



Correlates of anxiety and depression symptoms among patients and their family caregivers prior to allogeneic hematopoietic cell transplant for hematological malignancies

Donna M. Posluszny^{1,2} · Dana H. Bovbjerg^{1,2} · Karen L. Syrjala^{3,4} · Mounzer Agha^{1,2} · Mary Amanda Dew^{1,2}

Received: 26 January 2018 / Accepted: 6 July 2018 / Published online: 19 July 2018

© Springer-Verlag GmbH Germany, part of Springer Nature 2018

Abstract

Purpose Given the complexities and risks of allogeneic HCT, patients and their family caregivers may experience elevated psychological distress, including symptoms of anxiety and depression, in anticipation of the procedure. Patients and caregivers also bring with them their pre-HCT experiences of diagnosis, prior treatment, and associated burdens, thus potentially compounding their acute distress. Identification of clinical, psychosocial, and sociodemographic factors related to pre-HCT distress would allow targeting of patients and caregivers who may require assistance during the HCT process.

Methods Consecutive patients ($n = 111$) and their caregivers ($n = 110$) completed measures of anxiety, depression, cancer distress, perceived threat, perceived control, self-efficacy, relationship quality, and physical quality of life in the week before HCT. Multivariate linear regression analysis was used to identify factors associated with patient and caregiver anxiety or depression, including disease type, donor type, and patient and caregiver sociodemographic, health-related, and psychosocial factors.

Results Family caregivers had higher levels of anxiety and depression symptoms than patients. Thirty percent of caregivers vs. 17% of patients met criteria for clinically significant anxiety and a lesser amount (5% for both) met criteria for clinically significant depression. Patient anxiety was related to younger age ($b = -0.22$, $p = 0.005$) and greater cancer-related distress ($b = 0.59$, $p < 0.001$), while caregiver anxiety was related to lower self-efficacy ($b = -0.19$, $p = 0.011$) and greater cancer-related distress ($b = 0.58$, $p < 0.001$). Similarly, patient depression was related to lower perceived control ($b = -0.17$, $p = 0.050$), greater cancer-related distress ($b = 0.34$, $p = 0.005$), and lower physical functioning ($b = -0.26$, $p = 0.008$), while caregiver depression was related to greater cancer-related distress ($b = 0.46$, $p < 0.001$).

Conclusions Family caregivers may be more emotionally vulnerable than patients before HCT and in need of additional assistance. Cancer-related distress was the strongest correlate of anxiety and depression in both patients and caregivers, suggesting that distress related to their cancer experience and its consequences plays a major role in their emotional functioning prior to HCT.

Keywords Anxiety · Depression · Family caregiver · Hematological malignancies · Transplantation

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00520-018-4346-3>) contains supplementary material, which is available to authorized users.

✉ Donna M. Posluszny
poslusnydm@upmc.edu

¹ University of Pittsburgh, Pittsburgh, PA, USA

² UPMC Hillman Cancer Center, 5200 Centre Avenue, Suite 604, Pittsburgh, PA 15232, USA

³ Fred Hutchinson Cancer Research Center, Seattle, WA, USA

⁴ University of Washington, Seattle, WA, USA

Introduction

Allogeneic hematopoietic cell transplant (HCT) treatment for hematological malignancy and disease is a challenging medical procedure for patients and their family caregivers. It involves lengthy hospitalization for aggressive immunosuppressive chemotherapy treatment and immune system reconstitution and extensive post-discharge care to reduce the risk of potentially lethal complications such as infection [1]. Prior to HCT, patients must undergo comprehensive clinical evaluation to ensure they are good candidates for the procedure. In addition, patients need to identify a family caregiver who can help them participate in their care during the immediate post-HCT discharge period, during which successful

treatment requires careful and diligent attention to multiple factors (e.g., multiple daily medications, multiple outpatient clinic visits per week, vigilance to avoid potential sources of infection) [2].

Given the myriad psychological challenges associated with HCT, both patients [3–6]; and family caregivers [7–9] have been reported to be at risk for symptoms of anxiety and depression. Interestingly, the few studies that have concurrently examined patients and their family caregivers in this population prior to HCT have found that the severity of anxiety and depressive symptoms is similar or higher among the caregivers [9, 10]. To date, however, we know little about factors that may influence the severity of such symptoms in either patients or their family caregivers. During the course of treatment, patients and family caregivers have been reported to experience distress such as uncertainty and family strain associated with elements of the treatment process that they just finished (e.g., induction chemotherapy) and elements that lay ahead (e.g., transplant) [11]. These psychological factors may increase their risk for anxiety and depression, as their level of emotional burden grows. In addition, their perceptions of both the upcoming transplant and their psychological and relational resources to manage difficulties may also impact levels of anxiety and depression symptoms. Perceptions of high threat posed by the patient's disease, perceptions of having low/no control over outcome of the transplant, perceptions of low relationship quality and perceptions of low self-efficacy may all increase anxiety and depressive symptoms [12–15]. Finally, patients and family caregivers affect one another. For example, the level of cancer-related distress experienced by a patient, or the patient's self-efficacy, may be related to their caregiver's anxiety and/or depression levels or interactions between them may express this anxiety [16]. In the same way, caregiver characteristics and factors could be related to the patient's level of anxiety and depression.

