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Acquiescence to adjunctive experimental therapies may relate to psychological distress: pilot data from a bone marrow transplant center

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Summary:

Use of alternative therapy for breast cancer outside of the hospital setting has been identified as a marker of psychological distress. Whether acquiescence to experimental therapies within the medical setting might also be a sign of psychological distress is not well known. We therefore evaluated patients with breast cancer undergoing bone marrow transplantation (BMT), an experimental method for treatment, to determine if acquiescence to further adjunctive experimental therapy related to psychological distress. In order to do this, we studied psychological test results of 42 breast cancer patients undergoing BMT at the University of Florida between January and December 1997. These tests included the Medical Outcomes Short Form Health Survey, the Beck Depression Inventory, the State-Trait Anxiety Inventory and the Medical Coping Modes Questionnaire. Women who accepted adjunctive experimental therapy had significantly higher trait anxiety and poorer role functioning compared to women who did not (both $P < 0.001$). These findings suggest that psychological distress may be a factor in medical decision-making even within the medical setting and that prospective research in this area is warranted. *Bone Marrow Transplantation* (2000) **25**, 673–676.
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Several recent studies have shown that alternative medicine use is very high in the United States, particularly in patients who have cancer.[1–6] The reasons for which some people seek alternative therapy have been previously assumed to include failure of standard health treatment, to control choices, to maintain autonomy, and to use natural therapy. In a recent editorial, Holland summarized the typical image of the woman seeking alternative care as 'self-assertive, psychologically strong, and well adjusted'.[7]

However another reason for which patients may choose alternative therapy may be to calm psychosocial distress. Recently, Burstein and colleagues[1] showed that 28% of 480 newly diagnosed early-stage breast cancer patients undergoing surgery chose alternative medications in additional to standard therapy. Surprisingly, psychological testing in these women showed that those who used alternative therapy had a much higher incidence of depression, anxiety and physical symptoms and much lower overall life and sexual satisfaction than those who did not.

Whether psychological distress is also a factor in choosing experimental therapy in the hospital setting is not known. Yet the implications are immense in terms of detecting psychosocial distress in patients, offering appropriate mental health counseling, and in addressing the nationwide problem of low accruals to experimental trials. We therefore studied the psychological characteristics of women in our breast cancer population to determine if women who chose experimental therapies in a BMT setting may have high levels of psychological distress.

Methods

Patient population

All patients undergoing BMT for breast cancer during 1997 were considered for evaluation. Women were referred from their local oncologists for BMT. All met the criteria for BMT including chemosensitive stage IV disease, or stage II or III disease with involvement of multiple axillary lymph nodes.

Protocols

Psychological testing: All patients undergoing BMT at the University of Florida were offered psychological testing as a baseline measurement for further evaluation and management when needed. Testing was voluntary, and informed consent was obtained from all patients who agree to participate. The protocol for testing was approved by the University of Florida Institutional Review Board.

Health-related quality of life was assessed in two ways. First, the Medical Outcomes SF-36 Health Survey (SF-36) was used. This 36-item test assesses quality of life across eight domains: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health.[8] Higher scores represent a more satisfactory health status. Adequate test–retest reliability and internal consistency have been demonstrated.

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Second, physical and additional psychological symptoms were assessed using the Transplant Symptom Frequency Questionnaire (TSFQ), a measure designed for use in previous studies conducted in our center.[9] The TSFQ lists 32 symptoms common to transplant candidates and recipients, and asks the frequency that each is experienced. In addition, respondents indicate if symptoms are considered to be problematic, yielding both a frequency and problem total score.

Depressive symptomatology was measured by the Beck Depression Inventory (BDI), a 21-item measure that asks respondents to indicate their severity rating for both cognitive-affective and somatic symptoms of depression.[10] The State-Trait Anxiety Inventory (STAI) measured candidates' levels of anxiety.[11] The STAI is a 40-item measure that yields scores on both state (at the present time) and trait (in general) anxiety.

