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Physical Symptom Burden and its Association with Distress, Anxiety and Depression in Breast Cancer

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Abstract

Introduction—Physical symptom burden and psychological symptoms are highly prevalent in women with breast cancer. The Distress Thermometer and Problem List (DT&PL) is commonly used in oncology clinics to screen for distress and its accompanying Physical Problem List (PPL) identifies pertinent physical symptoms. However, the identification of physical symptoms found on the PPL has never been evaluated for its association with psychological symptoms in women with breast cancer.

Methods—Patients (*n*=125) with breast cancer (Stage 0-IV) completed the DT&PL and the Hospital Anxiety and Depression Scale (HADS). They reported bother from any of 22 PPL items on the DT&PL. PPL items were assessed for their associations with distress (DT), anxiety (HADS-A), and depression (HADS-D). The total number of PPL items endorsed per patient was evaluated for associations with psychological outcomes, controlling for relevant demographic factors.

Results—Most physical problems were associated with depression (n=13, 87%), and anxiety (n=8, 53%), but fewer were associated with distress (n=4, 27%). In multivariate analyses, higher total number of problems was associated with younger age (p=.03) and more depressive symptoms (p<.001).

Conclusion—Physical symptom burden detected by the DT&PL co-occurs with depression most commonly and to a lesser extent anxiety and distress in women with breast cancer. Depression is associated with more types of physical symptoms and a total number of physical symptoms. The endorsement of multiple PPL items on the DT&PL should prompt an evaluation for depression. Similarly, depression should prompt the evaluation and treatment of physical symptom burden.

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Introduction

Women with breast cancer have poor psychological outcomes compared to the general population.[1,2] Distress, anxiety, and depression are associated with high-risk patient features in the breast cancer setting such as previous psychological problems, chronic stress, and early childhood adversity, and uncontrolled physical symptoms.[3–5] Physical symptoms may be a consequence of surgery, radiation, chemotherapy, or anti-hormonal therapies and are associated with poor quality of life.[5,6] Enduring psychological symptoms have implications for worse adherence to anti-cancer therapies and possibly survival outcomes.[7,8] Adverse psychological outcomes such as distress, anxiety, and depression continue to be under-recognized and under-treated despite national and international initiatives and mandates.[9] In addition, physical symptom burden in breast cancer is not consistently ameliorated.[6,10] An increase in the use of patient reported outcomes (PROs) will be helpful in addressing this area of need, as PROs are more reliable indicators of physical symptom burden.[11,12] As such, this study examines the association between physical symptom burden as detected by the Physical Problem List (PPL) of the Distress Thermometer and Problem List (DT&PL) and distress, anxiety, and depression.

The DT&PL is endorsed by the National Comprehensive Cancer Network (NCCN) for the identification of psychological distress and to triage psychological symptoms in patients with cancer.[13] It is an ultra-short one-item measure that offers convenience and proven acceptability in bustling oncology clinics and has been the most broadly accepted and implemented measure of distress internationally.[14] Other standard measures such as the Brief Symptom Inventory or the Subjective Units of Distress Scale are less commonly used since they are more cumbersome for patients and staff.[14,15] The Problem List that accompanies the DT&PL is meant to be a convenient tool to identify pertinent real-time issues in the clinic and is organized into Practical, Family, Emotional, Spiritual/Religious Concerns, and Physical problems.[16,17]

Since the DT&PL is already in use in oncology clinics and provides a measure of physical symptom burden, it makes sense to understand the relationship between physical symptom burden as detected on the DT&PL and psychological symptoms. This has not been reported previously. That is, the DT&PL PPL variables that measure physical symptom burden have not been explored for their associations with distress, anxiety, or depression in the breast cancer setting. Identification of PPL items may provide readily accessible information on the patients' physical symptom burden and be associated with the presence of anxiety and/or depression as well. Physical symptom burden as identified on the DT&PL may point to psychological suffering. In addition, this information will be useful in understanding how psychological health may influence the perception of physical symptom burden as detected by the DT&PL. Information from this study should be clinically useful given that the DT&PL is already being used internationally to screen for distress and provides a measure of physical symptom burden that can be used to understand its relationship with the presence of psychological symptoms of distress, anxiety, and depression.

Methods and Materials

Details for the current study have been previously reported are reviewed in brief here.[18] The Mount Sinai Hospital Institutional Review Board approved this study. All participants provided informed consent prior to participation and data were collected from August 2014 to April 2015.

