives alone (% yes)	28.7 (176)
Working for pay (% yes)	44.4 (276)
Income >\$100,000 per year	41.2 (238)

Clinical Characteristics

Characteristic	Mean (SD)
Karnofsky Performance Status score	85.7 (10.6)
Body Mass Index	26.0 (5.4)
Number of comorbid conditions	2.6 (1.9)
Self-Administered Comorbidity Questionnaire	3.8 (3.3)
Years since cancer diagnosis	4.7 (4.8)
Number of prior cancer treatments	3.2 (1.0)
Total number of MSAS symptoms (out of 32)	9.1 (5.2)
Number of metastatic sites	0.7 (0.8)
Cancer diagnosis (% (n))	
Breast	55.7 (347)
Colon	8.0 (50)
Lung	3.0 (19)
Ovarian	8.7 (54)
Other	24.6 (153)

Top Symptoms

Symptom	Occurrence % (N)	Severity Mean (SD)	Distress Mean (SD)
Lack of energy	69.5 (432)	4.2 (2.2)	4.1 (2.7)
Pain	69.0 (429)	4.6 (2.2)	4.3 (2.8)
Difficulty sleeping	67.4 (419)	4.5 (2.4)	4.3 (2.7)
Numbness/tingling in hands/feet	67.2 (418)	5.3 (2.1)	4.5 (2.8)

OCCURRED IN OVER 65%

MODERATE SEVERITY AND DISTRESS

Three Symptom Clusters

Identified three symptom clusters across all three dimensions of occurrence, severity, and distress:

- **Fatigue**
- **Psychological**
- **Constitutional**



Symptom Cluster - Fatigue

Symptom	Occurrence	Severity	Distress
Lack of energy	x	x	x
Feeling drowsy	x	x	x
Difficulty concentrating		x	
Pain			x
Difficulty sleeping			x
Numbness of tingling in hands or feet			x
<i>Percent Agreement</i>	33%	50%	83%

Symptom Cluster - Fatigue

Two Consistent Symptoms

Symptom	Occurrence	Severity	Distress
Lack of energy	x	x	x
Feeling drowsy	x	x	x
Difficulty concentrating		x	
Pain			x
Difficulty sleeping			x
Numbness of tingling in hands or feet			x
<i>Percent Agreement</i>	<i>33%</i>	<i>50%</i>	<i>83%</i>

Symptom Cluster - Psychological

Symptom	Occurrence	Severity	Distress
Difficulty concentrating	X	X	X
Feeling nervous	X	X	X
Feeling sad	X	X	X
Sweats	X		
Worrying	X	X	X
Problems with sexual interest/activity	X		X
Feeling irritable	X	X	X
<i>Percent Agreement</i>	100%	71%	86%

Symptom Cluster - Psychological

Five Consistent Symptoms

Symptom	Occurrence	Severity	Distress
Difficulty concentrating	X	X	X
Feeling nervous	X	X	X
Feeling sad	X	X	X
Sweats	X		
Worrying	X	X	X
Problems with sexual interest/activity	X		X
Feeling irritable	X	X	X
<i>Percent Agreement</i>	100%	71%	86%

Symptom Cluster - Constitutional

Symptom	Occurrence	Severity	Distress
Pain	X	X	
Numbness or tingling in hands or feet		X	
Feeling bloated		X	X
Itching	X	X	X
Dizziness	X	X	X
Swelling of arms or legs	X	X	X
<i>Percent Agreement</i>	67%	100%	67%

Symptom Cluster - Constitutional

Three Consistent Symptoms

Symptom	Occurrence	Severity	Distress
Pain	X	X	
Numbness or tingling in hands or feet		X	
Feeling bloated		X	X
Itching	X	X	X
Dizziness	X	X	X
Swelling of arms or legs	X	X	X
<i>Percent Agreement</i>	67%	100%	67%

