ASSESMENT OF DISTRESS AMONG BREAST CANCER SURVIVORS FOLLOWING PRIMARY TREATMENT COMPLETION

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ABSTRACT

PURPOSE

To evaluate the presence of distress among breast cancer survivors and to investigate demographic, psychosocial, tumor and treatment related variables that may be associated with distress in this patient population. Although elevated levels of distress have been well documented among cancer patients receiving active treatment, the magnitude of and contributors to distress in cancer survivors have not been well established.

METHODS

This investigation is based on a retrospective chart review that includes 81 female breast cancer survivors, 21 years of age or older, who received care at the Stony Brook Cancer Center Survivorship Clinic and completed the National Comprehensive Cancer Network (NCCN) Distress Thermometer (DT) form between October 2012 and June 2014.

RESULTS

One-half of the breast cancer survivors reported a clinically significant distress level (4 or higher). Physical and emotional concerns were the most commonly reported problems among the sample of breast cancer survivors. Those who were on an anxiolytic or anti-depressant medication tended to have higher levels of distress (OR: 3.10; 95% CI: 0.90-10.74; P=0.07) and age greater than 60 years at the time of diagnosis was negatively correlated with distress (OR: 0.24; 95% CI: 0.07-0.84; P=0.03).

CONCLUSIONS

Findings from this study indicate that more than half of breast cancer survivors experienced

distress during the early survivorship phase. This distress was attributable to emotional and physical problems. Although preliminary, these data suggest the need to develop targeted screening strategies for early recognition and interventions to alleviate distress in this population.

Keywords—Distress Thermometer; Breast Cancer; Survivorship; Distress Screening; National Comprehensive Cancer Network

INTRODUCTION

Distress is well described among cancer patients, regardless of cancer type. The National Comprehensive Cancer Network (NCCN) defines distress as "a multifactorial unpleasant experience of a psychological (i.e., cognitive, behavioral, emotional), social, and/or spiritual nature that may interfere with the ability to cope effectively with cancer, its physical symptoms, and its treatment. Distress extends along a continuum, ranging from common normal feelings of vulnerability, sadness and fears, to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis" (National Comprehensive Cancer Network 2015). The Distress Thermometer (DT), a tool to evaluate the presence of and contributors to distress among cancer patients, was developed by the NCCN in response to the growing evidence that highlights the significant role that distress plays among cancer patients. It is recommended that this instrument be included at every cancer patient clinical encounter. As a result, there is more evidence about the prevalence and factors associated with distress during the treatment phase of cancer care. The data are limited, however, regarding the level of, and contributors to, distress during survivorship after primary treatment is completed.

There are approximately 3.1 million female breast cancer survivors (BCS) according to the American Cancer Society as of June 2014 (ACS 2014). Death from breast cancer has been declining over the past few decades, in part due to improvements in cancer treatment. These include various combinations of surgery, radiotherapy and systemic therapy (including chemotherapy and hormonal treatment). It is often assumed that once breast cancer treatment concludes, patients will return to their "pre-cancer" lifestyle. However, during the post-treatment period breast cancer survivors may experience not only long-term treatment-related physical problems, but also social and emotional problems including fear of recurrence, anxiety, depression, social isolation and altered relationships with family and friends (Ploos van Amstel et al. 2013, Costanzo et al. 2007, Garofalo et al. 2009, Stanton 2012). Limited evidence has shown that survivors experience clusters of symptoms after treatment completion including various combinations of fatigue, anxiety, depression, pain, sleep disturbances, and cognitive dysfunction (Brant et al. 2011, Berger et al. 2012). One population based study showed that one in four survivors with heterogeneous cancer types had high symptom burden one year after cancer diagnosis, even when free from cancer treatment (Shi et al. 2011). A patient's experience of distress can have a negative impact on the patient's and caregivers' quality of life (QOL) and success of recovery after treatment (Ploos van Amstel et al. 2013, Wu and Harden 2015).