The purpose of the present study was to provide a first critical test of factors we hypothesized would be associated with the severity of anxiety and depressive symptoms in a sample of hematological malignancy patients about to undergo allogeneic HCT and their family caregivers. We examined factors that previously have been reported to be important predictors in other cancer populations, including sociodemographic factors (e.g., age, sex); patient clinical status (e.g., disease type, donor type); self-reported health-related factors (e.g., physical functioning); and psychosocial factors (e.g., cancer-related distress, perceived control, self-efficacy). To our knowledge, the present study is the first to concurrently examine this set of factors in family caregivers along with patients scheduled for HCT. A better understanding of the factors contributing to heightened symptoms of anxiety and depression in patients and their family caregivers prior to HCT is critical for developing more effective interventions to improve the clinical management of this vulnerable population at this critical time in their treatment.

Method

Participants

Participants were adult patient-family caregiver dyads recruited prior to allogeneic HCT from the UPMC Hillman Cancer Center. Eligible patients were scheduled for their first allogeneic HCT, as part of a curative treatment protocol for hematological malignancy, were English-speaking, and had no medical record of serious mental illness (e.g., psychosis). Patients were asked to identify the one person who would serve as their main family caregiver during the transplant and follow-up process. All caregivers were also English speaking. Both the patient and family caregiver had to agree to participate in the study, as a dyad, to be enrolled.

Procedure

The study was approved by the University of Pittsburgh Institutional Review Board. All eligible patients were initially asked by the transplant treatment team if they would be willing to have study staff contact them to discuss the study. Participants provided written informed consent and responded to all study measures and questionnaires during face-to-face interview conducted 4–14 days prior to HCT. Patients and caregivers were each interviewed separately. Interviews were approximately 30–45 min in length, were arranged to coincide with medical visits when possible, and were conducted by a trained bachelor's-level study staff person. Data presented here reflect an analysis of baseline characteristics of a longitudinal descriptive study.

Measures

Sociodemographic information, including age, sex, ethnic group, financial status, education level, and type of patient-caregiver relationship, was obtained from all participants. Financial status was assessed with one item with the stem, "Thinking about your money situation, would you say you" with three completion options: "do not have enough for basic requirements," "have just enough to get along on," or "are comfortable" [17]. This item was developed for use in a large scale multinational World Health Organization study of social and health aspects of aging.

Clinical characteristics, including type of patient's disease and type of donor (matched unrelated, sibling, haploidentical, or cord), were obtained from patients' medical records.

Health-related characteristics included perceived physical functioning which was assessed in both patients and caregivers through self-report via physical component score of the Medical Outcomes Study 36-item Short Form Health Survey (SF-36; [18]). Patients and caregivers also completed the Brief Charlson Comorbidity Index, which is an 11-item

measure used to assess the presence of comorbid medical conditions [19]. A summary score was calculated, with a higher score indicating more serious and more comorbid conditions. For analyses, we removed the contribution of the cancer condition related to the transplant from the patients' scores for patient-caregiver comparisons.

Both patients and caregivers also completed the following measures.

Anxiety and Depression Symptoms The Hospital Anxiety and Depression Scale (HADS; [20]) contains two 7-item subscales to measure the severity of anxiety and depression symptoms and is widely used in medical populations. Subscale scores range from 0 to 21: scores of 8–10 indicate mild distress while 11–21 indicate clinically significant distress (among patients in the present sample, $\alpha = 0.85$ and 0.76 for anxiety and depression, respectively; among caregivers, $\alpha = 0.87$ and 0.74 for anxiety and depression, respectively).

Psychosocial characteristics

Cancer-related distress was assessed via the 35-item Cancer and Treatment Distress Scale, Acute version (CTXD) developed for HCT patients [11, 21]; family caregivers completed the caregiver version of the CTXD (CTXD-CG). Items in the patient version covered topics such as uncertainty, family strain, appearance and sexuality, health burden, managing the medical system, finances, and acute symptoms. Topics in the caregiver version covered uncertainty, burden, medical/financial issues, and changes due to cancer. For both measures, a total distress summary mean score was tabulated. This score ranges from 0 = no distress to 3 = severe distress for both patients and caregivers ($\alpha = 0.95$ for CTXD and 0.91 for CTXD-CG in the present sample).

Perceived threat was assessed using a 3-item measure [22]. These items concerned how serious, life threatening, and threatening to their well-being their (or their patient's) condition was (1 = not at all; 5 = extremely threatening). Items were averaged; $\alpha = 0.79$ and 0.75 for patients and for caregivers, respectively, in the present sample).

Perceptions of patient's control over transplant and long-term course of cancer was assessed via two items adapted from Christenson and colleagues' work in cancer [23]. We changed "cancer" in one item to "transplant." Participants rated items concerning how much control they thought the patient had over the effectiveness of the transplant and over the long-term course of the cancer (1 = absolutely no control; 5 = total control). Items were highly correlated ($r = 0.73$ and 0.78 for patients and for caregivers, respectively) and were averaged.

Relationship quality was reported by both the patient and caregiver via a 20-item measure adapted by Dew and Bromet [24] from the work of Spanier [25] and Pearlin and Schooler

[26], and used extensively in organ transplant candidates, recipients, and their family caregivers ([27–31]). This instrument yields an overall relationship quality score (1 = poor relationship, 5 = excellent relationship) ($\alpha = 0.95$ and 0.94 for patients and caregivers, respectively, in the present sample).

