How long does depression at cancer diagnosis affect a patient’s health?

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Abstract

PURPOSE OF THE STUDY: Many breast cancer patients report depressive symptoms at diagnosis. Although depressive symptoms improve, it is unknown whether women fully recover into the survivorship years, as previous studies have been cross-sectional or only short-term. RESEARCH METHOD: Breast cancer patients were accrued following surgery and prior to adjuvant therapy (baseline) and then followed for 5 years. Measures of psychological and physical functioning (both patient and nurse-rated) were used. Baseline CES-D scores (11-item version) were used to classify patients as clinically depressed (scores \( \geq 10; n = 45; \) DEP) or non-depressed (scores < 10; \( n = 182; \) NON-DEP). FINDINGS: Using mixed model analyses, trajectories of physical and psychological functioning over 5 years for the groups were compared. For physical functioning (KPS and signs/symptoms of illness/treatment), the DEP group had poorer outcomes from baseline through 12 months (\( ps < .01 \)). Over time, both groups gradually improved in physical functioning in a similar pattern (\( ps > .12 \)). The psychological trajectories--depressive symptoms (CES-D), stress (IES), and quality of life (SF-36 mental and physical components)--were of similar form. Across outcomes, the DEP group had poorer functioning at baseline (\( ps < .001 \)) and this difference was maintained through 24 months (\( ps < .05 \)). The groups were equivalent thereafter (\( ps > .39 \)). IMPLICATIONS: Significant depressive symptomatology at cancer diagnosis portends impaired functioning for years. For such individuals, physical symptoms remain

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significantly elevated through 12 months, and poorer quality of life and high levels of cancer-specific stress extend for another year. Only after 2 years do women depressed at diagnosis appear to attain a level of recovery similar to that of those not depressed at diagnosis. Thus, interventions are needed for patients vulnerable to slowed physical and psychological recovery from cancer.

Introduction

The human costs of cancer are overwhelming. The earliest of clinical studies described an ‘existential plight’ at diagnosis, characterized by bringing extreme shock, disbelief, and emotional turmoil (Weisman & Worden, 1976). Although negative events do not always produce stress, data from many studies document severe acute stress at cancer diagnosis and treatment (e.g., Andersen, Anderson, & deProsse, 1989; Maunsell, Brisson, & Deschenes, 1992; Stanton, Danoff-Burg, & Huggins, 2002). It is also clear that even after lengthy, difficult treatments have ended, individuals still report disruptions in major life areas and, for some, continuing problems with emotional distress (Carlson et al., 2004; Engel et al., 2003), role and social functioning (Kopp, Bauhofer, & Koller, 2004), fatigue (Anderson et al., 2003; Servaes, Verhagen, & Bleijenberg, 2002), pain (Dalton, Keefe, Carlson, & Youngblood, 2004), and sleep disturbance (Bower et al., 2000; Savard, Simard, Blanchet, Ivers, & Morin, 2001).

Cancer and comorbid Depression

The lifetime prevalence of any psychiatric disorder for those with a chronic medical condition is higher—42%—than is found for the general population (i.e., 33%; Wells, Golding, & Burnham, 1988). Mental health disorders among cancer patients are
prevalent, largely unrecognized, and in turn, untreated. In studies of the last 25 years, it is consistently estimated that 30-50% of cancer patients meet criteria for mood or anxiety disorders (Burgess et al., 2005; Derogatis & Melisaratos, 1983; Zabora, Brintzenhofssoc, Curbow, Hooker, & Piantadosi, 2001), with depression being the most common (Massie, 2004; van't Spiker, Trijsburg, & Duivenvoorden, 1997). Specifically, estimates for major depressive disorder (MDD) are 22 to 29% for patients with early stage disease (Raison & Miller, 2003), and range from 8 to 40% for patients with advanced disease (Hotopf, Chidgey, Addington-Hall, & Lan Ly, 2002), and increase further with recurrence (Burgess et al., 2005). Among common site for cancer among women, such as breast or gynecologic cancers, Zabora et al. (2001) found prevalence of 33% and 30%, respectively. Schairer et al. (2006) reported that breast cancer survivors may have an increased risk for suicide, even among those diagnosed as long as 25 years previously.