Although many studies have documented distress in breast cancer patients during time of initial diagnosis and treatment, few have evaluated prevalence of distress in breast cancer survivors post-treatment (Ploos van Amstel et al. 2013). The purpose of this investigation is to assess distress prevalence in breast cancer survivors after completion of primary treatment and to identify demographic, psychosocial, tumor and treatment related variables that may be associated with distress in this patient population.

The findings may assist in the development of strategies to address contributors to distress and improve health outcomes of breast cancer survivors in the future.

1. METHODS AND MATERIALS

1.1. STUDY DESIGN

A retrospective chart review was conducted to identify female breast cancer survivors attending the Stony Brook Cancer Center Survivorship Clinic between October 2012 and June 2014. Eligible patients were at least 21 years of age and had completed i) primary treatment for breast cancer with a curative intent and ii) the NCCN Distress Thermometer at their first survivorship care visit. Patients with incomplete treatment history were excluded. A total of 81 breast cancer survivors met the eligibility criteria and are included in the present investigation.

1.2. DATA COLLECTION

The Distress Thermometer is a modified visual analogue scale that resembles a thermometer recommended by NCCN for distress screening in cancer patients. This tool has an 11-point scale ranging from 0 (no distress) to 10 (extreme distress) with a cutoff score of greater than or equal to 4 indicating significant distress. This instrument also includes a problem checklist of 39 psychosocial stressors grouped into five categories (practical, family, emotional, spiritual/religious and physical) (Ploos van Amstel et al. 2013, Dabrowski et al. 2007). The Distress Thermometer has been shown to be comparable to other lengthier measures of psychosocial distress (Ma et al. 2014).

A nurse practitioner distributed the Distress Thermometer during the survivorship care visit following the completion of primary treatment. Although several participants had completed more than one assessment, only the first assessment completed was included in this analysis. Data was obtained from the patient's electronic medical record.

Variables abstracted for this study include age, marital status, living arrangements (whether the patient lived alone or not), race, parity, age of the youngest child, number of comorbidities, baseline history of depression or anxiety, use of anxiolytics or anti-depressants prior to being seen in the survivorship clinic, and family history of breast cancer. Tumor-related variables that were collected included stage, estrogen receptor (ER) expression, progesterone receptor (PR) expression, and human epidermal growth factor receptor 2 (HER2) status. Treatment-related variables included type of treatment in the form of surgery, radiotherapy, chemotherapy, hormonal therapy and HER2 directed therapy (whether or not the patient received Trastuzumab).

1.3 ETHICAL CONSIDERATIONS

The Stony Brook University Medical Center Institutional Review Board provided approval for this study.

1.4. STATISTICAL ANALYSIS

Descriptive statistics (numbers and percents) were used to describe the demographic, psychosocial, and tumor-related and treatment characteristics for the study sample, as well as those factors included in the Distress

Thermometer. A value of 4 or higher reported on the Distress Thermometer was used to define "clinically significant distress." Logistic regression models were used to evaluate the relationship between elevated distress and the factors outlined above. The regression results are presented as odds ratios (ORs) and 95% confidence intervals (CIs). Data were analyzed using SPSS version 21.

2. RESULTS

Characteristics of study participants

This investigation included 81 breast cancer survivors who attended a Survivorship Care visit at the Stony Brook Cancer Center and completed the Distress Thermometer during the study time period. The demographic and treatment variables for study participants are presented in Table 1. The mean (Standard Deviation/SD) age was 53.0 (8) years and the study sample was predominantly (85.0%) Caucasian. Seventy-six percent of the women were married, 9.0% lived alone and 87.0% were parous. Most patients had stage 1 (43.0%) or stage 2 (41.0%) breast cancer, and more than half (52.0%) received a regimen of combined treatment including surgery, chemotherapy and radiotherapy. Seventy-two percent received chemotherapy, 82.0% received hormonal treatment and only 16.0% were on Trastuzumab, which is a monoclonal antibody that interferes with HER2 receptor (Boekhout, Beijnen, and Schellens 2011). A total of 38.0% had a positive family history of breast cancer and 66.0% had one or more comorbidities. Twenty percent of these breast cancer survivors had baseline anxiety or depression, and 21.0% were either on an anxiolytic or anti-depressant**.** Seventy-three percent of breast cancer survivors were employed. The mean (SD) distress score among the sample of breast cancer survivors was 3.78 (3.02), and one-half reported a clinically significant distress level (4 or higher). The distribution of distress scores is presented in Figure 1.