Perceived self-efficacy was measured through the General Self-Efficacy Scale (GSE; [32]) which is a 10-item summed measure assessing beliefs about personal ability to handle new and difficult tasks ($\alpha = 0.86$ for both patients and caregivers in the present sample).

Statistical analysis

Descriptive statistics were used to characterize anxiety and depression symptoms, as well as potential patient-related and caregiver-related correlates of these symptoms (sociodemographic, health-related, and psychosocial factors). Paired *t* tests (for continuous variables) and McNemar χ^2 tests (for categorical variables) were conducted to compare patients and caregivers on HADS symptom severity scores, HADS caseness, the health-related and psychosocial factors, and sociodemographics. These types of tests keep each individual patient's score paired with their specific family caregiver during the analysis. Correlation coefficients were calculated to examine bivariate relationships between patient and caregiver anxiety and depressive symptom severity, as well as the relationships of symptom severity with patient and caregiver sociodemographic, patient clinical, and patient and caregiver health-related and psychosocial variables. In order to examine independent correlates of anxiety and depressive symptom severity, multiple linear regression analyses were then conducted, entering the sociodemographic, health-related, and psychosocial variables which showed correlations of at least modest size ($r \geq 0.20$) with a given outcome as predictors. Separate regression analyses were performed for patient depression and patient anxiety and for caregiver depression and caregiver anxiety. Like the bivariate analyses, the multiple regressions took the paired nature of the patient-caregiver data into account because caregiver variables within a given dyad were included as predictors for each patient symptom outcome variable and, similarly, patient variables within a given dyad were included as predictor for each caregiver symptom outcome variable. Data analysis was conducted using IBM SPSS version 24.

Results

One hundred eleven of the 121 consecutive eligible patients approached agreed to participate. Reasons for refusal included not wanting the caregiver to be burdened or caregiver refusal ($n = 4$), patient feeling too sick ($n = 3$), and patient not interested ($n = 3$). One patient-caregiver dyad withdrew prior to

questionnaire completion due to not wanting an additional burden, and one caregiver from another dyad was unable to complete the questionnaires due to time constraints. Thus, 111 patients and 110 caregivers provided data for the study. As shown in Table 1, most participants were European American and married, with 34–43% having at least a college education. Most dyads were spousal dyads (61%), and slightly more patients were male (56%) consistent with the transplant population, while more caregivers were female (71%). A majority of patients had acute myelogenous leukemia (AML; 61%) and about half (51%) had an unrelated donor. Patients and caregivers did not differ on age (53.7 vs. 53.2 years) or on self-endorsed financial situation (about half from each group described being comfortable). Table 1 also shows descriptive statistics for patient and caregiver health-related and psychosocial characteristics. Caregivers reported higher levels of perceived threat and physical function but no differences in perceived control or self-efficacy. Patients reported higher relationship quality than caregivers. We also provide descriptive data separately for each specific type of patient-caregiver relationship (please see Supplementary Table 1). We could not do formal comparisons of patient-caregiver subgroups because the groups are too small.

Anxiety and depression symptoms

Table 2 shows mean severity of anxiety and depression symptoms in both patients and caregivers, as well as caseness in each domain. Caregivers reported greater symptom severity in both areas compared to patients. In terms of caseness, 30% of caregivers had clinically significant anxiety compared with 17% of patients. Patients and caregivers were less likely to meet the caseness criterion on the depression scale, with 5% of each group endorsing clinically significant depression.

Correlates of anxiety and depression symptom severities

We first examined whether patient sociodemographic factors (age, sex, financial situation, education, type of relationship with caregiver), clinical characteristics (disease type, donor type), and health-related and psychosocial characteristics (physical functioning, comorbidity, perceived threat, perceived control, relationship quality, cancer distress) as well as the corresponding caregiver sociodemographic, health-related, and psychosocial characteristics were related to the severity of anxiety and depressive symptoms in either the patients or the caregivers. Results are shown in Table 3 (see columns showing *r*s, the simple correlation coefficient between each factor and the depression and anxiety variables). It is noteworthy that the severities of patient anxiety and depression were not significantly correlated with caregiver anxiety and depression severities. In patients, younger age was

related to higher severity of anxiety but not depression. Having a poorer financial situation was related to both higher anxiety and depression. None of the clinical characteristics were related to patient anxiety or depression. For the health-related and psychosocial characteristics, patients with higher perceptions of threat, lower perceptions of control, and higher cancer distress had higher depression and anxiety symptom levels. No caregiver health-related or psychosocial factors were related to the severity of patient anxiety and depression symptoms.

Turning to the correlations for caregiver anxiety and depression symptom levels, younger age and lower self-efficacy were related to higher anxiety severity, while younger age and having at least a college education were related to higher depression severity. Caregivers who were spouses of patients had lower depression levels than other types of caregivers. No patient clinical factors (including patient depression and anxiety) were related to caregiver anxiety or depression severities. Among the psychosocial factors, caregivers having more cancer-related distress also had higher anxiety levels. Caregiver depression levels were not related to either patient or caregiver health-related or psychosocial factors.