Factors Associated with Fatigue Severity

Characteristic* (*only significant characteristics reported on table)	Group	Severity score (mean (SE)) range 0-9	Unstandardized regression coefficient (BC-CI)
Age	Younger (<65)	3.33 (0.12)	-1.12* (-1.49 – -0.77)
	Older (≥ 65)	2.20 (0.13)	
Gender	Female	3.02 (0.10)	-0.72* (-1.19 – -0.26)
	Male	2.30 (0.21)	
History of depression	No	2.49 (0.10)	1.93* (1.51 – 2.35)
	Yes	4.42 (0.19)	
Multimorbidity	No (<2 comorbidities)	2.46 (0.13)	0.87* (0.49 – 1.23)
	Yes (≥ 2 comorbidities)	3.23 (0.14)	
			W(df); p-value**
Cancer diagnosis	Breast (1)	3.22 (0.13)	22.65 (4); p<0.01
	Colon (2)	2.28 (0.28)	
	Lung (3)	1.58 (0.44)	
	Ovarian (4)	2.76 (0.30)	1 > 2, 3
	Other (5)	2.63 (0.18)	

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	Lung (3)	1.58 (0.44)	
	Ovarian (4)	2.76 (0.30)	
	Other (5)	2.63 (0.18)	1 > 2, 3

Factors Associated with Psychological Severity

Characteristic* (*only significant characteristics reported on table)	Group	Severity score (mean (SE)) range 0-9	Unstandardized regression coefficient (BC-CI)
Age	Younger (<65)	3.90 (0.17)	-1.68* (-2.16 – -1.22)
	Older (\geq 65)	2.22 (0.17)	
Gender	Female	3.41 (0.14)	-0.94* (-1.53 – -0.26)
	Male	2.47 (0.29)	
History of depression	No	2.61 (0.12)	3.08* (2.45 – 3.78)
	Yes	5.69 (0.32)	
Multimorbidity	No (<2 comorbidities)	2.91 (0.17)	0.73* (0.23 – 1.22)
	Yes (\geq 2 comorbidities)	3.64 (0.20)	

Factors Associated with Psychological Severity

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	Male	2.47 (0.29)	
History of depression	No	2.61 (0.12)	3.08* (2.45 – 3.78)
	Yes	5.69 (0.32)	
Multimorbidity	No (<2 comorbidities)	2.91 (0.17)	0.73* (0.23 – 1.22)
	Yes (≥2 comorbidities)	3.64 (0.20)	

Factors Associated with Constitutional Severity

Characteristic* (*only significant characteristics reported on table)	Group	Severity score (mean (SE)) range 0-9	Unstandardized regression coefficient (BC-CI)
History of depression	No	2.38 (0.07)	1.00* (0.62 – 1.40)
	Yes	3.79 (0.17)	
Multimorbidity	No (<2 comorbidities)	2.08 (0.10)	1.01* (0.72 - 1.30)
	Yes (≥2 comorbidities)	3.07 (0.11)	
W(df); p-value**			
BMI	Low to normal weight (1)	2.17 (0.10)	32.27 (2); p<0.001
	Overweight (2)	2.92 (0.14)	
	Obese (3)	3.14 (0.19)	1 < 2, 3

Factors Associated with Constitutional Severity

Characteristic* (*only significant characteristics reported on table)	Group	Severity score (mean (SE)) range 0-9	Unstandardized regression coefficient (BC-CI)
History of depression	No	2.38 (0.07)	1.00* (0.62 – 1.40)
	Yes	3.79 (0.17)	
Multimorbidity	No (<2 comorbidities)	2.08 (0.10)	1.01* (0.72 - 1.30)
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W(df); p-value**			
BMI	Low to normal weight (1)	2.17 (0.10)	32.27 (2); p<0.001
	Overweight (2)	2.92 (0.14)	
	Obese (3)	3.14 (0.19)	1 < 2, 3

Conclusions

- **Three clusters: Fatigue, Psychological, Constitutional**
- **Number and types of symptom clusters are relatively similar regardless of the symptom dimension used to create the clusters.**
- **For all three symptom clusters, severity scores were significantly higher in survivors who reported a history of depression and had multiple morbidities.**

¹Cataldo et al., BMC Cancer 13:6, 2013

Limitations

- **Cross-sectional**
- **Convenience sample**
- **Parent study different aim**
- **Limits to generalizability**
 - **Women with breast cancer**
 - **Caucasian**
 - **Well-educated**



Implications for Practice

- **Target symptom assessment and management.**
 - **Reduction of polypharmacy**
- **Anticipatory symptom education throughout survivorship.**
- **Multiple symptom assessment tools that could be integrated in to the electronic health record.**

Implications for Research

- **Symptom clusters – still so much to learn**
 - **Longitudinal studies**
 - **Identification of underlying mechanisms**
 - **Intervention trials aimed at treating multiple symptoms within a cluster**



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