Table 1 Demographic, Psychosocial, Tumor and Treatment variables of study participants

	N=81
Age: years, mean (SD)	53.0 (8.4)
Marital status	
Single	6.3%
Married	76.2%
Divorced	12.5%
Widowed	5.0%
Living alone or cohabiting	
Living alone	9.1%
Cohabiting	90.9%
Employment	
Student	1.6%

Paid work	72.6%
Housewife	4.8%
Disability insurance	1.6%
Retirement	16.1%
Unemployed	3.2%
Race	
Caucasian	84.8%
African American	7.6%
Hispanic	5.1%
Asian	2.5%
Children (Y/N)	
Yes	86.8%
No	13.2%
Age of youngest child (in years)	
0-10	17.9%
11-20	39.3%
21-30	25.0%
31-40	10.7%
41-50	7.1%
Family history of breast cancer	
Yes	38.0%
No	62.0%
Number of comorbidities	
0	33.0%
1-3	54.0%
>3	12.0%
History of anxiety or depression	
Yes	20.0%
No	80.0%
On anxiolytics or antidepressant	
Yes	21.1%
No	78.9%
Tumor stage	
0	3.7%
1	43.2%
2	40.7%
3	11.1%
4	1.2%
Estrogen receptor status	
Positive	79.0%
Negative	21.0%
Progesterone receptor status	
Positive	64.5%
Negative	35.5%

HER2 receptor status	
Positive	18.5%
Negative	81.5%
Treatment	
Surgery alone	8.6%
Surgery and Chemotherapy	18.5%
Surgery and Radiotherapy	21.0%
Surgery, Chemotherapy and Radiotherapy	51.9%
Chemotherapy given	
Yes	71.6%
No	28.4%
Hormonal therapy given	
Yes	81.5%
No	18.5%
Traztuzumab given	
Yes	16.0%
No	84.0%

