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Distress and quality of life in patient and caregiver dyads facing stem cell transplant: identifying overlap and unique contributions

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Abstract

Purpose Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is a demanding treatment requiring caregiver support. The pre-transplant period is particularly stressful. How patient and caregiver dyads respond to these stressors can impact post-transplant outcomes. The purpose of this cross-sectional study was to assess pre-transplant patient and caregiver distress, patient quality of life (pQoL), and simultaneously investigate relationship between caregiver distress, patient distress, and patient QoL.

Methods We measured caregiver anxiety, depressive symptoms, perceived stress, sleep quality, caregiver burden, and pQoL in 148 dyads compared to clinical thresholds or population norms. To reduce comparisons, we created a composite distress score from affective measures. Associations within dyads were examined via correlation and path analysis.

Results Most dyads scored above norms for psychological measures. Patient distress was positively associated with caregiver distress. Higher caregiver distress significantly predicted poorer pQoL after accounting for the interdependence of patient and caregiver distress. Specifically, patients' physical functioning was the primary driver of this interrelationship.

Conclusions Allo-HSCT patients and their caregivers reported elevated distress pre-transplant. Both patient and caregiver distress contributed to pQoL, with patients' physical functioning accounting significantly for caregiver well-being. Supporting the patient-caregiver dyad before transplantation is a priority for supportive services.

Keywords Cancer · Caregivers · Dyads · Dyadic relationships · Oncology · Hematology

Background

Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is an aggressive form of treatment for malignant and non-malignant disorders. The number of Allo-HSCT transplants conducted nationally is increasing as indications for its clinical application broaden [1]. Patients undergoing transplant face significant physical and emotional challenges before, during, and after the transplantation [2]. As patients approach the transplant, levels of uncertainty are high as transplant carries significant risk for morbidity and mortality due to lack of disease response, disease relapse, or treatment-related side effects such as infection or graft-versus-host disease (GvHD) [3]. Therefore, distress of Allo-HSCT patients is high, especially in the days immediately before and after stem cell infusion [4].

Unlike many cancer therapies, Allo-HSCT requires patients to identify a caregiver who will provide critical support during the first 100 days post-transplant. Caregivers are almost always a partner, close family, or friend of the patient. In addition to managing the demands of having a loved one endure this life-changing procedure, caregivers are responsible for ensuring compliance to complicated medication regimens, assessing for post-transplant side effects, providing emotional support, and transporting the patient to/from

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frequent clinic appointments. Given these high demands, it is not surprising that caregivers experience elevated levels of distress in the peri-transplant period [5] that are comparable or greater than those experienced by Allo-HSCT patients [6].

As transplant survival improves [7], quality of life (QoL) is increasingly recognized as a critical outcome [8]. Most of transplant QoL research has focused on the post-transplant period [9]. Factors related to pre-transplant QoL have not received as much attention to date. Pillay et al. [10] found that half of patients pre-transplant had impaired physical QoL, and almost half reported lower psychological and social QoL compared to population norms. Further, pre-transplant QoL is relat-ed to the rate of QoL improvements across the course of transplant [11]. Importantly, others have demonstrated an association between pre-transplant QoL and critical out-comes, such as post-transplant relapse and mortality [9].

In addition to patient factors, research has demonstrated the importance of the interrelatedness of patient-caregiver dyads on QoL [12]. Increased duration and frequency of visits by the caregiver during the transplant process is related to increased patient survival [13]. Ratings from pre-transplant assessment on whether patients had adequate support predicted longer overall survival [14]. In addition to the patient-caregiver dyad being important to consider in relation to these clinical out-comes, others have called for targeting the dyad in supportive interventions in cancer at large, with the argument that there is potential for more efficient and impactful interventions [15]. Given the importance of the patient-caregiver relationship, there is a need for more dyadic research during the pre-transplant period in HSCT.

This cross-sectional study focuses on pre-transplant dis-tress in Allo-HSCT patients and their caregivers and how distress in the dyad relates to patient QoL pre-transplant. The purpose is to: (1) compare patient and caregiver pre-transplant psychosocial, sleep, and patient QoL variables to established norms; (2) examine the relationship between pre-transplant caregiver distress and patient QoL, while control-ling for pre-transplant patient distress, and (3) examine how these dyadic relationships relate to specific domains of patient QoL.

Methods

The cross-sectional findings described in this study uti-lized pre-transplant baseline data from part of a larger study assessing the effectiveness of a randomized stress management intervention for caregivers of Allo-HSCT patients and its effects on patients' QoL (currently un-der review; all data presented here are collected prior to randomization).

