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Anxiety and depression in young women with metastatic breast cancer: A cross-sectional study

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Abstract

Background—Young adults with cancer experience disruptions in their normal developmental trajectories and commonly experience psychological distress related to their diagnoses. Young women with metastatic breast cancer (MBC) are at particular risk of adverse mental health outcomes.

Objective—We sought to determine the prevalence of and factors associated with anxiety and depression symptoms in young women with newly diagnosed *de novo* MBC.

Methods—Fifty-four women with newly diagnosed *de novo* MBC were identified from an ongoing, prospective, multi-center cohort of women diagnosed with breast cancer at age <40. Depression and anxiety symptoms were assessed using the Hospital Anxiety and Depression Scale

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(HADS). Items assessing socio-demographics, physical symptom burden, social support, and disease and treatment history, with complementary medical record review, were used to assess variables potentially associated with anxiety and depression symptoms.

Results—Mean HADS Depression score was 4.4 (SD, 3.7) and mean HADS Anxiety score was 7.9 (SD, 5.0). Eleven (20%) women scored ≥8 on the HADS Depression subscale, the suggested threshold for depression/anxiety screening, and 24 (44%) women scored ≥8 on the HADS Anxiety subscale. In a multivariable model of anxiety, higher physical symptom scores (OR=4.41, p=0.005) was significantly associated with higher anxiety scores. None of the other variables improved the model fit.

Conclusion—In this study, a considerable proportion of young women with newly diagnosed MBC experience anxiety symptoms, although depression is less common. Future strategies focused on distress reduction in young MBC patients should focus on physical symptom management as well as anxiety identification and management.

Keywords

Anxiety; Depression; Cancer; Oncology; Psycho-Oncology

INTRODUCTION

Breast cancer is an important source of morbidity, mortality, and health care utilization for women in the United States (US).[1] Among US adult women younger than 40 years old, breast cancer is the most frequently diagnosed cancer[2] and the leading cause of cancer-related death.[3] Biologically, young women are more likely to develop aggressive phenotypes of breast cancer and present with advanced disease, resulting in worse prognosis and lower survival rates compared to older adults.[4] Over the past thirty years in the US, rates of metastatic breast cancer (MBC) at diagnosis have disproportionately increased in younger women, from 1.53 per 100,000 to 2.90 per 100,000, without a corresponding increase in older women.[5] Young women with MBC are also surviving longer; in the US, 5-year survival rates for women aged 15–49 with *de novo* breast cancer have increased to 36%.[6] Despite the increasing prevalence of MBC in young women, limited research has evaluated the psychological distress at diagnosis for young women with metastatic disease.

Due to their young ages and life-limiting diagnoses, young women with any metastatic cancer or advanced hematologic malignancy may be particularly vulnerable to distress given that they experience unique psychosocial stressors. In addition to disruptions in their expected life roles and responsibilities, they must contemplate the loss of an imagined future and early mortality at a young age.[7] Such practical, existential, and psychological concerns are a major source of distress for patients and may contribute to the higher prevalence of depression and anxiety disorders in young adults with cancer.[8] Among women with breast cancer in general, available data suggest that young women are more vulnerable to negative psychological outcomes than older women.[9–11]

Much of the extant literature on psychiatric outcomes in young women with breast cancer focuses on those with early stage cancer or for those in survivorship.[9, 12] Yet, extrapolating from the experiences of young women with early stage disease may not be valid for the MBC patient population who experience greater physical symptom burden, greater cumulative treatment toxicity, and awareness of a life-limiting prognosis. No prior study has focused on the psychological distress of young women with *de novo* MBC (diagnosed with MBC at initial diagnosis).

The objectives of this study were to identify the prevalence of depression and anxiety symptoms in a cohort of young women with newly diagnosed *de novo* MBC and examine whether sociodemographic and disease characteristics were associated with anxiety and depression. We hypothesized that younger women would experience a high prevalence of anxiety as compared to published prevalence norms among all adult women with MBC and that women who were parents of dependent children would endorse higher anxiety symptom severity.