FIGURE 1 DISTRIBUTION OF DISTRESS SCORES AMONG BREAST CANCER SURVIVORS

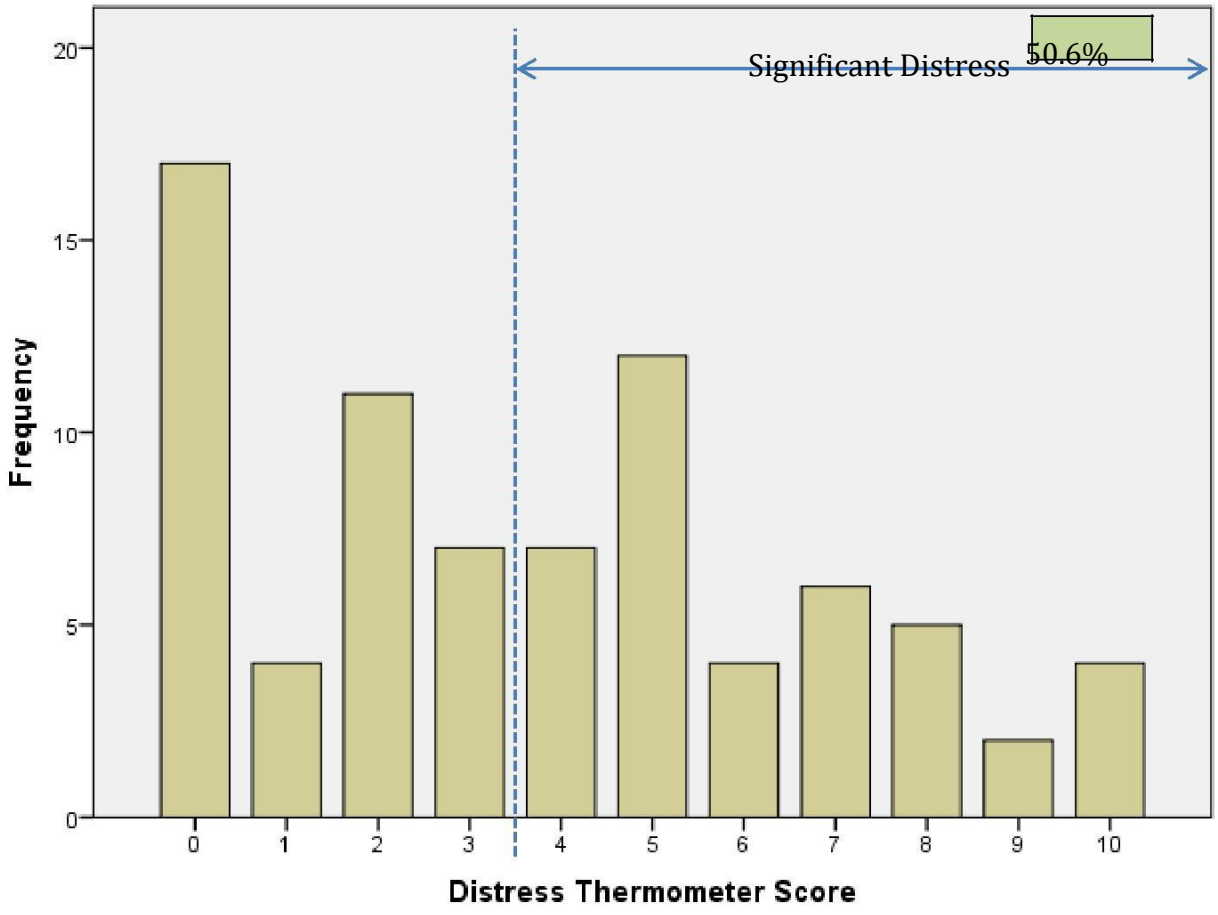


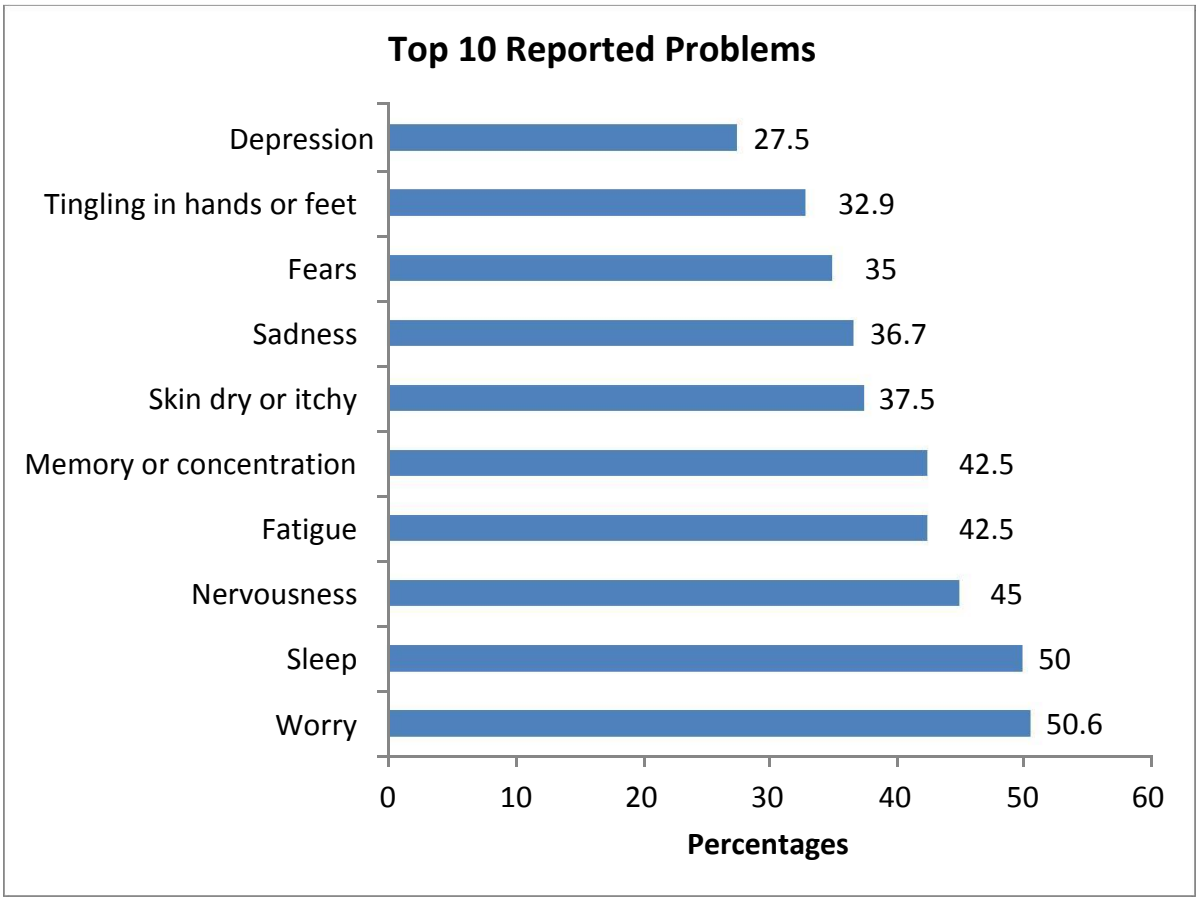
Table 2 lists all factors included in the Distress Thermometer and presents the distribution of "yes" responses for each factor as a contributor to an overall feeling of distress. Physical and emotional concerns were commonly reported among the sample of breast cancer survivors. The top ten reported problems as shown in Figure 2 include worry (51.0%), impaired sleep (50.0%), nervousness (45.0%), fatigue (43.0%), impaired memory or concentration (43.0%), dry skin (38.0%), sadness (37.0%), fears (35.0%), tingling in hands/feet (33.0%) and depression (28.0%).

Table 2 Distress Thermometer Breakdown

	Percentages
PRACTICAL PROBLEMS	
Child care	0.0%
Housing	6.3%
Insurance or financial	17.7%
Transport	2.5%
Work or school	5.0%
Treatment decisions	15.2%
FAMILY PROBLEMS	
Dealing with children	10.0%
Dealing with partner	16.3%
Ability to have children	1.3%
Family health issues	16.3%
EMOTIONAL PROBLEMS	
Depression	27.5%
Fears	35.0%
Nervousness	45.0%
Sadness	36.7%
Worry	50.6%
Loss of interest in usual activities	20.5%
SPIRITUAL OR RELIGIOUS CONCERNS	
Yes	2.6%
No	97.4%
PHYSICAL PROBLEMS	
Appearance	22.5%
Bathing or dressing	2.5%
Breathing	11.3%