Participants

Patients with Stage 0-IV breast cancer within five years of diagnosis were recruited and consented to participate from a dedicated breast cancer clinic in this survey-based study. Inclusion criteria consisted of a confirmed tissue diagnosis of breast cancer within the previous five years, as indicated by the patient.

Procedure

Participants were asked to participate by either a clinic receptionist or an infusion suite nurse. They were told that the survey was anonymous as part of a research initiative and that it would not be part of their ongoing care. Available psychological services were listed in the survey and patients were asked to bring up any concerns with clinic staff and, in particular, to tell a staff member if they felt severely depressed or had suicidal ideation. A board-certified psychiatrist oversaw the study and was available for consultation. Participants completed surveys while waiting in the clinic office space prior to their appointments or during chemotherapy infusion.

Measures

Patient demographic and medical characteristics—Patients reported demographic information including age, race/ethnicity, and marital and employment status, as well as medical information including whether they had received surgical treatment, chemotherapy, and anti-hormonal therapy.

Distress, anxiety, and depression—Patients completed the Distress Thermometer (DT) to assess for distress and the Hospital Anxiety and Depression Scale (HADS) to assess for anxiety and depression.

The DT is a one-item measure of distress, ranging from 0 (Not at all distressed) to 10 (Extremely distressed) and a cut-off of ≥4 has been accepted by the NCCN to indicate clinically meaningful distress.[19] The DT&PL (including the DT and Problem List) has been validated among international cancer populations.[20]

The HADS is a 14 question psychometric measure that was developed to identify ‘caseness’ (possible and probable cases) of anxiety and depressive disorders among patients in hospital clinics.[21] The HADS is divided into an anxiety subscale (HADS-A) and a depression subscale (HADS-D). Responses are scored 0 to 3 points such that each individual subscale (i.e., HADS-A and HADS-D) may garner between 0 and 21 points. Multiple cut-offs have been identified, but a cut-off of 8 and over (on each subscale) shows highest sensitivity and

specificity and therefore is most commonly used to identify caseness of both depression and anxiety.[22]

Physical Problems—Patients reported whether a physical symptom had been a problem for them over the past week using the PPL accompaniment to the DT&PL. Problem List items are potentially modifiable depending on clinic needs. The standard PPL contains 22 separate items (see Table 2 for items) to which patients endorse whether or not a particular physical symptom has been a problem for them in the past week.

Statistical Analysis

The primary outcome of this study was the association of 22 Physical Problem List items with the psychological outcomes distress, anxiety, and depression. Associations with distress, anxiety, and depression were examined if at least 10% of patients endorsed that particular physical symptom (to ensure adequate power). Independent t-tests were used to assess the bivariate associations between patient age and endorsement of physical problems.

The effect of psychosocial distress variables on total number of items endorsed from the PPL was tested using negative binomial regression, as our outcome variable (total PPL items) represents a count variable, which was over-dispersed (i.e., Pearson's chi square value for the model using Poisson regression $\chi^2/df = 2.18$).[23] Demographic factors that were found to be significantly related to the endorsement of specific physical problems in our prior work were included as covariates.[18] These statistical procedures were performed using the SPSS version 24 software (SPSS, Chicago, IL 2013) and statistical tests were two-tailed with a 5% significance level.

Results

One hundred and twenty five participants completed the survey. As previously reported, Table 1 highlights patient characteristics and their psychological symptoms (e.g., distress, anxiety, and depression).[18] Women had an average age of 55.4 years, ranging from 26 to 84 years. Approximately half of the women endorsed white race/ethnicity (51.2%) and were married (49.2%), and most were employed (64.1%). Approximately half of the women reported having received chemotherapy (55.6%). Screening criteria were met by 55.1% of patients for distress, 36.8% for anxiety, and 20.8 for depression.

Fifteen of the 22 PPL items were reported by more than 10% of women (Table 2). The median number of PPL variables endorsed by patients was 3.0 (M=3.43, SD=3.42) with a range from 0 to 14. Approximately one-fourth endorsed no physical symptoms while three-fourths reported at least one problem, and three-fifths endorsed 2 or more problems. The five most commonly reported physical problems were fatigue (40.0%), sleep (34.7%), skin dry/itchy (22.9%), pain (19.5%), and feeling swollen (19.5%). Problems with changes in urination, fevers, and substance abuse were not common (all <2.5%). Patients who met psychological screening criteria endorsed more PPL variables. For example, the number of endorsed PPL variables was 4.38 (3.9) versus 2.5 (2.6) for patients who met distress screening criteria, 4.51 (4.1) versus 2.67 (2.6) for patients who met anxiety screening criteria, and 6.29 (4.7) versus 2.54 (2.6) for patients who met depression screening criteria.