Next, we completed the multivariate analyses. Given the need to ensure an appropriate ratio of study participants to variables considered in multivariate analysis examining the outcomes of HADS anxiety scores and depression scores, only variables showing correlations of at least modest size ($r \geq 0.20$) with a given outcome were included in the multiple regression analysis. Thus, for patient anxiety, patient age, patient financial situation, patient perceived threat, patient perceived control, patient cancer-related distress, and patient general self-efficacy were included in the regression. As a set, the variables were significantly related to the severity of patient anxiety symptoms ($F(6,102) = 20.10$, $p < 0.001$; $R = 0.74$), with younger age and greater cancer distress having significant independent associations with greater patient anxiety (see Table 3, column with beta coefficients for patient anxiety). For patient depression, patient financial situation, patient perceived threat, patient perceived control, patient cancer-related distress, patient physical functioning, patient self-efficacy, and caregiver perceived threat were included in the regression. This group of factors was significant as a set for the severity of patient depression symptoms, ($F(7,94) = 9.31$, $p < 0.001$; $R = 0.64$), with less patient perceived control, greater patient cancer distress, and worse patient physical functioning showing significant independent effects for greater depression severity (see Table 3, column with beta coefficients for patient depression).

For caregiver anxiety symptom severity, caregiver age, caregiver sex, caregiver distress, and caregiver self-efficacy were included in the regression. As a set, the factors were significantly associated with anxiety severity ($F(4,102) = 22.18$, $p < 0.001$; $R = 0.68$). As shown in Table 3, with caregiver cancer

Table 1 Descriptive characteristics of participants ($N = 221$)

	Patients ($n = 111$)	Caregivers ($n = 110$)	Test statistic, ^a p value
Sociodemographic characteristics			
Age (mean; range; SD)	53.7; 22–71; 10.3	53.2; 18–86; 13.6	0.345, 0.731
Sex, female % (n)	44 (49)	71 (78)	
Ethnic group, European American % (n)	95 (106)	95 (104)	^b 0.000
African American % (n)	5 (5)	5 (5)	
Native American % (n)	0	1 (1)	
Financial situation ^c			
Do not have enough for basic requirements	10 (11)	7 (7)	– 1.111, 0.269
Have just enough to get along on	41 (46)	40 (42)	
Are comfortable	49 (54)	53 (56)	
Highest education level, \geq college graduate	34 (38)	43 (47)	0.121, < 0.001
Marital status, married/partnered % (n)	77 (85)	81 (89)	0.286, < 0.001
Type of Pt-C relationship, spousal % (n)			
Pt parent-cg adult child % (n)	11 (12)		
Pt adult child-Cg parent % (n)	13 (14)		
Sibling/sibling in law % (n)	13 (14)		
Friend % (n)	3 (3)		
Clinical characteristics			
Disease type, AML % (n)			
ALL % (n)	61 (68)		
MDS % (n)	7 (8)		
Other % (n)	16 (18)		
Type of donor, MUD % (n)			
Sibling % (n)	15 (17)		
Haploidentical % (n)	37 (41)		
Cord % (n)	11 (12)		
1 (1)			
Health-related characteristics, M (SD)			
Perceived physical functioning	37.69 (9.8)	50.68 (9.3)	10.078***, < 0.001
Brief Charlson Comorbidity ^d	0.97 (1.3)	0.50 (0.9)	3.090**, 0.003
Psychosocial characteristics, M, range, (SD)			
Perceived disease threat	4.32 (0.7)	4.37 (0.6)	– 0.540, .590
Perceptions of patient's control over transplant and long-term course of cancer	3.11 (0.9)	3.17 (0.9)	– 0.438, .662
Relationship quality	4.43 (0.5)	4.27 (0.5)	2.908**, .004
Cancer treatment-related distress ^e	1.25 (0.6)	1.13 (0.5)	N/A ^c
Self-efficacy	3.27 (0.4)	3.21 (0.3)	0.870, .386

AML acute myelogenous leukemia, ALL acute lymphocytic leukemia, MDS myelodysplastic syndrome, MUD matched unrelated donor

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

^a χ^2 for nominal variables and paired t tests for continuous variables

^b No test statistic is reported because Fishers exact test p value is reported; all five African American patients had African American caregivers

^c n may not total group number as some demographic data missing

^d Patients' mean score including cancer condition related to the transplant was 2.96; $t = 17.891$; $p < 0.001$

^e Patient and caregiver versions of this scale are not comparable

distress and caregiver general self-efficacy were significant independent correlates: greater caregiver cancer distress and lower caregiver general self-efficacy were related to greater anxiety

severity (see beta coefficients shown for caregiver anxiety). For caregiver depression symptom severity, type of relationship, caregiver age, caregiver education, caregiver cancer distress,

Table 2 HADS Anxiety and Depression Scores and caseness for patients and caregivers

Characteristic	Patients (<i>n</i> = 110) ^a	Caregivers (<i>n</i> = 107) ^a	Test statistic ^b
Anxiety ^b , (mean; range; SD)	6.64; 0–19; 4.1	8.62; 0–21, 4.1	−3.653***
Caseness: normal % (<i>n</i>)	66 (73)	42 (45)	15.56***
Mild % (<i>n</i>)	16 (18)	28 (30)	
Clinically significant % (<i>n</i>)	17 (19)	30 (32)	
Depression ^b , (mean; range; SD)	4.10; 0–14; 3.2	5.14; 0–13; 2.9	−2.717**
Caseness: normal % (<i>n</i>)	87 (96)	79 (85)	3.86
Mild % (<i>n</i>)	8 (9)	16 (17)	
Clinically significant % (<i>n</i>)	5 (5)	5 (5)	