Participants

From March 7, 2014 to November 2, 2016, we approached 407 Allo-HSCT patients/caregivers dyads admitted for treat-ment to two transplant programs in the Denver area for par-ticipation in this study: a university-based NCI-designated comprehensive cancer center and a private community-based hospital.

Eligibility criteria for both patient and their primary care-giver facing Allo-HSCT included: (1) ability to speak/read English and (2) 18 years or older. In addition, for caregivers, eligibility included willingness to use a smartphone and avail-ability to participate in the intervention (if randomized). Exclusion criteria included: (1) uncontrolled psychiatric dis-order in patient or caregiver in the past 18 months; (2) serious medical condition of the caregiver likely to influence bio-markers assessed in the RCT; and (3) caregiver alcohol con-sumption greater than two drinks/day. We defined the caregiv-er as the person in the patient's life primarily responsible for post-transplant care, emotionally invested in the patient, and responsible for major decisions regarding their care.

Of those approached, 331 dyads met the eligibility criteria. Of those eligible, 159 consented to participate (48%). Complete baseline (pre-transplant) data, used for this study, was available on 148 dyads. All subjects provided informed consent and were given monetary reimbursement for partici-pation. The Colorado Multiple Institutional Review Board approved this study (COMIRB#13-2639) and the randomized trial was registered at ClinicalTrials.gov (NCT02037568).

Assessment measures

At consent, patients and caregivers completed paper question-naires (less than 25%) or online via a HIPAA-compliant website, RedCap [16]. Patients and caregivers completed the same assessment measures except patients completed the FACT-BMT (Functional Assessment of Cancer Therapy—Bone Marrow Transplant [17, 18]), and caregivers completed the Caregiver Reaction Assessment (CRA) [19].

Center for Epidemiologic Studies—Depression

The Center for Epidemiologic Studies—Depression (CES-D) is a 20-item depression scale anchored to the past week. Test-retest validity ranges from 0.51 to 0.67 with an internal valid-ity of 0.85 for a normal population [20]. Scores of 16 and above reflect significant depressive symptomatology [21].

State-Trait Anxiety Inventory

The State-Trait Anxiety Inventory (STAI) [22] is a 40-item scale that asks subjects to rate how they feel "right now" (STAI-S used for this study) on a 4-point Likert scale.

Internal consistency ranges from 0.89 to 0.92, and test-retest correlations range from 0.73 to 0.86. The scale has been used in both patient and caregiver populations [23]; higher scores reflect greater anxiety.

Perceived Stress Scale

The 14 item Perceived Stress Scale (PSS) measures the degree to which subjects feel their lives are unpredictable, uncontrollable, and overwhelming during the past month on a 5-point Likert scale [24]. The measure has good reliability and validity [25] and normative data from the general population [26]; higher scores reflect greater perceived stress.

Pittsburgh Sleep Quality Index

The Pittsburgh Sleep Quality Index (PSQI) [27] is a measure of sleep quality anchored to the past month. It has acceptable reliability and validity with diagnostic sensitivity of 89.6% and specificity of 86.5%. [28] Scores ≥ 5 indicate sleep difficulty and poorer sleep quality.

Caregiver Reaction Assessment

The Caregiver Reaction Assessment (CRA) [19], which includes 24 items measuring caregiver burden scored on a 5-point Likert scale with subscales of self-esteem, family support, finances, schedule, and health [29]. It has an excellent test-retest reliability of 0.9 [19] as well as normative data for a caregiver population [30]. Only the Schedule and Health subscales were analyzed as having greater relevance to this study based on the recommendation by the scale's developer (William Given, personal communication, 4/2017). Higher scores signify greater burden.

Functional Assessment of Cancer Therapy—Bone Marrow Transplant

The FACT-BMT (Functional Assessment of Cancer Therapy-Bone Marrow Transplant) [13] consists of the FACT-G (Functional Assessment of Cancer Therapy-General) [14] developed to assess cancer patient QoL in the areas of physical, social/family, emotional, and functional well-being, and a BMT subscale specific to bone marrow transplant. Anchored to the past week, the FACT-G has 27 items and the BMT subscale has 10 items. Both scales have been used extensively in cancer populations [31], and in comparisons with other measures of QoL; the FACT-BMT is one of the more comprehensive instruments of QoL available [32]. Higher scores indicate better quality of life.