MATERIAL AND METHODS

Participants and study design

Helping Ourselves, Helping Others: The Young Women's Breast Cancer Study is an ongoing multi-center prospective cohort study to explore the biological, medical, and quality of life issues specific to young women diagnosed with breast cancer at any stage. Description of study procedures has been previously reported.[13] Briefly, eligible women with newly diagnosed breast cancer who received care from one of nine academic and community hospitals in Massachusetts and academic sites in Denver, Colorado, Rochester, Minnesota, and Toronto, Ontario, Canada, although Toronto participants received a modified version of all the surveys and were not included in this analysis. After providing informed consent, enrolled participants completed a mailed self-report baseline survey and complete a follow-up survey every six months for the first three years following initial cancer diagnosis and then annually thereafter. Overall eligibility criteria includes women who are English speaking, have stage 0 – IV breast cancer diagnosed within six months before enrollment, and are age ≤ 40 years at time of initial diagnosis. This analysis focuses on the 54 women with *de novo* MBC who completed the baseline survey between November 2006 and April 2016. The study was approved by the Institutional Review Board at the Dana-Farber/Harvard Cancer Center and all other study sites.

Data and Instruments

Participants provided their sociodemographic information and clinical illness histories and completed several measures of psychosocial functioning at study baseline. Financial comfort was defined by participants answering the question, "how would you describe your household's financial situation right now?" with the response choice of having enough money to buy special things after paying bills (vs. "not").[14, 15] Overall religiousness/spirituality was assessed using two questions from the Multidimensional Measurement of Religiousness/Spirituality for Use in Health Research. These two questions are from the "Religious Intensity" domain of the Multidimensional Measurement of Religiousness/Spirituality for Use in Health Research. When included in the 1997–1998 General Social

Survey of the National Data Program for the Social Sciences, the reliability for the two questions was 0.77 when combined as a domain, and 0.63 for each individual question.[16]

Depression and anxiety symptoms were measured using the Hospital Anxiety and Depression Scale (HADS). The HADS is a 14-item self-report instrument that assesses anxiety and depressive symptoms in populations with medical conditions.[17] It has two 7-item subscales: HADS Depression and HADS Anxiety. Each item is scored on a 4-point scale (0=not at all to 3=nearly all the time); thus, each sub-scale can range from 0–21. Scores are interpreted as no (0 – 7), mild (8 – 10), moderate (11 – 14) or high (15 – 21) symptoms. The HADS has been extensively validated in oncology populations.[18]

Quality of life. The Cancer Rehabilitation Evaluation System-Short Form (CARES-SF) is a 59-item instrument evaluating QOL issues among individuals with cancer. The CARES has five summary scales addressing (1) physical function; (2) psychosocial function; (3) marital interaction; (4) sexual function; and (5) medical interactions over the past month.[19, 20] Its reliability, validity, factor structure, and other psychometric properties have been studied extensively.[21] Each item is scored on a 5-point scale (0=none, 4=very much). For this study, we used the physical functioning subscale, designed to measure the physical changes and disruption of daily activity caused by the disease to estimate physical symptom burden (subscale score range 0–4, higher scores are worse).[22]

Perceived social support was measured by the Medical Outcomes Study Social Support Survey (MOS). The MOS is a 20-item self-administered multi-dimensional survey of perceived social support frequently used in patients with chronic medical conditions. It is scored on a 5-point scale and has four subscales addressing tangible, affectionate, emotional or information support, and positive social interaction.[23] Scores are calculated by averaging items and transforming the mean score to a 100-point scale. Higher scores reflect greater support. The MOS has good internal consistency and reliability [24, 25] and is frequently used in oncology populations.