Table 2 shows the psychological associations of each PPL item, and Table 3 reviews independent t-test results. Thirteen of the 15 most commonly reported PPL items (i.e., those PPL items with endorsement from over 10% of patients) were significantly associated with depression (87%), while 8 of the 15 (53%) were associated with anxiety, and only 4 of the 15 (27%) were associated with distress (Tables 2). All PPL items that were associated with either distress or anxiety were also associated with depression (Table 3). For example, problems with Memory/Concentration were associated with all three psychological outcomes while problems with Eating, Breathing, and Nausea were associated with distress and depression, but not anxiety. Problems with Sleep, Pain, Indigestion, Constipation, Getting Around, Tingling in Hands/Feet, and Feeling Swollen were associated with both anxiety and depression but not distress. Problems with Fatigue and Nose Dry were only associated with depression and not distress or anxiety. Tingling in Hands/Feet and Appearance had no psychological associations.

Results from hierarchical negative binomial regression analyses predicting the number of PPLs endorsed are reported in Table 4. Age was the only covariate that was related to the total number of problems endorsed. Controlling for all other covariates and psychosocial distress variables, older women tended to endorse *fewer* physical problems. Depression was the only psychosocial association that was related to total number of problems endorsed. Controlling for covariates, distress, and anxiety, women endorsing more depressive symptoms tended to endorse *more* physical problems.

Discussion

Physical problems are very common among patients with breast cancer and are also frequently associated with at least one psychological outcome. Depression and younger age were associated with the greatest number of endorsed physical symptoms. Depression was associated with both the most individual physical problems and greater number of physical problems endorsed by the patient. That is, the most common psychological association with any physical symptom was depression. Depression was also associated with actual number of endorsed physical symptoms per participant. This study provides evidence that physical symptom burden identified on the DT&PL is associated with psychological co-morbidity, and most strikingly with depression. From an opposite perspective, the presence of depression over distress or anxiety most commonly was associated with both an increasing number of physical symptom complaints and the most varied types of physical complaints.

Findings fit with those from comparable studies of breast cancer or general cancer populations where depression is associated with the presence of physical symptoms. A study by Breen et al. found that the presence of anxiety or depression was associated with physical symptoms most commonly in the form of fatigue, pain, sleep, and gastroenterological problems in women with breast cancer.[24] Another study also found that appetite changes and issues with memory or concentration were the physical symptoms most strongly associated with depression in a population of general cancer patients.[25] A previous study of 487 cancer patients found a synergistic relationship between depression and the presence and severity of physical symptoms independent of cancer type, functional status, chemotherapy status, and survival time.[26] Overall, the most commonly endorsed physical symptoms across these

studies were associated with depression, and anxiety to a lesser extent in distinct cancer populations similar to our study.

Although the association between physical symptom burden and depression is well described in the literature, it has not been described using the DT&PL. This is important information since this distress measure is readily accessible in oncology clinics and its usefulness may be expanded. This has implications for consult liaison psychiatrists working in breast cancer clinics who may be able to evaluate these measures that were collected in previous clinics or will be collected moving forward in their patients care in the oncology clinic. This may provide a convenient measure of physical symptom burden with concomitant depression or psychological burden. Latent physical symptom burden should be addressed in order to alleviate concomitant psychological symptom burden.[27] While this idea in itself is not novel, using the DT&PL to describe the physical symptom burden is and should be explored more thoroughly.

Of note, particular types of physical problems were associated with distinct psychological outcomes. For example, patients highlighted cognitive issues (memory/concentration) and biological functions (sleep, pain) that are known to be associated with mood. In addition, they highlighted gastroenterological functioning (problems with eating, indigestion, nausea), and problems of global functioning (getting around, breathing, feeling swollen, pruritus) that were association with psychological symptoms, most commonly depression. Results that may be considered surprising include the following: 1) fatigue was associated with only depression since it is a marker of mood and global functioning and 2) problems with Appearance and Tingling in Hands/Feet (neuropathy) were not associated with psychological outcomes since these problems may influence global functioning. Although 18.6% of the cohort experienced neuropathy, which is a known complication of paclitaxel chemotherapy used on breast cancer, it was not associated with adverse psychological outcomes.