HADS Hospital Anxiety and Depression Scale

** $p < 0.01$; *** $p < 0.001$

^a One patient and three caregivers were missing HADS data

^b McNemar-Bowker χ^2 test for nominal variables and paired *t* tests for continuous variables

and caregiver general self-efficacy were included in the regression. The factors as a set were significant ($F(5,101) = 7.84$, $p < 0.001$; $R = 0.53$); only caregiver cancer distress had a significant independent effect, with greater caregiver cancer distress related to greater caregiver depression severity (see Table 3, column with beta coefficients for caregiver depression).

Because cancer distress was a central factor for both patient and caregiver anxiety and depression, we explored which subscales of the measure might have been relatively more important or that accounted for the impact of the total cancer distress measure. We found that the cancer distress subscales were highly intercorrelated (median correlation of 0.57; range of 0.48–0.82), and we therefore had to add each subscale individually to each of the four regressions that included all of the other factors (i.e., the factors included in the regressions shown in Table 3). The results were that all the subscales were similarly strongly associated with patient outcomes (median regression coefficient = 0.41; range = 0.26–0.52; for anxiety = 0.28; range = 0.18–0.32 for depression) and with caregiver outcomes (median regression coefficient = 0.41; range = 0.31–0.56; for anxiety = 0.31; range = 0.24–0.39 for depression).

Discussion

This study identified some important distinctions between and correlates of patient and caregiver anxiety and depression that add to the growing literature on understanding how patients and caregivers approach medical challenges. We found that clinically significant levels of anxiety symptoms were more common than clinically significant levels of symptoms of depression in both patient and family caregivers prior to allogeneic HCT. We found that in both groups, just 5% met criteria for clinically significant levels of depressive symptoms. However, 17% of patients and 30% of family caregivers reported anxiety symptoms in the clinically significant range.

Comparisons of the severity of anxiety and depression symptoms treated as continuous variables showed the same pattern, with anxiety symptoms experienced as more severe, on average, than depressive symptoms. Further, from the standpoint of clinical significance, the 2-point difference we found between mean anxiety scores for patients and caregivers can be considered as having met the threshold of a “minimally important difference” on the HADS anxiety scale, based on recommendations of 1.5 to 2.5 points in other medically ill populations [33, 34]. Overall, these findings may reflect the impact of uncertainty and worry about the upcoming treatment on general levels of anxiety.

Novel to the present study was our attempt to explore possible differences between caregivers and patients in the predictors of anxiety and depression symptom severity. We assessed a number of sociodemographic, clinical, and health characteristics and psychological characteristics in both patients and their family caregivers that have been reported to serve as important correlates of anxiety and depressive symptoms in other patient populations. Several key findings emerged. First, the severity of symptoms of patient anxiety and depression was unrelated to the severity of caregiver anxiety and depression symptoms. Second, none of the caregiver factors were related to anxiety or depression symptom severity in the patients, and none of the patient factors were related to anxiety or depression in the caregiver. However, we observed several patient-related correlates of patient anxiety and depression symptom severity. Patients who were younger and reported greater cancer-related distress endorsed higher levels of anxiety. These results are consistent with other reports showing that younger patients experience more anxiety and depression in other cancer populations, potentially due to cancer diagnosis being an “off life course” event for them, meaning it is an event that tends to happen during a different (i.e., older) phase of life [35]. We found that patients who felt they had less control over their transplant and disease outcomes, those

Table 3 Correlates of HADS anxiety and depression symptom severity in patients and family caregivers

	Patient				Caregiver			
	Anxiety		Depression		Anxiety		Depression	
	<i>r</i>	<i>b</i>	<i>r</i>	<i>b</i>	<i>r</i>	<i>b</i>	<i>r</i>	<i>b</i>
Patient (Pt) factors								
Sociodemographic characteristics								
Pt age	−0.32***	−0.22**	−0.09		−0.09		−0.08	
Pt sex, female	0.13		0.11		−0.19		−0.14	
Financial situation ^a	−0.31***	−0.03	−0.23**	−0.09	−0.01		.05	
Education, ≥ college degree	−0.05		0.15		0.07		0.126	
Type of relationship, spousal	−0.14		0.06		0.18		−0.20*	0.01
Clinical characteristics								
Disease type, AML (vs. all others)	−0.02		0.11		−0.03		−0.02	
Donor type, MUD (vs. all others)	−0.05		0.08		0.15		0.13	
Health-related characteristics								
Pt SF36 physical composite	−0.15		−0.37***	−0.26**	−0.08		−0.14	
Pt Brief Charlson Comorbidity Index	0.08		0.11		0.09		0.05	
Psychosocial characteristics								
Pt perceived threat	0.21*	0.06	0.25**	0.06*	0.10		0.11	
Pt perceived control	−0.29**	−0.12	−0.34***	−0.17	−0.08		−0.14	
Pt relationship quality	−0.09 ^b		−0.14 ^b		0.01 ^b		−0.06 ^b	
Pt cancer distress	0.69***	0.59***	0.52***	0.34**	0.11		0.02	
Pt anxiety					0.06		0.03	
Pt depression					0.15		0.16	
Pt general self-efficacy	−0.35***	−0.14	−0.39***	−0.15	0.08		0.07	
Caregiver (Cg) factors								
Sociodemographic characteristics								
Cg age	0.01		0.10		−0.28**	−0.11	−0.20*	−0.08
Cg sex, female	−0.08		−0.16		0.24*	0.15	0.14	
Financial situation ^a	−0.06	−0.05	0.03	0.15	−0.05	0.07	−0.12	0.08
Education, ≥ college degree	0.07		0.11		0.17		0.24*	0.16
Health-related characteristics								
Cg SF36 physical composite	−0.06		−0.13		0.13		−0.05	
Cg Brief Charlson Comorbidity Index	0.08		0.12		0.11		0.07	
Psychosocial characteristics								
Cg perceived threat	0.19*		0.25*	0.06	−0.04		0.07	
Cg perceived control	−0.15		−0.11		−0.02		−0.04	
Cg relationship quality	0.07 ^b		0.01 ^b		−0.05 ^b		−0.02 ^b	
Cg cancer distress	0.00		0.07		0.62***	0.58***	0.49***	0.46***
Cg anxiety	0.06		0.16					
Cg depression	0.03		0.16					
Cg general self-efficacy	0.02		−0.01		−0.34***	−0.19*	−0.25*	−0.09