Statistical analysis

We used descriptive statistics to characterize the study sample. Scoring for the HADS, CARES-SF and MOS were calculated using standard algorithms. Univariable logistic regression analyses were performed to assess the relationship between HADS Anxiety or Depression scores – and psychosocial and clinical predictor variables: age, race, education, employment (at time of survey completion), level of religious and spiritual intensity, marital status, household financial situation, number of children prior to diagnosis, perceived social support, and physical functioning. Independent variables that were significant at $p < 0.2$ (2-tailed) were entered into the multivariable logistic regression model. The stepwise forward sequence was used, keeping all variables in the model that achieved significance at $p < 0.05$ (2-tailed), to identify the most parsimonious models. The analyses were conducted using SAS Software, Version 9.4 (SAS Institute, Cary, N.C).

RESULTS

Table 1 contains the demographic and illness characteristics of the sample. Mean age at time of MBC diagnosis was 35.2 (range, 23 – 40) years. Median time between diagnosis and baseline survey completion was 143.5 days (range, 58 – 305).

Anxiety and associated factors

Mean HADS Anxiety score was 7.9 (SD 5.0) and 24 (44%) women scored 8 or higher on the HADS Anxiety subscale. Nearly a third (n = 15, 28%) reported moderate-high (scores > 11) levels of anxiety symptoms (see Table 2).

In univariable logistic regression analyses, higher physical symptom score (CARES-SF physical subscale), Caucasian race, having at least a college education, less financial comfort, lower social support scores (MOS), and lower spirituality were associated with more anxiety at a $p < 0.2$. In the multivariable model (see Table 3), only higher physical symptom burden (OR = 4.41, $p = 0.005$) was statistically significantly associated with higher HADS Anxiety scores. None of the other variables improved the model fit.

Depression and associated factors

Mean HADS Depression score for the sample was 4.4 (Standard deviation, SD 3.7). A total of 11 (20%) women scored 8 or higher on the HADS Depression subscale, the suggested threshold for depression screening (see Table 2). Nine percent (n = 5) of women had moderate-high (scores ≥ 11) levels of depressive symptoms. Similar to the HADS Anxiety subscale, women who had at least a college education, a higher physical symptom score, Caucasian race, lower social support scores, and lower spirituality were more likely to report higher depression scores at a $p < 0.2$. Given the relatively low numbers of women with clinically significant depressive symptoms, further regression analyses were not conducted for the HADS Depression scores as the outcome variable.

DISCUSSION

In this cross-sectional evaluation of young women with recently diagnosed *de novo* MBC, participants frequently experienced anxiety symptoms, although depression was less common. The results of this study add to the literature in three important ways. First, to our knowledge, this is the only study designed to examine the prevalence of psychological distress in young women with MBC. While the HADS is not a diagnostic instrument for anxiety or depression disorders, scores above eight reflect clinically significant morbidity and identify at-risk patients who benefit from clinical evaluation.

Second, this study confirms the psychological vulnerability of young women with *de novo* MBC. Reported rates of clinically significant anxiety symptom burden in women with MBC typically range from 20–40%.[26, 27] The prevalence of clinically significant anxiety symptoms among women in this study exceeded rates seen among mixed-age populations of women with MBC[28, 29] or populations of newly diagnosed cancer patients,[30] though similar studies exclusively focused on older women with *de novo* MBC have not been conducted. Prevalence of depression, while not as high as anxiety, was also higher than other populations of cancer patients using similar symptom severity scales.[29, 31] It is possible that the 44% point prevalence of clinically significant anxiety symptoms and the 20% point prevalence of clinically significant depression symptoms in this study are a function of sampling women with recent diagnoses of *de novo* metastatic cancer. Yet, cross-sectional evidence suggests that anxiety and depression symptoms are prevalent among advanced cancer patients even beyond the time of initial diagnosis.[32]