Statistical analyses

Data were entered and analyzed in SPSS v24 (IBM, Armook, NY). Path analyses described below were conducted with Mplus version 1.5 [33]. Outcomes included patient and caregiver scores on the CES-D, STAI-State, PSS, PSQI and patient FACT-BMT, and caregiver Schedule and Health subscales of the CRA. All outcomes displayed adequate characteristics of normality. To reduce the number of variables and simplify comparisons, a principal component analysis (PCA) extracted the first principal component from three variables (CES-D, STAI-State, and PSS) individually for the caregiver and their patient. This was conducted with a priori hypotheses and an analytic plan consistent with prior work indicating that these measures provide the highest factor loadings [5]. This PCA yielded composite distress scores for patients (PT-distress) and caregivers (CG-distress). Focused comparisons with Bonferroni correction to reduce type 1 error applied Pearson correlations to PT-Distress and FACT-BMT with aforementioned psychological measures collected from the caregiver—hereafter, referred to as CG well-being. Additional targeted Pearson correlations examined CG-distress with subscales of the FACT-BMT. We applied path analysis to simultaneously account for a hypothesized interdependence of CG-distress and PT-distress in the prediction of FACT-BMT in a single model. This approach, while only focusing on one outcome in the FACT-BMT (not measured in caregivers), is similar to the Actor-Partner Interdependence Model [34] appropriate for dyadic analyses.

Results

Patient and caregiver demographics

Patient illness variables as well as patient and caregiver demographics are shown in Table 1. Most patients were male (65%), average age 53 years old, ranging from 19 to 76 years old. In contrast, most caregivers were female (79%) with similar age (54 years old) and age range (18–82 years old). Most caregivers were spouses of patients (64%). Leukemia was the most common diagnosis (61%). The patient population mirrors national trends for racial distribution as reported by the Center for International Blood and Marrow Transplantation [35].

Pre-transplant patient and caregiver distress

Means and standard deviations of pre-transplant patient and caregiver measures of well-being (depression, anxiety, perceived stress, sleep, patient QoL, and caregiver burden) are shown in Table 2 along with established norms. Numbers/percentages of patients and caregivers who exceeded clinical threshold scores or were above reported population means by ± 1 SD are indicated. Over 65% of patients scored above threshold scores on the CESD and the PSQI. Nearly half of the patients fell above population norms by one SD for STAI and PSS. Sixty-nine percent of patients scored below the pre-

Table 1 Baseline characteristics of patient and caregiver (N = 159)

Variable	N (%)
Patient[b]	
Mean age (sd), years	53.3 (14.8)
Range	19–76
Sex	
Female	56 (35.2)
Male	103 (64.8)
Race	
White	125 (78.6)
Black or African-American	2 (1.3)
Native Hawaiian or other Pacific Islander	2 (1.3)
More than one race	5 (3.1)
Another group not listed	6 (3.8)
Ethnicity	
Hispanic or Latino	13 (8.2)
Non-Hispanic or Latino	121 (76.1)
Annual income, $	
< 25,000	45 (28.3)
25,000–44,999	28 (17.6)
45,000–64,999	19 (11.9)
> 65,000	30 (18.9)
Diagnosis[a]	
Leukemia	97 (61.0)
Lymphoma	21 (13.2)
MDS/MPS	35 (22.0)
Other	6 (3.8)
Mean Duration of Illness (sd), month	19.9 (34.2)
Range	1.6–195.3
Transplant conditioning intensity	
Myeloablative	88 (55.3)
Non-myeloablative	17 (10.7)
Reduce intensity	40 (25.2)
Donor source	
Matched related donor	48 (30.2)
Matched unrelated donor	57 (35.8)
Mismatched unrelated donor	8 (5.0)
Cord	39 (24.5)
Other	5 (3.1)
Caregiver[c]	
Mean age (sd), years	54.1 (13.7)
Range	18–82
Sex	
Female	125 (78.6)
Male	31 (19.5)
Race	
White	130 (81.8)
American Indian or Alaska Native	1 (0.6)
Black or African-American	2 (1.3)
More than one race	6 (3.8)
Another group not listed	6 (3.8)

Table 1 (continued)

Variable	N (%)
Ethnicity	
Hispanic or Latino	14 (8.8)
Non-Hispanic or Latino	129 (81.1)
Education	
College graduate or above	116 (73.0)
Annual income (reported by patient), $	
< 25,000	50 (31.4)
25,000–44,999	27 (17.0)
45,000–64,999	31 (19.5)
> 65,000	29 (18.2)
Relationship	
Spouse/partner	102 (64.2)
Parent	20 (12.6)
Other	29 (18.2)
Employment status (before caregiving)	n (%)
Full-time	65 (40.9)
Part-time	27 (17.0)
Unemployed	16 (10.1)
On leave	2 (1.3)
Retired	40 (25.2)