Changes in urination	6.3%
Constipation	12.5%
Diarrhea	5.0%
Eating	7.5%
Fatigue	42.5%
Feeling swollen	16.3%
Fevers	0.0%

Getting around	5.1%
Indigestion	13.8%
Memory or concentration	42.5%
Mouth sores	5.0%
Nausea	6.3%
Nose dry or congested	18.8%
Pain	22.5%
Sexual	13.9%
Skin dry or itchy	37.5%
Sleep	50.0%
Tingling in hands or feet	32.9%
Substance abuse	0.0%

FIGURE 2 TOP TEN REPORTED PROBLEMS AMONG BREAST CANCER SURVIVORS



A comparison of Distress Thermometer components between survivors with high and low distress respectively is presented in Table 3. Breast cancer survivors with clinically significant distress reported more problems in the emotional domain components, whereas patients with low distress (less than 4) reported more problems on the physical domains. The most common problem reported was worry, which was approximately 3 times higher in the high distress group as compared to the low distress group: 75.0% versus 26.0%. Most commonly reported emotional problems among breast cancer survivors with clinically significant distress in addition to worry included nervousness (61.0%), sadness (58.0%), fears (51.0%), depression (46.0%) and loss of interest in usual activities (36.0%). Commonly reported physical problems included impaired memory/concentration, sleep, fatigue, appearance and pain.