Experimental therapy protocols: All patients underwent high-dose chemotherapy (cyclophosphamide, thiotepa, carboplatinum) and autologous stem cell support (HDC-ASCT) as previously described.[12–14]

Patients were also offered one of three 'adjunctive' experimental protocols ongoing in our transplant unit. One of these was a prophylactic platelet transfusion study in which patients were randomized to receive prophylactic platelet transfusions when their platelet counts reached either 10 000/mm^3 or alternatively, 20 000/mm^3. Some were also offered a trial evaluating an experimental growth factor at varying doses to determine maximally tolerated doses of the growth factor. These were given as daily injections after stem cell infusion until neutrophil recovery occurred. Others were offered a randomized trial of a new growth factor compared to G-CSF prior to stem cell collection to determine efficacy of the factor in enhancing stem cell engraftment.

Written informed consent forms for each of the adjunctive experimental therapies were signed if the patient agreed to participate. All studies and consent forms were approved by the University of Florida Institutional Review Board.

Statistical analyses

Statistical Program for the Social Sciences (SPSS) for Windows was used to analyze the quantitative data. Independent sample *t* tests and chi square analyses were used to examine group differences on continuous and categorical variables, respectively. To control for family-wise error rates, the Bonferroni correction was used when examining group differences on psychological measures.

Results

The patients consisted of 42 women between the ages of 31 and 65 years. Ten women had stage II disease, 17 had stage III and 15 had stage IV disease. Women were studied together as a group and then separately into one of two groups: those who agreed to adjunctive experimental therapy and those who did not.

Table 1 Patient characteristics

	Agreed (n = 25)	*Did not agree (n = 17)*	*P value between groups*
Age	48.0 ± 7.5	46.4 ± 9.4	0.2
Race	22W, 2AA, 1H	16W, 1AA	—
Education (No. of years in school)	13.3 ± 2.1	12.7 ± 2.3	0.8
Miles from hospital	133.1 ± 80	108.9 ± 75	0.5
Other medications	1.2 ± 1.3	0.9 ± 0.9	0.03
Never married	1	1	0.5
Married	15	14	0.3
Widowed	2	1	0.5
Separated or divorced	7	1	0.5

W = white; AA = African American; H = Hispanic.

Of the 42 patients, 25 (60%) agreed to adjunctive experimental therapy and 17 (40%) declined. Age of patients ranged from 31 to 65 years, with mean 47.3 ± 8.3, and median 47 years (Table 1). When analyzed separately, women who agreed to clinical trials had a mean age of 48.1 ± 7.5 years, median 48, and women in the group who did not agree to such treatments had a mean age of 46.4 ± 9.4 years, median 47 ($P = 0.2$).

Patients smoked between 0 and 60 pack years in their entire lifetimes, with one patient alone who accounted for 60 pack years (Table 2). Mean pack years was 8 ± 14.5. In the women who accepted adjunctive therapy, mean pack years was 0 to 60 smoke pack years with mean 11.3 ± 16.8; and in the other women who declined was 0 to 32, mean 3.2 ± 8.4 pack years ($P = 0.5$). The heaviest smokers (those with 35, 40 and 60 pack years) all agreed to participate in the study and the mean values were higher in the group of women who agreed to participate compared to those who did not. These differences although striking were not statistically significant, because of the small number of study subjects and because of the variability of data.

Alcohol use was also higher in the group of women who accepted adjunctive trials. Overall, patients consumed between 0 and 140 ounces of alcohol per week; with mean 17.5 ± 35.6 ounces per week. Among women who accepted adjunctive trials, alcohol intake ranged from 0 to 140

Table 2 Behavioral characteristics of patients

	Agreed (n = 25)	*Did not agree (n = 17)*	*P value between groups*
Stressful events in prior year	2.8 ± 2.1	0.9 ± 1.0	0.003*
Currently smokes	6	0	0.08
Smoking (pack years)	11.2 ± 16.8	3.2 ± 8.4	0.5
Alcohol use in past 6 months (Y/N)	13	5	0.5
Amount alcohol in past 6 months	21.5 ± 40.3	11.6 ± 27.4	0.41
Illicit drug use	3	0	0.4

*$P < 0.05$.

ounces, with mean of 21.5 ± 40.3 ounces; and among the others range was between 0 and 84 with mean 11.6 ± 27.4 ounces per week ($P = 0.5$). As for smoking use, women who had the highest amount of alcohol consumption (140 and 84 ounces) were those who accepted the adjunctive trials. These differences between the groups were also not statistically significant because of the small number of study subjects and the variability of data.