Finally, other morbidity comes with depression, such as comorbid anxiety (e.g. Dausch et al., 2004; Schwartz & Drotar, 2006), poorer quality of life (e.g. Deshields, Tibbs, Fan, & Taylor, 2006; Peters & Sellick, 2006; Yen et al., 2006), fatigue (e.g. Sadler et al., 2002; Smith, Gomm, & Dickens, 2003), and more distress from physical symptoms (e.g. Mystakidou et al., 2005).

Unfortunately, cancer patients with comorbid depression are not readily identified. For example, among 112 women with major depression undergoing cancer treatment, Ell and colleagues (2005) found that few were being treated: only 12% were receiving antidepressants and only 5% receiving psychological therapy. Excepting the most obvious symptoms (e.g., suicidal ideation, Oquendo et al., 2004), indications of psychopathology may not be familiar to oncology professionals, there may be insufficient
time for analysis during medical appointments, symptoms may be trivialized as a ‘normal’ reaction, or, even when recognized they may seen as due only to impaired physical status (Evans et al., 2005). Indeed, studies show that oncologists and nurses detect depressive symptoms in only a third of the patients who have them, and, further, underestimate symptom severity (Keller et al., 2000; McDonald et al., 1999; Newell, Sanson-Fisher, Girgis, & Bonaventura, 1998). Even when treated with antidepressant medication, patients may not receive an adequate dose (Ashbury et al., 2003; Sharpe et al., 2004).

Little is known about how those with elevated depressive symptoms during the diagnostic or treatment period fare with follow up. Data come only from cross-sectional (e.g. Golden-Kreutz & Andersen, 2004) or short-term follow-up studies (Akechi et al., 2006; Kurtz, Kurtz, Stommel, Given, & Given, 2002). One study compared rates of depressive symptoms in cancer survivors to similar-aged individual without cancer and found no differences between groups at 8 years after diagnosis (Schroevers, Ranchor, & Sanderman, 2006). However, a meta-analysis suggests that depression does not decline (van't Spiker et al., 1997).

**Method**

Data was used from ongoing follow up of patients from a randomized clinical trial (Andersen et al., 2004) to examine the stability of depressive symptomatology and concurrent life disruption. Newly diagnosed breast cancer patients \((N = 227)\) with regional disease were accrued after diagnosis but prior to adjuvant therapy, assessed at that time (baseline), and then followed for 5 years. The sample was primarily Caucasian.
middle aged ($M = 51, SD = 11$ years), married or partnered (74%), with some college ($M = 14$ years of education, $SD = 3$), and above average income (median = $51,000). The majority of individuals was diagnosed with Stage II disease (90%), had a mastectomy (57%) versus lumpectomy (43%), was pre-menopausal (54%), and had positive nodal status (68%). Assessments included measures of psychological and physical functioning. Women ($n = 45$; DEP) meeting the clinically significant cutoff for elevated depressive symptoms [scores $\geq 10$ on the 11-item Center for Epidemiological Studies Depression Scale (CES-D)] at baseline were compared to the remaining patients scoring $<10$ ($n = 182$; NON-DEP).

Mixed-effects modeling was used to compare the two groups. This analysis is advantageous for analyzing longitudinal data as it accounts for correlations among repeated assessments within an individual and allows the number of repeated assessments to vary across individuals. Using this framework, fixed-effects were estimated to test for average group differences in baseline and changes over time. Six fixed effects were tested: Intercept, Linear Slope, Quadratic Change, and Group differences in Intercept, Slope, and Quadratic Change. The form of change, linear versus quadratic, was determined by comparison of relative fit of models using a likelihood ratio test. If the fit of the quadratic model was not significantly better ($\alpha = .05$), the linear model was retained. No sociodemographic (i.e. age, education level, marital status, race, income, and intervention arm), disease (i.e. stage and nodal status), or treatment (i.e. lumpectomy vs. mastectomy, chemotherapy, radiation, and hormone therapy) variables were found to differ between the groups in the preliminary analyses; therefore, none were included in the multilevel models. Time was coded in months.
The follow-up trajectory of psychological and physical functioning of those women who reported elevated depressive symptoms at breast cancer diagnosis was compared with the trajectory of those without symptoms at diagnosis. Preliminary analyses revealed that, across groups, psychological and physical functioning improved primarily within the first 24 months after diagnosis. Based on this general pattern, one model was estimated for each outcome, describing the period of chemotherapy and the year thereafter (pre-chemotherapy baseline, 4, 8, 12, 18, and 24-month assessments). Figures provide graphical representation of the predicted trajectories from the mixed model analyses. A linear model was used for health status and a quadratic model for all others.

