

Longer Life Foundation Final Report History of Mental Health Treatment and Survival Among Newly Diagnosed Women with Breast Cancer Principal Investigator: Mark Walker, Ph.D.

Abstract

Research has shown an association between psychological status and survival in some cancers. This study examined current distress, history of mental health problems (MHP), and history of mental health treatment (MHT) as predictors of overall survival among newly diagnosed patients with breast cancer.

Methods: Eligible patients (N=302) were women, 18 and older, recently diagnosed with stage 0 – IV breast cancer, and had completed psychosocial surveys between May 2000 and October 2003. The survey included self-reported history of MHP and MHT. Survey data were linked with death records from the state departments of health, and with data abstracted from the outpatient medical record. Planned methods included Cox regression models of overall survival among patients with and without MHP and MHT. Models of MHP and MHT were constructed separately. Covariates in each model included stage of disease, comorbidities, treatment adherence, health behaviors, and a composite measure of general distress.

Results: Patients were 73.5% Caucasian, with mean age of 53.5 years (SD=11.9), and 84.7% had stage II or earlier disease. Thirty-four patients (11.3%) had died by early 2007. Overall, 20.2% of patients reported a history of MHP, and 24.8% reported a history of MHT. Results for models of MHP and MHT showed that longer survival was associated with higher education, less comorbid disease, earlier stage of disease, and less distress at diagnosis. MHP and MHT both showed patterns in which patients with a positive history showed longer survival. The effect was nonsignificant for MHP, but significant for MHT ($p=.016$). Subsequent evaluation showed that the number of predictors used in the models was inappropriate for the number of observed events (deaths). Because the primary aims require covariates for control of relevant patient characteristics, revised statistical modeling cannot easily address this limitation. Results should be interpreted with caution.

Conclusions: Findings support a link between either mental health treatment or treatment seeking, and breast cancer survival, and are at odds with some existing research. However, findings are subject to important methodological limitations.

Lay Summary

Research has shown that for some types of cancer, patients who are more psychologically distressed tend not to survive as long. However, little research has been done that examines whether mental health history might be related to survival. This study examined two characteristics of mental health history as predictors of survival among newly diagnosed patients with breast cancer. The two characteristics are history of mental health problems, and history of mental health treatment. Eligible patients included 302 women, 18 and older, who were recently diagnosed with stage 0 – IV breast cancer. All of the patients had completed surveys related to emotional distress and mental health history at the time of their diagnosis. Surveys were completed between May 2000 and October 2003. The survey information was linked with death records from the state departments of health, and with other information drawn from each patient's medical record. The analysis took several other variables into

account, including stage of disease, other medical conditions, whether patients followed their doctor's treatment recommendations, and the patients level of emotional distress at the time of diagnosis.

Results showed that 73.5% of patients were Caucasian, and that patients were an average of 53.5 years of age. Most (84.7%) had stage II or earlier disease. Of the 302 patients, 34 (11.3%) had died by the time of the analysis. Approximately 1 in 4 patients reported a history of mental health problems, and 1 in 5 reported a history of mental health treatment. The analysis showed that patients tended to live longer if they had more education, fewer medical problems of other kinds, earlier stage disease, and if they were less distressed at diagnosis. All of these findings were expected. However, the results also showed that patients who reported having had mental health problems and mental health treatment were likely to live longer. These findings were not expected. The effect of mental health treatment was stronger than the effect of mental health problems, and did not appear likely to be just a chance finding. However, careful outside review of the methods concluded that the research tried to draw too many conclusions with too few patients. Because of this, the findings should be viewed as interesting but not conclusive in any way. They should not lead to any strong conclusions about the importance of mental health history. They should instead suggest possible avenues for research in the future.

Introduction

A large body of research has investigated psychological functioning in patients with cancer. Much of this concerns the emotional impact of cancer¹⁻⁴, or the role of emotional distress during/after cancer treatment^{5,6}. However, at least one study has examined the impact of a history of emotional problems at the time of diagnosis, and found that a history of depression was associated with shorter survival⁷.