Table 3 COMPARISON OF DISTRESS THERMOMETER COMPONENTS BETWEEN BREAST CANCER SURVIVORS WITH HIGH AND LOW DISTRESS SCORES

DT components	High distress (4 or greater)	Low distress (less than 4)
Emotional problems		
Worry	75.0%	26.0%
Nervousness	61.0%	28.0%
Sadness	58.0%	15.0%
Fears	51.0%	18.0%
Depression	46.0%	8.0%
Loss of interest in usual activities	36.0%	5.0%
Physical problems		
Memory/concentration	61.0%	23.0%
Sleep	60.0%	40.0%
Fatigue	59.0%	26.0%
Appearance	42.0%	3.0%
Tingling in hands/feet	40.0%	26.0%
Skin dry/itchy	39.0%	36.0%
Pain	34.0%	10.0%
Feeling swollen	24.0%	8.0%
Constipation	24.0%	0.0%
Nose dry/congested	20.0%	18.0%
Indigestion	20.0%	8.0%
Sexual	18.0%	10.0%
Breathing	17.0%	5.0%

Eating	15.0%	0.0%
Changes in urination	12.0%	0.0%
Getting around	7.5%	3.0%
Diarrhea	7.0%	3.0%
Mouth sores	7.0%	3.0%
Nausea	7.0%	5.0%
Bathing/dressing	5.0%	0.0%
Fevers	0.0%	0.0%
Substance abuse	0.0%	0.0%
Practical problems		
Treatment decision	30.0%	0.0%
Insurance/financial	25.0%	10.0%
Housing	12.0%	0.0%
Work/school	10.0%	0.0%
Transportation	5.0%	0.0%
Child care	0.0%	0.0%
Family problems		
Dealing with partner	29.0%	3.0%
Family health issues	29.0%	3.0%
Dealing with children	15.0%	5.0%
Ability to have children	2.0%	0.0%
Spiritual/religious concerns	5.0%	0.0%

Independent factors associated with clinically significant distress were identified using a multivariable linear regression analyses. Breast cancer survivors who were on an anxiolytic or anti-depressant tended to have higher levels of distress (OR: 3.10; 95% CI: 0.90-10.74; P=0.07) but this did not reach statistical significance. Multivariate regression analyses showed that age greater than 60 years was associated with less distress (P<0.05). However, breast cancer survivors who were on anxiolytics or anti-depressants and number of comorbidities did not correlate with distress levels as determined by multivariate regression analyses (P<0.07). No significant correlations were found between clinically significant distress and any other demographic, psychosocial, tumor or treatment related variables.

DISCUSSION

Significant distress was experienced in 50.6% of breast cancer survivors in this investigation. As the number of cancer

survivors continues to grow, psychological screening is critical for providing these survivors with appropriate psychosocial care. The NCCN has supported this initiative with recommendations for distress screening and early referrals to psychosocial services if needed. Guidelines recommend routinely screening all cancer patients for distress during various periods of their cancer course (Dabrowski et al. 2007, Boyes et al. 2013). In our study, we have used a score of 4 or greater to indicate clinically significant distress, which has been shown in various studies to be the optimal cutoff with maximum sensitivity and specificity for general psychosocial morbidity (Gil et al. 2005, Ma et al. 2014). However some studies have used a cutoff ≥5 and there is still a need to establish standard criteria for future evaluations.