**Results**

*Depressive Symptoms*

Depressive symptoms were measured with the CES-D. As expected, the score for the DEP group was significantly higher (“worse”) at baseline, with a mean score of 11.6 as compared to the NON-DEP group, whose average was 4.7, or more than half of the DEP group (see Figure 2). A significant quadratic change over time was observed for the DEP group ($p < .001$). This indicates that, for the DEP group, depressive symptoms declined below the clinical cutoff of 10, plateaued, and increased with a nadir (the lowest point) seen around 18 months ($p < .001$) at a score of 7.1. In contrast, the NON-DEP group showed little change over time (Difference in Group X Quadratic Time, $p = .002$), with their average at 4 for the two year period. Follow-up ANOVAs reveal significant group differences at each time point.
Figure 2. Depressive Symptoms from baseline to 24 months post-diagnosis, categorized by group.

Cancer-specific stress was measured with the Impact of Events Scale (IES; Horowitz, Wilner, & Alvarez, 1979). Total scores range from 0 to 75 and scores above 19 reflect clinically relevant levels of traumatic stress (Horowitz, 1982). The result of the mixed model analysis was similar to the results for depressive symptoms (see Figure 3). Both groups scored above the cutoff, but the DEP group scored significantly higher (“worse”) at baseline, with a mean predicted score of 37, as compared to the NON-DEP group, with a mean predicted score of 22 ($p < .001$). A significant quadratic change was observed for the DEP group ($p < .001$) but the pattern of change did not differ by group ($p = .083$). For both the DEP and NON-DEP group, stress declined, plateaued, and increased with a nadir seen at 18 months. Follow-up ANOVAs revealed significant
group differences at each time point. Notably, the DEP group remained above the clinically significant cut-off of 19 throughout the 2 year follow-up.

**Figure 3.** Cancer-specific stress from baseline to 24 months post-diagnosis, categorized by group.

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**Quality of Life: Mental and Physical Health**

Quality of life was assessed using the mental and physical component summary of the Medical Outcomes Study SF-36 [MCS and PCS respectively; (Ware, Kosinski, & Keller, 1994)]. Higher scores on the SF-36 indicate better, and not worse, functioning. In the model, the score for the DEP group was significantly lower (“worse”) at baseline ($p < .001$), with an average score 2 standard deviations (or 20 points) lower than the population mean of 50 (Ware et al., 1994), as compared to the NON-DEP group, whose scored was approximately 0.5 SD lower than the population mean. A significant quadratic change was observed for the DEP group ($p < .001$) and the pattern of change differed by group ($p < .001$). For the DEP group, mental health quality of life improved,
plateaued, and decreased somewhat with a nadir seen around 18 months \( (p < .001) \). In contrast, the NON-DEP group showed less change over time \( (p < .001) \) and remained in the range of 50. Follow-up ANOVAs revealed significant group differences at each time point.

**Figure 4.** Mental health quality of life from baseline to 24 months post-diagnosis, categorized by group.

Results for physical health quality of life are somewhat different. There were no significant differences for the baseline PCS \( (p = .319) \). Both groups scored approximately one standard deviation (or 10 points) below the population mean of 50. The DEP group showed no statistically significant improvement over time \( (p = .373; \) see Figure 5). However, the NON-DEP group life improved, plateaued, and decreased somewhat with a nadir seen around 18 months \( (p = .029) \). Follow-up ANOVAs reveal group differences at each time point. In summary, although both groups had poor
physical health quality of life at baseline, the NON-DEP group exhibited faster recovery, with scores approaching the population mean.