[a] MDS, myelodysplastic syndrome; MPS, myeloproliferative syndrome

[b] Patient information was not available for the following variables: race (n = 19), ethnicity (n = 25), annual income (n = 37), duration of illness (n = 17), transplant conditioning intensity (n = 14), and donor source (n = 2)

[c] Caregiver information was not available for the following variables: age (n = 3), sex (n = 3), race (n = 14), ethnicity (n = 16), education (n = 8), annual income (n = 22), relationship (n = 8), employment status before caregiving (n = 9), and after caregiving (n = 11)

transplant norm for FACT-BMT, reflecting worse quality of life. For caregivers, nearly three quarters scored above the clinical threshold for depressive symptoms, and 68% scored above the threshold for sleep difficulties. Over half scored above the population norm for state anxiety and perceived stress, 58 and 65%, respectively. Caregiver responses to burden exceeded population norms on the CRA Schedule (61%) and Health (40%) subscales [30].

Bivariate relationship between patients' FACT-BMT and caregiver well-being

As expected, bivariate comparisons between caregiver psychological measures and their patient's distress yielded a number of significant relationships. After applying a Bonferroni correction for repeated comparisons, caregivers' Perceived Stress Scale scores (r = .32) and STAI-State (r = .33) were significantly (p's ≤ .001) related to the composite patient distress measure. However, there were no significant relationships with caregivers' CESD scores, PSQI scores, or the two selected markers

Table 2 Descriptive statistics of patient and caregiver behavioral measures (N = 159) at baseline compared to normative samples

Assessment measure	Mean (SD)	Population mean (SD)	N (%) caregivers ≥ threshold or > population mean by 1 SD
Patients			
CES-D	20.4 (6.8)	Depression threshold ≥ 16	N = 107 (67%)
STAI-S	36.8 (11.6)	35.96 (1.1)	N = 66 (42%)
PSS	21.6 (7.9)	19.1 (7.1)	N = 40 (25%)
PSQI	8.9 (4.3)	Sleep difficulty threshold ≥ 5	N = 109 (69%)
FACT-BMT*	97.9 (18.3)	113.7 (17.9)	N = 63 (40%)
PWB	16.9 (6.5)	21.6 (5.3)	N = 65 (41%)
SWB	23.2(4.3)	24.0 (3.8)	N = 30 (19%)
EWB	18.4 (3.6)	15.2 (3.1)	N = 12 (8%)
FWB	14.2 (5.1)	17.7 (5.5)	N = 59 (37%)
BMTS	25.2 (5.7)	27.9 (5.4)	N = 46 (29%)
Caregivers			
CES-D	20.3 (6.6)	Depression threshold ≥ 16	N = 117 (74%)
STAI-S	40.6 (12.9)	35.96 (1.1)	N = 79 (50%)
PSS	25.0 (8.4)	19.1 (7.1)	N = 67 (42%)
PSQI	8.0 (3.9)	Sleep difficulty threshold ≥ 5	N = 108 (68%)
CRA			
Schedule	2.86 (3.9)	2.44 (0.84)	N = 51 (32%)
Health	1.86 (0.66)	1.98 (0.62)	N = 25 (16%)

CES-D, Center for Epidemiologic Studies—Depression; *STAI-S*, State-Trait Anxiety Inventory—State Anxiety; *PSS*, Perceived Stress Scale; *PSQI*, Pittsburgh Sleep Quality; *FACT-BMT*, Functional Assessment of Cancer Therapy—Bone Marrow Transplant; *PWB*, physical well-being; *SWB*, social well-being; *EWB*, emotional well-being; *FWB*, functional well-being; *BMTS*, Bone Marrow Transplant Subscale; *CRA*, Caregiver Reaction Assessment

*For FACT, higher scores are better QoL

of caregiver burden (impact on schedule and health, Table 3). Patients' FACT-BMT scores showed a number of significant relationships, all in the anticipated direction, such that greater caregiver well-being was related to higher patient FACT-BMT (in a negative direction based on coding). First, the CRA Impact Health was significantly correlated with patient FACT-BMT scores (r = − .31; p ≤ .001), which appeared to be driven by the patient's physical well-being (r = − .28; p ≤ .001). Other FACT subscales were nonsignificant following the Bonferroni correction. Second, caregivers' PSS, CESD, and STAI-State scores were all significantly related to their patients' total FACT-BMT score (r's between − .31 and − .35; all p's ≤ .001), as well as the patient's physical well-being subscale (r's between − .28 and − .30; all p's ≤ .001). There were no significant correlations between measures of caregiver well-being and patient's social well-being nor functional well-being scores. Finally, there were no significant relationships between caregiver PSQI and any domain of the FACT-BMT.