Psychological testing revealed differences in the two groups of women in several ways (see Table 3). First, trait anxiety was significantly higher in the women who undertook adjunctive trials compared to those who did not. Trait anxiety, expressing baseline characteriological anxiety as opposed to situational anxiety, was expressed as score of 36.2 ± 10.6 in the women who agreed to further therapy and only 33.1 ± 4.9 in the other group ($P < 0.001$). Also, although physical functioning was similar in the two groups, role functioning was significantly more impaired in the women who agreed to further experimental therapy than in the other group (mean 13.1 ± 25.7 *vs* 33.4 ± 44.1, $P < 0.001$). Thus, although the women had similar physical abilities, their ability to do precisely what they had done in their specified roles as mother, daughter, wife, etc was perceived to be more impaired in those women who agreed to more therapy compared to the others. Finally, the number of stressful events in the prior year was significantly higher in the patients who accepted adjunctive experimental therapy compared to those who did not (2.8 ± 2.1 compared to 0.9 ± 1.0, $P = 0.003$) (see Table 2). All other measures of psychological functioning were similar between the two groups (see Table 3).

Discussion

This study supports the findings of others that decision-making may be based on psychological distress as well as rational thinking.[1,7,15–22] Indeed in our study, women who agreed to participate in the adjunctive studies were more likely to have high trait anxiety, to have experienced more stressful life events in the prior 12 months, and to have demonstrated poorer role functioning than the other women who declined additional research studies. The women who readily accepted the adjunctive experimental therapies also had a greater likelihood of having experimented with smoking, alcohol and illicit drugs.

These findings parallel findings of psychological distress as motivating factors in use of alternative therapies in patients with cancer and with other diseases. Thus, although some studies have shown that patients who use alternative therapy are younger and more educated,[5,19] emotional characteristics may be as, or more, important. These emotional characteristics included need for control of therapy,[17] psychological factors,[18–20] and feelings of being coerced into specific treatments.[21] Users of alternative therapy felt unhappy with the medical information and care they received,[18] had a higher incidence of somatization disorders,[19] experienced more hopelessness,[20] and were psychologically more labile with high anxiety and depression.[1]

Our study has several important limitations, including the small number of patients (42 women) and the retrospective nature of the study. However, as a pilot study it suggests that decision-making, even within a medical setting, may relate to psychological distress as much as to cognitive decision-making. Better recognition of the association of acquiescence to experimental studies and psychosocial distress could help physicians to understand the decision making process of their patients and to recommend mental health counseling when and if appropriate. More research is needed in larger numbers of patients to confirm our findings in a variety of settings in which patients need to make difficult decisions.

Table 3 Psychological test scores between women who agreed or did not agree to adjunctive experimental therapy

Test	*Agreed (n = 25)*	*Did not agree (n = 17)*	*P value*
Depression score	11 ±11	7 ± 6	0.12
State anxiety	38 ± 12	34 ± 8	0.11
Trait anxiety	36 ± 11	33 ± 52	0.001*
Life satisfaction	23 ± 7	26 ± 5	0.21
Symptom frequency	40 ± 12	32 ± 14	0.30
No. of problem symptoms	8 ± 5	6 ± 5	0.94
SF 36 physical functioning	65 ± 29	63 ± 38	0.76
Physical role functioning	13 ± 26	33 ± 44	0.001*
Bodily pain	56 ± 26	65 ± 25	1.00
Vitality	42 ± 19	47 ± 20	0.94
Gen. health	58 ± 24	58 ± 24	0.81
Social functioning	63 ± 28	61 ± 27	0.91
Emotional role functioning	63 ± 43	71 ± 39	0.29
Mental health	64 ± 18	74 ± 16	0.56

*$P < 0.05$.

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