HADS Hospital Anxiety and Depression Scale, AML acute myelogenous leukemia, MUD matched unrelated donor, Pt patient $n = 110$, Cg caregiver $n = 107$

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

^a Participants endorsed financial situation as 1 = not enough for basic requirements; 2 = just enough to get along on; 3 = comfortable

^b Taking type of dyad (spousal vs. not) into account did not affect the significance of the correlation between relationship quality and symptoms

who had more cancer-related distress, and those reporting poorer physical functioning reported greater levels of depression. The relationship between perceived control and depression has substantial roots in the literature (e.g., [36]), and our findings here add to that literature although it is surprising that the relationship between perceived control and anxiety in patients did not bear out in the multivariate analyses. Perceptions of poorer physical functioning may reflect negative cognitive beliefs that are associated with depression, or conversely, physical impairment could increase risk for depression. Further, it is noted that patient-reported factors examined here, such as patient depression and perceived physical functioning, as well as emotional support, have all been associated with patient health outcomes following HCT [3, 37, 38].

For the caregivers, we found fewer reliable associations of factors to anxiety and depression symptom severity. Lower levels of perceived efficacy and higher levels of cancer-related distress were related to anxiety. As the caregiver is tasked with providing care to the patient both after hospital discharge, as well as in an ongoing manner, a positive sense of self-efficacy may be important for their emotional well-being. The relationship between self-efficacy and anxiety has been observed in other cancer and cancer caregiver populations as well [39–41]. Higher levels of cancer-related distress were also associated with anxiety, and it was the only factor reliably associated with caregiver depression. It is possible that those caregivers who were more burdened and dealing with many stressors were more vulnerable to experiencing other types of distress including anxiety and depression.

It is notable that we found cancer-related distress to be a key correlate for both patient and caregiver anxiety and depression symptom severity. The mean levels on the cancer-related distress measures in our sample were similar to scores reported in other HCT samples [21, 42]. In our sample, cancer-related distress was moderately to strongly correlated with patient anxiety and depression and caregiver anxiety and depression in the range of $r = 0.49$ – 0.69 . Although one might suggest that they are measuring overlapping concepts, we do not believe that is the case as our choice of cancer-related distress measure, the CTXD and CTXD-CG version, encompasses broad aspects of the cancer and cancer-treatment experience such as distress related to physical symptoms, appearance, financial strain, family strain, and uncertainty. Thus, it can be considered reflective of both emotional sequelae from pre-transplant disease and treatment processes as well as the upcoming transplant. We also did not find any evidence that any one subscale of the CTXD or CTXD-CG was more important than the others; thus, there was no specific type of cancer distress (e.g., uncertainty, changes in appearance) that stood out. Overall, patients and caregivers who had a more difficult time during the pre-transplant cancer treatment process may be at higher risk for anxiety and depression and

should potentially be targeted for additional assistance as they approach transplant.

Although this study's inclusion of caregivers and assessment of variables that are relatively novel to this study population in the literature are strengths, the cross-sectional design limits inferences regarding the direction of the effects. Although we had a large subgroup within our sample of spousal patient-caregiver dyads, our nonspousal dyads were heterogeneous. Thus, while we could examine differences in patient and caregiver depression and anxiety as a function of spousal vs. nonspousal dyads, we did not have enough dyads with each nonspousal type (e.g., adult child caregiver, parent caregiver) to be able to examine whether certain types of these dyads bore different patterns of associations with respondent anxiety and depression levels. Further, most of the sample was Caucasian and non-Hispanic, making it impossible to examine associations between symptoms of anxiety and depression and race and ethnicity.