The third way that results from this study inform our understanding of psychological distress in breast cancer are the confirmation of anxiety as the most clinically prevalent psychological problem in this population, and the role of physical symptom burden in anxiety and depression severity.[31, 33] Despite the known high prevalence of anxiety symptoms in breast cancer patients, the influence of anxiety disorders on cancer outcomes is less studied than the impact of depression. In studies of patients with chronic medical illness, anxiety disorders are strongly associated with increased healthcare utilization, reduced physical well-being, and physical disability.[34] The psychosocial and demographic risk factors for anxiety and depression among young women with *de novo* MBC are similar and there is likely a bidirectional relationship between all mental health disorders and health outcomes. Thus, there are several compelling reasons to specifically identify and address untreated anxiety when screening for depression in MBC patients. The link between physical symptom burden and higher anxiety and depression severity in young women with *de novo* MBC mirrors relationships found in patients with chronic medical illness[35] and advanced cancers.[36, 37] While we do not know how much of their physical functioning impairment was due to illness burden versus anti-neoplastic therapy side effects, clinicians may want to consider the consequences of higher treatment toxicity in highly anxious and/or depressed patients. In the era of shared decision-making and personalized medicine, young women with *de novo* MBC reflect a population where treatment decisions must consider the toxicity on the whole person. Individualized assessment of physical symptoms with mental health patient-reported outcome measures could aid decision-making for these patients at high risk of clinically significant distress.

We had hypothesized that the presence of dependent children would be associated with anxiety as previous studies have found high cross-sectional rates of anxiety in adult advanced cancer patients with dependent children[38] and higher rates of anxiety among patients with dependent children compared to those without children.[39] However, we did not find this association in our study. This lack of association may be due to the small sample size; it is also possible that parental status serves as both a psychologically protective factor for individuals as well a source of psychological distress for young women with a *de novo* diagnosis of MBC. It is possible that patients with access to robust parenting support services (not captured in this dataset) found ways to address their parenting concerns and therefore reduce their overall psychological distress.

Mitigation of the psychosocial effects of life disruption is a large unmet need among young adult cancer patients. Zebrack et al. demonstrated that nearly 41% of newly diagnosed (within four months) adolescent and young adult cancer patients reported a counseling need (e.g. mental health counseling, family counseling) and that these mental health needs increased for those with more treatment-related symptoms.[8] Data from this study corroborate this need for enhanced mental health services for young adult cancer patients. The growing number of psychosocial interventions to reduce cancer-associated psychological distress among young adults is encouraging[40]; yet, there remain large gaps in research, clinical, and resource delivery. In particular, many psychosocial interventions for young adult cancer patients focus on exercise and activity-based resources. These interventions are ideal for many cancer survivors but may not address their counseling needs. In addition, they may be less accessible for patients who cannot fully participate in physical activity-based interventions. For young women with MBC, physical symptoms may interfere with many of the interventions clinicians recommend to patients to ameliorate psychological distress and improving overall functioning. Thus, psychosocial interventions tailored to young adults with incurable illness or functional limitations are needed, particularly for the young adults with MBC.

This was a small study that aimed to more fully characterize the clinical and psychosocial correlates of psychological distress in young women presenting with *de novo* MBC. Assessment of prior psychiatric history were not included in the survey, so it is not possible to know whether participants' depression and anxiety symptoms preceded their MBC diagnosis. The majority of respondents were Caucasian and were well-educated. Thus, the demographic characteristics of his cohort may limit generalizability of our results to other populations. This study reports on the results of a cross-sectional analysis limited to women with *de novo* MBC responding to the baseline survey on the study. As the Young Women's Breast Cancer Study cohort matures, additional data will become available on the psychosocial effects and supportive care needs of women who develop progression of MBC from early stage breast cancer, how these differ from women with *de novo* metastatic disease, and how they change over time.

CONCLUSIONS

Knowledge of the risk factors associated with psychological distress among young women with *de novo* MBC can help clinicians and researchers alike to systematically identify vulnerable patients and provide targeted psychosocial interventions to improve these young women's mental health outcomes.