This study provides evidence of an association between physical symptom burden and depression using two of the most commonly used scales to screen for psychological issues in cancer populations, the DT&PL, and HADS.[14,28,29] Therefore, these findings should be repeated in patients with breast cancer to test for validity and evaluated in other cancer populations. Evaluating this association with commonly used scales enhances the clinical application of these findings. Of note, there is no overlap in physical symptoms between the DT&PL and the HADS since the HADS does not ask about physical symptoms and is therefore a preferred measure of psychological states in medically ill patients with significant physical symptoms. As well, the DT&PL and HADS have been found to correlate well as screening tools for distress, anxiety, and depression.[15,30] The co-occurrence of endorsing PPL items and concomitant distress, depression, and/or anxiety using these scales is also notable since the HADS does not use any physical symptoms. These data may reinforce the need to investigate the presence of psychological issues, and depression in particular, in patients who report ongoing problems with physical symptoms, especially in younger patients. Alternatively, the presence of distress, anxiety, or depression may point to unmet physical symptom needs. Although this study was not powered to study causation, directionality would be a worthy investigation.

A limitation of this study is the lack of another validated measure of physical symptom burden in order to ensure the validity of our results, as opposed to measures such as the Edmonton Symptom Assessment System (ESAS) or the Functional Assessment of Cancer Therapy-Breast Cancer (FACT-B), which have been validated as patient-reported outcome measures. Also, stage and length of time with breast cancer was not captured and may have provided more information on the association of physical and psychological symptoms. Future studies should compare these psychological associations with other standard measures of physical symptom burden and quality of life measures, as well as include longitudinal assessments to better determine the directionality of this co-occurrence.

In summary, this study has provided evidence for the association between physical symptom burden and poor psychological outcomes, most notably depression in patients with breast cancer. Efforts should be made to identify and treat concurrent depression in the breast cancer setting. The DT&PL may be a fast and convenient tool to evaluate for physical symptoms that point to concomitant psychological comorbidity that should be further investigated.

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Table 1

Demographic and Psychological (distress, anxiety, and depression) Information of Breast Cancer Patient Cohort.

	Mean	***SD***
Age	55.4	13.2
Distress (DT&PL)	4.0	2.60
Anxiety (HADS-A)	6.21	4.04
Depression (HADS-D)	4.08	3.79
	N	%
Race/Ethnicity		
Black	26	21.1
White	63	51.2
Latina	22	17.8
Other	12	10.1
Married (Yes)	61	49.2
Working (Yes)	66	64.1
Chemotherapy (Yes)	67	55.6

Table 2

Number and Percentage of Breast Cancer Patients Endorsing Physical Problem List Variables on the Distress Thermometer and Problem List.

Physical Problem List Variables	*N*	%	Psychological Association
Fatigue	46	40.0	Depression
Sleep	41	34.7	Anxiety, Depression
Skin Dry/Itchy	27	22.9	Anxiety, Depression
Pain	23	19.5	Anxiety, Depression
Feeling Swollen	23	19.5	Anxiety, Depression
Memory/Concentration	22	18.6	Distress, Anxiety, Depression
Tingling in Hands/Feet	22	18.6	-
Eating	21	17.8	Distress, Depression
Appearance	20	16.9	-
Constipation	20	16.9	Anxiety, Depression
Nose Dry	16	13.6	Depression
Breathing	15	12.7	Distress, Depression
Getting Around	14	11.9	Anxiety, Depression
Nausea	13	11.0	Distress, Depression
Indigestion	12	10.2	Anxiety, Depression

Table 3

Comparison of Distress, Anxiety, and Depression among Patients who do or do not the Endorse Problems with the Most Common Physical Problems on the DT&PL in Patients with Breast Cancer.