In conclusion, the period prior to allogeneic HCT can be distressing to both patients and caregivers, mainly in the form of anxiety and to a lesser extent depression. Caregivers appear to experience more anxiety and depression than patients, although anxiety is a larger concern with 30% of the caregiver sample clinically anxious. This posits a focus on the well-being of family caregivers may be of critical importance, and efforts to help improve their self-efficacy may decrease their anxiety. For patients, those who are younger may be at greater risk anxiety, and those who feel a lack of control and physically debilitated may be at greater risk for depression. The strongest association to anxiety and depression was cancer-related distress, suggesting that patients' and caregivers' personal experiences with cancer, and its consequences such as family and financial strain, are highly relevant for their general psychological functioning prior to HCT. Thus, screening for cancer-related distress could be important for identifying areas of difficulty for both patients and caregivers as well as identifying patients (and caregivers) at higher risk for anxiety and depression. It may be prudent to target those patients, and particularly caregivers, with the most difficult disease experiences prior to HCT for additional assistance, including referrals for psychological care and support.

Funding information This study was supported by grants K23CA149082 and P30CA047904 from the National Cancer Institute.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This research was conducted in compliance with ethical standards.

References

- Majhail NS, Farnia SH, Carpenter PA, Champlin RE, Crawford S, Marks DI, Omel JL, Orchard PJ, Palmer J, Saber W, Savani BN, Veys PA, Bredeson CN, Giralat SA, LeMaistre CF (2015) Indications for autologous and allogeneic hematopoietic cell transplantation: guidelines from the American Society for Blood and Marrow Transplantation. *Biol Blood Marrow Transplant* 21(11):1863–1869
- National Marrow Donor Program (NMDP) (2015) Patient Care Guidelines: Allogeneic transplant: How to plan and what to expect. <http://www.marrow.org>
- El-Jawahri A et al (2017) Impact of pre-transplant depression on outcomes of allogeneic and autologous hematopoietic stem cell transplantation. *Cancer* 123(10):1828–1838
- Pillay B, Lee SJ, Katona L, Burney S, Avery S (2014) Psychosocial factors associated with quality of life in allogeneic stem cell transplant patients prior to transplant. *Psychooncology* 23(6):642–649
- Syrjala KL, Langer S, Abrams J, Storer B, Martin P (2004) Physical and mental recovery after hematopoietic stem cell transplantation. *Discov Med* 4(23):263–269
- Prieto JM, Atala J, Blanch J, Carreras E, Rovira M, Cirera E, Gastó C (2005) Patient-rated emotional and physical functioning among hematologic cancer patients during hospitalization for stem-cell transplantation. *Bone Marrow Transplant* 35(3):307–314
- Simoneau TL, Mikulich-Gilbertson SK, Natvig C, Kilbourn K, Spradley J, Grzywa-Cobb R, Philips S, McSweeney P, Laudenslager ML (2013) Elevated peri-transplant distress in caregivers of allogeneic blood or marrow transplant patients. *Psychooncology* 22(9):2064–2070
- Beattie S, Lebel S (2011) The experience of caregivers of hematological cancer patients undergoing a hematopoietic stem cell transplant: a comprehensive literature review. *Psychooncology* 20(11):1137–1150
- Bevans M, Wehrlen L, Prachenko O, Soeken K, Zabora J, Wallen GR (2011) Distress screening in allogeneic hematopoietic stem cell (HSCT) caregivers and patients. *Psychooncology* 20(6):615–622
- El-Jawahri AR et al (2015) Quality of life and mood of patients and family caregivers during hospitalization for hematopoietic stem cell transplantation. *Cancer* 121(6):951–959
- Syrjala KL, Yi JC, Langer SL (2016) Psychometric properties of the Cancer and Treatment Distress (CTXD) measure in hematopoietic cell transplantation patients. *Psychooncology* 25(5):529–535
- Baliouis M, Rennoldson M, Dawson D, Mills J, das Nair R (2017) Perceptions of hematopoietic stem cell transplantation and coping predict emotional distress during the acute phase after transplantation. *Oncol Nurs Forum* 44(1):96–107
- Fife BL, Monahan PO, Abonour R, Wood LL, Stump TE (2009) Adaptation of family caregivers during the acute phase of adult BMT. *Bone Marrow Transplant* 43(12):959–966
- Sarkar S, Scherwath A, Schirmer L, Schulz-Kindermann F, Neumann K, Kruse M, Dinkel A, Kunze S, Balck F, Kröger N, Koch U, Mehnert A (2014) Fear of recurrence and its impact on quality of life in patients with hematological cancers in the course of allogeneic hematopoietic SCT. *Bone Marrow Transplant* 49(9):1217–1222
- Wells KJ, Booth-Jones M, Jacobsen PB (2009) Do coping and social support predict depression and anxiety in patients undergoing hematopoietic stem cell transplantation? *J Psychosoc Oncol* 27(3):297–315
- Langer SL, Yi JC, Storer BE, Syrjala KL (2010) Marital adjustment, satisfaction and dissolution among hematopoietic stem cell transplant patients and spouses: a prospective, five-year longitudinal investigation. *Psychooncology* 19(2):190–200
- Ferraro KF, Su Y (1999) Financial strain, social relations, and psychological distress among older people: a cross-cultural analysis. *J Gerontol B Psychol Sci Soc Sci* 54(1):S3–S15
- Ware JE Jr, Sherbourne CD (1992) The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 30(6):473–483
- Katz JN et al (1996) Can comorbidity be measured by questionnaire rather than medical record review? *Med Care* 34(1):73–84
- Zigmond AS, Snaith RP (1983) The hospital anxiety and depression scale. *Acta Psychiatr Scand* 67(6):361–370
- Syrjala K (2005) The Cancer and Treatment Distress Scale (CTXD). Scoring manual obtained from the author
- Witte K et al (1996) Predicting risk behaviors: development and validation of a diagnostic scale. *J Health Commun* 1(4):317–341
- Christensen AJ, Moran PJ, Ehlers SL, Raichle K, Karnell L, Funk G (1999) Smoking and drinking behavior in patients with head and neck cancer: effects of behavioral self-blame and perceived control. *J Behav Med* 22(5):407–418
- Dew MA, Bromet EJ (1991) Effects of depression on social support in a community sample of women. In: Exner JE (ed) *The social context of coping*. Plenum, New York, pp 189–208
- Spanier GB (1978) Measuring dyadic adjustment: new scales for assessing the quality of marriage and similar dyads. *J Marriage Fam* 38(1):15–28
- Pearlin LI, Schooler C (1978) The structure of coping. *J Health Soc Behav* 19(1):2–21
- Dew MA, DiMartini AF, DeVito Dabbs AJ, Fox KR, Myaskovsky L, Posluszny DM, Switzer GE, Zomak RA, Kormos RL, Toyoda Y (2012) Onset and risk factors for anxiety and depression during the first 2 years after lung transplantation. *Gen Hosp Psychiatry* 34(2):127–138
- Myaskovsky L, Posluszny DM, Schulz R, DiMartini AF, Switzer GE, Dabbs ADV, McNulty ML, Kormos RL, Toyoda Y, Dew MA (2012) Predictors and outcomes of health-related quality of life in caregivers of cardiothoracic transplant recipients. *Am J Transplant* 12(12):3387–3397
- Myaskovsky L, Dew MA, Switzer GE, Kormos RL, Hall M, Goycoolea JM, DiMartini AF, Manzetti JD, KR MC (2003) Avoidant coping is related to poorer quality of life among lung transplant candidates. *Prog Transplant* 13(3):183–192
- Dew MA et al (2004) Onset, timing and risk for depression and anxiety in family caregivers to heart transplant recipients. *Psychol Med* 34(6):1065–1082
- Dew MA, Kormos RL, DiMartini A, Switzer GE, Schulberg HC, Roth LH, Griffith BP (2001) Prevalence and risk of depression and anxiety-related disorders during the first three years after heart transplantation. *Psychosomatics* 42(4):300–313
- Jerusalem RSM (1995) Generalized self-efficacy scale. In: Weinman SWJ, Johnston M (eds) *Measures in health psychology: a user's portfolio. Causal and control beliefs*. NFER-NELSON, Windsor, pp 35–37
- Puhan MA, Frey M, Büchi S, Schünemann HJ (2008) The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. *Health Qual Life Outcomes* 6:46
- Chan KS, Aronson Friedman L, Bienvenu OJ, Dinglas VD, Cuthbertson BH, Porter R, Jones C, Hopkins RO, Needham DM (2016) Distribution-based estimates of minimal important difference for hospital anxiety and depression scale and impact of event scale-revised in survivors of acute respiratory failure. *Gen Hosp Psychiatry* 42:32–35
- Lang MJ, David V, Giese-Davis J (2015) The age conundrum: a scoping review of younger age or adolescent and young adult as a risk factor for clinical distress, depression, or anxiety in cancer. *J Adolesc Young Adult Oncol* 4(4):157–173
- Taylor SE, Helgeson VS, Reed GM, Skokan LA (1991) Self-generated feelings of control and adjustment to physical illness. *J Soc Issues* 47(4):91–109