In a cross-sectional study performed by Van Amstel et al. a lower percentage of breast cancer survivors reported clinically significant distress compared to our study: 36.0% versus 50.0%. This discrepancy may be due to a higher cutoff score of greater than 4 and use of other additional screening tools in addition to the Distress Thermometer. We noted that age greater than 60 years at the time of diagnosis was negatively correlated with distress (OR: 0.24; 95% CI: 0.07-0.84; P=0.03). This is similar to the results published by Costanzo et al. in which younger age predicted greater distress in breast cancer patients following treatment completion (Costanzo et al. 2007). Howard-Anderson et al., who found that quality of life (QOL) is reduced in younger breast cancer survivors due to greater psychological distress from a variety of issues such as change in employment status and fertility related concerns is similar to our findings (Howard-Anderson et al. 2012).

We further explored the relationship between clinically significant distress and various demographic, psychosocial, tumor and treatment related variables. Breast cancer survivors who were already on anxiolytics or anti-depressants tended to have higher levels of distress (P =0.07) but this finding did not achieve statistical significance likely due to a small sample size. This is similar to results published by Dabrowski et al who noted that underlying mental health disorders were associated with higher levels of distress detected using the NCCN Distress Thermometer (Dabrowski et al. 2007). No significant correlations were found between clinically significant distress and tumor stage, receptor status, treatment modality, family history, marital status, whether the patient lived alone or not, race and number of comorbidities. This is similar to findings reported by Roerink et al. in thyroid cancer survivors in whom no significant correlation was noted between Distress Thermometer scores and clinical or demographic characteristics except for employment status (Roerink et al. 2013). However, in their study a higher cutoff score (greater than or equal to 5) and additional distress screening tools were employed which may contribute to the difference in findings.

Breast cancer survivors with significant distress were more likely to report emotional problems, whereas patients with low levels of distress indicated that physical issues were of greater concern. The Institute of Medicine (IOM) report, “From cancer patient to cancer survivor: Lost in transition”, underscores shortfalls

in meeting the unique psychosocial and healthcare needs of cancer survivors (Hewitt et al. 2006). Many cancer survivors experience negative psychosocial effects from their disease along with feelings of abandonment as they transition from cancer patient to survivor. Improving cancer survivors' access to psychosocial care remains a significant concern (Holland and Reznik 2005). Efforts to improve psychosocial care for cancer survivors should begin by including screening for distress and should be integrated into routine patient care.

This study has several limitations. Inherent to the study design, the retrospective chart review did not enable monitoring of changes in distress levels over time and did not include a control group for comparative purposes. Additionally, the sample size was limited and was a predominantly Caucasian population with mostly early stage cancer survivors initiating from a single survivorship clinic, thereby limiting generalizability. Furthermore, the Distress Thermometer provides an overview of problems experienced by breast cancer survivors in the form of yes or no responses but is unable to discern severity of reported problems. Moreover, we were not able to differentiate whether if patients were on anxiolytics or anti-depressants prior to starting treatment or during treatment as this was a retrospective chart review and included patients who had received treatment elsewhere. Finally, survivors had a wide variation in time since treatment ranging from one to several years which could have attributed to differences in distress levels.

Mental health issues represent higher health and economic burdens among cancer survivors compared to those without a cancer history (Li et al. 2015). Additionally, survivors who were diagnosed one year earlier or more had significantly higher annual per capita mental health expenditures (Li et al. 2015). In studies published by Islam et al., socio-demographic, treatment-related and psychological factors, including elevated distress levels, were barriers for returning to work in breast cancer survivors, which can indirectly affect the economy (Islam et al. 2014). It is important to encourage dialogue between healthcare professionals and patients regarding distress, so that timely referrals for psychosocial counseling can be made (Holland and Reznik 2005). Strategies to address and prevent elevated distress levels will not only improve QOL for the individual breast cancer survivor, they may also reduce health care system expenditures. Results of our study indicate that clinically significant distress was present in a high percentage (>50.0%) of breast cancer survivors. These results support the use of Distress Thermometer by healthcare professionals to screen for distress in breast cancer survivors. Future prospective studies are needed to quantify distress severity over time and develop strategies to reduce the burden of such distress among cancer survivors.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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