There are several plausible processes by which current or past psychological problems could influence survival. First, patients with a history of mental health problems (MHP) might delay seeking medical treatment after onset of symptoms⁸. Second, patients with a history of MHP may be more likely to engage in unhealthy behavior, which might in turn affect survival⁹⁻¹². Third, patients experiencing emotional distress or those with a history of MHP may be less likely to adhere to recommended treatment^{3,13}, which might lead to a poorer outcome¹⁴⁻¹⁸. Fourth, emotional distress during and after cancer treatment might influence survival through a psychoneuroimmunological (PNI) pathway that affects response to treatment or course of disease¹⁹⁻²². If previous MHP is associated with distress during and after diagnosis, then history of MHP might be associated with survival.

If psychological functioning influences survival through one or more of these paths, then interventions that reduce distress or enhance psychological functioning might also improve survival. In fact, most studies that have investigated interventions to enhance psychological functioning among cancer patients have failed to show an effect on survival^{6,23-26}. Groenvold and colleagues theorize that the association of emotional distress and cancer survival is attributable to a shared common cause—an underlying robustness that reduces psychological distress and enhances resistance to breast cancer²⁷. This robustness model would account for the prognostic significance of emotional distress and quality of life, but also the nonsignificant effect of psychosocial interventions in previous research.

The current study sought to explore further these issues by examining current distress at diagnosis, and self-reported history of MHP and history of mental health treatment (MHT) among newly diagnosed patients with breast cancer. We hypothesized that current distress, a history of MHP, and a history of MHT would be associated with shorter survival.

Methods

Setting and Participants: Participants for this study were adult women (18 years and older), who were seen in the Breast Health Center in the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine between May 2000 and October 2003. Inclusion was limited to patients who underwent a routine psychosocial evaluation as part of their outpatient visit, had not previously been seen through the Breast Health Center, and had not yet had treatment other than biopsy. The sample was also limited to Missouri and Illinois residents, the primary states served by the Siteman Cancer Center.

Procedure: Data collection for this study involved the abstraction and collection of data from four existing data sources, and the linking of databases. The primary data source was a psychosocial survey database developed as part of routine clinical care in the Breast Health Center at Siteman Cancer Center. The database included records from self-reported survey measures of psychosocial functioning and mental health history administered during the first 1 - 4 weeks after the diagnosis of breast cancer. This database was linked by social security number with three data sources: 1) vital records obtained from the Missouri Department of Health and Senior Services and Illinois Department of Health; 2) summary psychosocial data abstracted from psychosocial evaluation reports of each patient who completed the psychosocial survey; and 3) medical and adherence data abstracted from the outpatient medical record. This study was conducted following Washington University School of Medicine's guidelines for ethical conduct of research involving human subjects. All study procedures were approved by the Institutional Review Boards at Washington University School of Medicine and Siteman Cancer Center.

Study Measures: The primary outcome for this study was overall survival. Vital records were obtained through the Missouri Department of Health and Senior Services and the Illinois Department of Public Health. Vital records searches were conducted separately for each state, with different possible latencies for appearance of death records in each database. Cases for which no record of death was found (the vast majority) were considered censored on the latest observed date of death in each state.

Individual demographic characteristics collected from the medical record included age and race/ethnicity (Caucasian vs. Minority). Disease and treatment related variables included date of diagnosis, stage of disease, comorbid medical conditions, and adherence to recommended adjuvant/neoadjuvant chemotherapy and radiation treatment. Stage of disease was coded as Stage 0 to Stage 4. The burden of comorbid medical conditions was graded using the Katz adaptation of the Charlson Index^{28,29}. Treatment adherence was computed as the proportion of planned chemotherapy and radiation therapy treatments that were delivered during the first year after diagnosis.

The psychosocial survey collected from breast cancer patients as part of routine care following diagnosis at Siteman Cancer Center included the Center for Epidemiological Studies—Depression scale (CESD)³⁰, the state section of the State-Trait Anxiety Inventory (STAI-s)³¹, and the Functional Assessment of Cancer Therapy-General measure (FACT-G)³². A

composite of the CESD, STAI-s, and Emotional Well Being subscale of the FACT-G was used as a measure of general distress in this study³³.

Patient self-reported history of MHP was assessed with the single item: “Have you ever had problems with nerves, tension, depression, or other emotional problems?” Responses on the 5-point response scale were dichotomized with “infrequently” or “never,” representing a negative history, and “often”, “very frequently”, or “all the time,” coded as a positive history. Patient self-reported history of MHT was assessed with the yes-no item: “Have you ever consulted with a professional person about problems with nerves, tension, depression, or other emotional problems.” Items not answered were coded as indicating a negative history. Several items were abstracted from the psychosocial evaluation report that was completed as a routine part of the patient’s outpatient evaluation at diagnosis. These included marital status (married vs. not or unknown), educational level (≤ 12 years vs. some college), number of sources of social support (0 -1, > 1, unknown), and several health behaviors.