Figure 5. Physical health quality of life from baseline to 24 months post-diagnosis, categorized by group.

Physical Functioning

Physical functioning included two measures. The Karnofsky Performance Status Scale (KPS; Karnofsky & Burchenal, 1949) measures performance status. Higher scores indicate better functional status (e.g., 90 = Able to carry on normal activity, minor signs/symptoms of disease; 80 = Normal activity with effort, some signs/symptoms of disease). In these analyses, a linear model was used. The DEP group reported worse functioning at baseline, with an average predicted score of 81 as compared to the NON-DEP group, whose mean predicted score was 86 ($p < .001$; see Figure 6). By the 24-month assessment, both groups had reached a mean predicted score of 90. A significant linear change was observed for the DEP group ($p < .001$) and the pattern of change
differed by group ($p < .001$). The NON-DEP group showed less change over time ($p < .01$). Follow-up ANOVAs reveal group differences up to the 12-month assessment.

**Figure 6. Health status from baseline to 24 months post-diagnosis, categorized by group.**

The second measure of physical functioning rates signs and symptoms of toxicities related to cancer treatments (SWOG; Moinpour et al., 1989). Higher scores indicate poorer functioning. In these analyses, a linear model was used. The DEP group reported worse functioning at baseline as compared to the NON-DEP group ($p < .01$; see Figure 7). There were no significant differences in time or its interaction with group ($ps > .3$). Follow-up ANOVAs reveal group differences up to the 12-month assessment. Thus, physical functioning was worse in the DEP group and this difference appeared to be maintained throughout the first year after cancer diagnosis.

**Figure 7. Signs/symptoms of treatment toxicities from baseline to 24 months post-diagnosis, categorized by group.**
Discussion

Psychological stress is a near-universal experience after a cancer diagnosis. For some, stress can develop into a depressive disorder. If untreated, depression can negatively impact quality of life, treatment adherence, physical health status, and even disease outcome. Our data indicate that women with elevated depressive symptoms at breast cancer diagnosis continued to report difficulties in psychological and physical functioning for the next two years. The DEP group had more cancer-specific traumatic stress and poorer mental health quality of life at baseline. The rates of improvement for psychological functioning within the groups differed as well. While the DEP group improved at a significantly faster rate, it was unable to reach the same level of recovery as the NON-DEP group. Regarding physical health quality of life, the NON-DEP group improved over time, while the DEP group did not.

Differences in physical functioning were found between the two groups in the
first year after diagnosis. It is interesting to note that although the two groups had similar physical functioning after the first 12 months, the DEP group continued to report worse psychological functioning and poorer quality of life for an additional year.

The mechanisms of the development/maintenance of depression in cancer patients are not well understood. For example, those fatigued from cancer treatments may withdraw from pleasurable activities, which promotes the occurrence/maintenance of depression (Jacobson et al., 1996). It is also plausible that those with a history of depression generate may generate more stress when facing a current negative event, which in turn makes them more susceptible to a recurrence of a depressive episode (Hammen). In addition, biological pathways, such as inflammation, may contribute to the development of depression. Such an immune response could be triggered by stress, disease processes, and/or cancer treatment.

Psychological interventions for cancer patients can reduce stress and improve quality of life (Andersen et al., 2004). A meta-analysis of psychooncological interventions suggested that they are more effective for alleviating anxiety than they are for depression (Meyer & Mark, 1995). Thus, interventions designed specifically for depressed cancer patients may be needed. Also, our data support the identification and treatment of individuals suffering from high levels of psychological distress at cancer diagnosis. Additionally, populations with risk factors associated with high psychological distress, such as those who do not have a romantic partner, are of low socioeconomic status, or are younger, should also be targeted for intervention (Spijker, Trijsburg, & Duivenvoorden, 1997). Thus, interventions are needed for patients vulnerable to slowed physical and psychological recovery from cancer.
References