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DISCLOSURES

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Table 1

Patient Characteristics and Mean HADS Anxiety and Depression Scores

Variable	N*	HADS Anxiety score	HADS Depression score
Total	54	7.9	4.4
Age at Diagnosis			
≤30	9	8.0	4.9
31–35	14	8.1	4.1
≥36	31	7.8	4.4
Race			
Caucasian	48	8.3	4.7
Non-Caucasian	6	4.3	2.0
Married or partnered			
Yes	36	8.1	4.5
No	18	7.4	4.3
College educated			
Yes	42	8.6	5.1
No	12	5.3	2.0
Full Employment			
Yes	18	8.4	4.9
No	26	7.6	4.2
Has children			
Yes	33	7.6	4.7
No	21	8.3	4.0
Comfortable finances			
Yes	18	6.4	4.3
No	33	8.9	4.8
Spiritual person			
Yes	23	6.3	3.1
No	11	8.8	5.7
Religious person			
Yes	13	6.4	3.5
No	21	7.6	4.2
CARES-SF physical			
0 to <1	22	7.1	2.6
1 to <2	23	8.1	5.6
2+	5	13.8	9.2
MOS Social Support			
<80	7	11.9	8.4
80 to <90	15	6.6	3.9

Variable	**N***	**HADS Anxiety score**	**HADS Depression score**
90 to <100	19	9.1	4.8
100	13	5.5	2.2

*N varies due to missing data

Abbreviations: HADS=Hospital Anxiety and Depression Scale (range, 0–21, higher scores indicate more symptoms); CARES-SF=Cancer Rehabilitation Evaluation System-Short Form (higher scores indicate more symptoms); MOS=Medical Outcomes Study Social Support Survey (higher scores indicate better social support).

Table 2

Participant HADS Scores (n = 54)

	HADS Anxiety	**HADS Depression**
Mean (S.D)	7.9 (5.0)	4.4 (3.7)
Median Score	6	3.5
Observed range	0 – 20	0 – 14
Grouped results (n, %)		
Low (0 – 7)	30 (56)	43 (80)
Mild (8 – 10)	9 (17)	6 (11)
Moderate – High (11 – 21)	15 (28)	5 (9)

Abbreviations: HADS=Hospital Anxiety and Depression Scale (range, 0–21, higher scores indicate more symptoms)

Table 3

Univariable and Multivariable Logistic Regression Model for Clinically Significant HADS Anxiety Scores (≥8)

Variable	Univariable Models			Multivariable Model*		
	OR	95% CI	p-value	OR	(95% CI)	p-value
CARES physical subscale	4.41	(1.57, 12.37)	0.005	4.41	(1.57, 12.37)	0.005
Age at diagnosis (continuous)	1.01	(0.89,1.15)	0.89			
College educated vs. less	5.50	(1.07, 28.19)	0.04			
Full employment vs. less	1.96	(0.62, 6.18)	0.25			
Married or partnered vs. not	1.00	(0.32, 3.12)	1.00			
Have children vs. none	0.81	(0.27, 2.44)	0.71			
Caucasian vs. other	4.60	(0.50, 42.36)	0.18			
Comfortable finances vs. less	0.42	(0.13, 1.38)	0.15			
MOS social support score	0.94	(0.89, 0.99)	0.03			
Religious vs. not	0.59	(0.14, 2.55)	0.48			
Spiritual vs. not	0.37	(0.08,1.61)	0.18			

[*] Variables with p-values <0.20 were evaluated in the stepwise regression model.

Abbreviations: HADS=Hospital Anxiety and Depression Scale (higher scores indicate more symptoms); CARES= Cancer Rehabilitation Evaluation System-Short Form (higher scores indicate more symptoms); MOS=Medical Outcomes Study Social Support Survey (higher scores indicate more social support).