		Distress		Anxiety		Depression	
		Mean (SD)	***t***	***Mean (SD)***	***t***	***Mean (SD)***	***t***
Fatigue	Yes	4.28 (2.5)	0.970	6.66 (4.1)	0.962	5.07 (3.8)	2.596 *
	No	3.74 (2.6)		5.9 (3.9)		3.2 (3.7)	
Sleep	Yes	4.38 (2.5)	1.467	8.44 (4.0)	4.566 **	6.15 (4.0)	4.854 **
	No	3.54 (2.5)		4.89 (3.6)		2.66 (3.2)	
Skin Dry/Itchy	Yes	4.57 (2.3)	−1.331	8.31 (3.9)	−3.102 **	6.62 (4.3)	−3.562 **
	No	3.74 (2.7)		5.63 (3.9)		3.38 (3.3)	
Pain	Yes	3.55 (2.6)	1.634	8.57 (4.5)	3.559 **	7.0 (4.3)	5.062 ***
	No	4.63 (2.3)		5.27 (3.6)		2.83 (3.1)	
Feeling Swollen	Yes	4.43 (2.5)	−0.936	8.00 (4.4)	−2.348 *	6.59 (4.0)	−3.607 ***
	No	3.83 (2.6)		5.79 (3.9)		3.51 (3.5)	
Memory/concentration	Yes	4.72 (1.8)	2.252 *	7.95 (4.0)	2.973 **	7.1 (4.0)	5.675 **
	No	3.51 (2.6)		5.25 (3.6)		2.68 (2.8)	
Tingling in hand/feet	Yes	4.45 (2.8)	−0.990	6.77 (4.4)	−0.724	5.09 (4.6)	−1.386
	No	3.81 (2.6)		6.08 (4.0)		3.86 (3.6)	
Eating	Yes	5.21 (2.5)	−2.442 *	7.75 (4.5)	−1.891	7.10 (3.4)	−4.161 ***
	No	3.63 (2.5)		5.9 (3.9)		3.48 (3.6)	
Appearance	Yes	3.67 (1.5)	0.184	6.74 (3.9)	0.989	4.58 (3.1)	1.254
	No	3.8 (2.7)		5.73 (3.9)		3.42 (3.7)	
Constipation	Yes	4.25 (3.1)	−0.524	7.95 (4.8)	−2.145 *	6.35 (4.5)	−3.031 **
	No	3.68 (2.5)		5.86 (3.8)		3.63 (3.5)	
Nose Dry	Yes	3.79 (2.0)	0.236	7.06 (3.7)	−0.908	5.88 (4.3)	−2.060 *
	No	3.96 (2.4)		6.08 (4.1)		3.81 (3.6)	
Breathing	Yes	6.00 (1.9)	−3.267 **	8.10 (3.1)	−1.505	7.50 (3.5)	−3.077 **
	No	3.77 (2.6)		6.10 (4.1)		3.77 (3.7)	

		Distress		Anxiety		Depression	
		Mean (SD)	*t*	*Mean (SD)*	*t*	*Mean (SD)*	*t*
Getting Around	Yes	5.08 (1.8)	−1.716	8.43 (4.1)	−2.225*	7.71 (4.2)	−4.057***
	No	3.78 (2.7)		5.92 (4.0)		3.60 (3.5)	
Nausea	Yes	6.00 (2.4)	−2.902**	8.00 (5.1)	−1.708	7.08 (3.5)	−3.127**
	No	3.67 (2.5)		5.99 (3.9)		3.72 (3.7)	
Indigestion	Yes	5.40 (2.3)	−2.117	9.67 (3.7)	−3.251**	9.17 (4.1)	−5.462***
	No	3.77 (2.6)		5.82 (3.9)		3.52 (3.3)	

* p<.05,

** p<.01,

*** p<.001

Table 4

Hierarchical Negative Binomial Regression Analysis Predicting Total Items Endorsed on the Physical Problem List

	B	Std Error	Exp(B)	95% CI for Exp(B)	*p*
Covariates					
Age	−0.02	0.01	0.98	0.97 – 1.00	.03*
Race/Ethnicity					
Black	0.46	0.33	1.58	0.83 – 3.01	.16
Latina	0.24	0.25	1.27	0.79 – 2.06	.33
Other	0.30	0.40	1.35	0.61 – 2.98	.46
Married	−0.02	0.21	0.98	0.65 – 1.49	.94
Working	0.33	0.28	1.39	0.80 – 2.41	.24
Received chemotherapy	−0.07	0.24	0.93	0.58 – 1.50	.77
Psychosocial Distress Variables					
Distress Thermometer	−0.001	0.05	1.00	0.91 – 1.09	.99
Depressive Symptoms	0.18	0.03	1.20	1.12 – 1.28	<.001***
Anxiety Symptoms	−0.03	0.04	0.97	0.91 – 1.04	.44

Note. Ethnicity: effect compared to that for white participants; Married, Working, Received chemotherapy: 0 = No, 1 = Yes.

* $p<.05$,

** $p<.01$,

*** $p<.001$