37. Wood WA, le-Rademacher J, Syrjala KL, Jim H, Jacobsen PB, Knight JM, Abidi MH, Wingard JR, Majhail NS, Geller NL, Rizzo JD, Fei M, Wu J, Horowitz MM, Lee SJ (2016) Patient-reported physical functioning predicts the success of hematopoietic cell transplantation (BMT CTN 0902). *Cancer* 122(1):91–98
38. Ehrlich KB, Miller GE, Scheide T, Baveja S, Weiland R, Galvin J, Mehta J, Penedo FJ (2016) Pre-transplant emotional support is associated with longer survival after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant* 51(12):1594–1598
39. Ugalde A, Krishnasamy M, Schofield P (2014) The relationship between self-efficacy and anxiety and general distress in caregivers of people with advanced cancer. *J Palliat Med* 17(8):939–941
40. Mystakidou K, Tsilika E, Parpa E, Gogou P, Panagiotou I, Vassiliou I, Gouliamos A (2013) Relationship of general self-efficacy with anxiety, symptom severity and quality of life in cancer patients before and after radiotherapy treatment. *Psychooncology* 22(5):1089–1095
41. Curtis R, Groarke A, Sullivan F (2014) Stress and self-efficacy predict psychological adjustment at diagnosis of prostate cancer. *Sci Rep* 4:5569
42. Syrjala KL, Sutton SK, Jim HSL, Knight JM, Wood WA, Lee SJ, Jacobsen PB, Abidi MH, Yi JC (2017) Cancer and treatment distress psychometric evaluation over time: a BMT CTN 0902 secondary analysis. *Cancer* 123(8):1416–1423

The authors retain full control of all primary data and agree to allow this journal to review the data if requested.