Resource limitations made it impossible to abstract the medical records of all patients on whom we had psychosocial survey results. To address this limitation, we randomly ordered patients in the database, and abstracted the records of as many as possible following the random order. This assured that disease stage, comorbidity, and adherence data would be missing completely at random. To address the missing predictor information statistically, we modeled these variables with use of “plugged” means and missingness indicators³⁴, which allowed all cases to be included in the analyses.

Statistical Methods: Descriptive statistics were calculated for all study variables. T-tests and chi-square tests of independence were used to examine the association of mental health history variables with other individual characteristics. Cox proportional hazard regression was used to predict overall survival after diagnosis. Because history of MHP and history of MHT were moderately correlated, separate models were examined for each. Within each model, demographic characteristics, disease stage, health behaviors, social support, adherence, comorbidity burden, and general distress were planned as possible covariates. The significance of each covariate was assessed with the standard likelihood ratio tests between nested models, and the proportional hazard assumption was examined for each variable in the models³⁵.

Results

Three hundred two patients completed psychosocial assessments as part of multidisciplinary treatment planning during the study period, had not been seen previously at the clinic, and represent the final study sample. Abstraction of medical records was completed for a random subsample of 145 patients. Ages ranged from 26 to 90 (mean age = 53.5 years) and the majority were Caucasian (74%), married (58%), and had early stage disease (85%). Of patients for whom there was a record of treatment (132 of the random subsample of 145), 64.4% received radiation therapy, 58.3% received chemotherapy, and 41.7% received both. Vital records showed that 34 of the 302 patients (11.3%) had died during the follow-up period. Breast cancer was a primary or contributing cause of death for 21 patients.

History of MHP	History of MHT			Total N (%)
	No	Yes	Not reported	
Never to Infrequently	160	40	14	214 (70.9%)
Often to All the time	17	30	14	61 (20.2%)
Not reported	10	5	12	27 (8.9%)
Total N (%)	187 (61.9%)	75 (24.8%)	40 (13.2%)	302

Overall, 20.2% of patients reported a positive history of MHP. A slightly larger proportion, 24.8%, reported having received MHT. Surprisingly, there was only moderate correspondence between these groups, with 9.9% of the sample (30 of 302) reporting a history of problems and of treatment, and just over half (53%) reporting neither (see Table 1).

Educational level, alcohol use, tobacco use, and social support were unrelated to history of MHP. Unmarried patients were more likely than married patients to report a history of MHP, $\chi^2(1, N = 302) = 5.582, p = .018$, but no more likely to report a history of MHT. Caucasians were more likely than minorities to report a history of MHP, $\chi^2(1, N = 302) = 7.137, p = .007$ and of MHT, $\chi^2(1, N = 302) = 7.510, p = .006$.

Mental health history (MHP and MHT) was unrelated to treatment adherence and unrelated to the Charlson Index of Comorbidity. However, positive history of MHP was associated with earlier stage of disease at diagnosis, $t(300) = 2.531, p = .012$, (stage = 1.54 vs. 1.76 for patients with and without a history of MHP). Likewise, positive history of MHT was associated with earlier stage, $t(300) = 2.187, p = .03$, (stage = 1.59 vs. 1.76 for patients with and without a treatment history).

Cox regression analysis showed that history of MHP did not significantly predict survival ($p = .229$). Greater likelihood of survival in the sample was associated with higher education ($p = .004$), lower comorbidity index ($p = .001$), lower stage of disease ($p = .003$) and less current distress at the time of diagnosis ($p = .001$), each variable controlling for the others. Age, marital status, sources of social support, and health behaviors were nonsignificant for inclusion in the model. Adherence to recommended treatment was also nonsignificant. Although history of MHP was not significant, the direction of the observed effect was unexpected, with patients positive on mental health history nominally more likely to survive ($HR = .53$).

Cox regression analysis showed that history of MHT was significant in predicting survival, with previous receipt of treatment associated with greater likelihood of survival ($p = .016$; see Figure 1). Covariates that were significant in the previous model were significant here (see Table 2). Minority race/ethnicity status also reached significance in this model, with minority status predicting a lower likelihood of survival ($p = .049$). Other variables examined were nonsignificant for inclusion in the model.

We also examined whether mental health history (either MHP or MHT) interacted with current distress in predicting survival. Findings were nonsignificant. We had also theorized that an effect of history of MHP might be mediated by current distress.

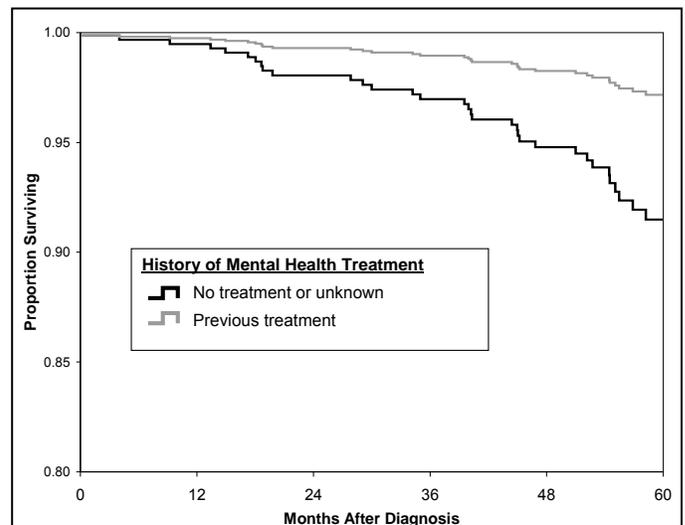


Figure 1. Survival, by History of Mental Health Treatment

Table 2. Cox Regression Model of Survival by History of MHT.			
Variables	HR	p	95% CI
Race = minority (vs Cauc)	2.06	.049	(1.02 - 4.15)
Educ <= 12 yrs (vs. some college)	0.34	.005	(0.15 - 0.77)
Charlson comorbidity index	3.05	<.001	(1.9 - 4.89)
Stage of disease	2.36	.005	(1.33 - 4.21)
Current distress	1.78	.001	(1.28 - 2.49)
History of MHT	3.22	.016	(1.09 - 9.09)

Note. All effects are adjusted for other variables in the model.

However, the effect of history of MHP was itself nonsignificant, whether adjusted or unadjusted, so a mediation model was not supported.

External Review: External review of the findings from this study identified methodological issues that limit the conclusions that should be drawn. The primary issue is the number of events that were observed relative to the number of covariates that were included in analysis. When too many covariates are included, overfitting results, and findings cannot be trusted. In a binary logistic regression, the number of events is the frequency of cases in the smaller of the two dependent variable categories. In a survival analysis, it is the number of terminal events. The investigators were aware of this methodological issue with respect to logistic regression, which was described in earlier literature³⁶, but were not aware of its application to survival analysis methods, which were reported more recently³⁷. Two possible approaches to addressing the limitation in the current study would involve drastically reducing the complexity of the model, and reanalyzing the data after the number of events had increased. The former approach has limitations, and if used, would preclude addressing the primary aims of the study. Given the relatively high rate of survival of breast cancer, the second approach is not practical.

Discussion

This study examined the association of mental health and behavioral issues with survival among patients with breast cancer. Overall survival in the sample was associated with being Caucasian, more highly educated, having less comorbid illness, less advanced stage of disease, and being less distressed at diagnosis. Survival was also associated with having received MHT, the opposite of the effect expected. It was not significantly related to self-reported history of MHP.

This effect of a positive history of MHT suggests that, whereas psychological distress may convey risk of reduced survival, treatment of mental health problems may have a beneficial effect. However, patients were self-selected for MHT—they were not assigned. It is possible, therefore, that differences exist between patients who seek MHT and those who do not, and that it is these differences that influence survival rather than treatment itself. This interpretation of the findings would be consistent with Groenvold et al.'s robustness hypothesis²⁷.

There were important limitations to this study, including that it was observational, that it did not examine the role of distress or of mental health care after diagnosis and treatment, and the important methodological limitation described under External Review, above. The observed effect of MHT on survival may in fact reflect statistical overfitting, but indicators of such overfitting are not apparent. Specifically, the effect of mental health history was a primary focus of the study rather than one 'discovered' during data mining. Also, the observed effect was present in univariate analysis, and was essentially unchanged when controlling for other significant covariates, including stage of disease, comorbidities, and current distress. Given these considerations, the finding that mental health treatment, or the propensity to seek treatment, may convey benefit, should be considered worthy of further study.

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