Bivariate relationship among caregiver distress and FACT-BMT

Bivariate comparisons of the PCA-derived composite measure of CG-distress yielded several significant relationships with subscales of patient FACT-BMT as well as total FACT-BMT (Table 4). Physical well-being (r = − .32, p < .001), emotional well-being (r = − .29, p < .001), and physical functioning specific to BMT-related symptoms (r = − .33, p < .001) were negatively related to CG-distress as was the total score (r = − .36, p < .001). These relationships fit expectations such that greater distress was related to lower scores. Caregiver PSQI was unrelated to the FACT-BMT and its' subscales.

Relationship of caregiver distress to patient FACT-BMT

Path analyses simultaneously measured the shared contribution of PT and CG-distress to PT-FACT scores, the results of which are displayed in Fig. 1. Results indicated that CG-distress remained a significant predictor of patient overall QoL (β = − .15, p < .05) after accounting for the stronger association between PT-distress and patient QoL (β = .64; p < .001) and the shared variance of PT and CG-distress (r = .33; p < .05). In examining the subscales of the FACT, CG-distress was only significantly related to the patients' physical functioning subscale (β = − .18; p < .05) after controlling for the shared variance of PT and CG-distress (r = .33; p < .05).

Table 3 Caregiver measures of well-being compared across domains of patients' quality of life and distress (N = 144*)

Psychological measure	FACT-BMT	PWB	SWB	EWB	FWB	BMTS	PT-distress
Caregiver							
CRA							
Schedule	− .177	− .227	− .029	− .215	.006	− .165	.136
Health	− .302**	− .283**	− .137	− .206	− .200	− .228	.167
PSS	− .353**	− .302**	− .116	− .283**	− .248	− .304**	.320**
CES-D	− .318**	− .276**	− .087	− .190	− .173	− .342**	.253
STAI-S	− .309**	− .292**	− .103	− .294**	− .161	− .255	.328**
PSQI	− .270	− .236	− .079	− .117	− .207	− .277	.193

FACT-BMT, Functional Assessment of Cancer Therapy—Bone Marrow Transplant; *PWB*, physical well-being; *SWB*, social well-being; *EWB*, emotional well-being; *FWB*, functional well-being; *BMTS*, Bone Marrow Transplant Subscale; *CRA*, Caregiver Reaction Assessment; *PSS*, Perceived Stress Scale Global Scale Score; *CES-D*, Center for Epidemiologic Studies—Depression; *STAI-S*, State-Trait Anxiety Inventory—State Anxiety; *PSQI*, Pittsburgh Sleep Quality Index; CG-distress = factor analysis score of CES-D, STAI-S, PSS

*Complete data was not available on all patients and caregivers

**p ≤ .001 (2-tailed)

Discussion

A large proportion of patients and caregivers reported elevated anxiety and stress pre-transplant, and over half of patients and caregivers reported depressive symptoms and sleep difficulties above clinical thresholds similar to previous studies [4, 5]. In addition, most transplant patients reported poor QoL (below population norms). Elements of patients' QoL suggest that while PT and CG-distress are interrelated and significantly impact the total FACT-BMT, the primary contributor to this relationship appears to be the patient's pre-transplant physical functioning (physical well-being subscale of the FACT). Interestingly, when shared PT and CG-distress are accounted

Table 4 Bivariate relationships among patient and caregiver distress and patient quality of life subscales (N = 144*)

Psychological measure	CG-distress
Patient	
FACT-BMT	− .364**
PWB	− .315**
SWB	− .114
EWB	− .288**
FWB	− .221
BMTS	− .332**

CG-distress = first principle component of CES-D, STAI-S, PSS. *FACT-BMT*, Functional Assessment of Cancer Therapy—Bone Marrow Transplant; *PWB*, physical well-being; *SWB*, social well-being; *EWB*, emotional well-being; *FWB*, functional well-being; *BMTS*, Bone Marrow Transplant Subscale

*Complete data was not available for all dyads

**p ≤ .001 (2-tailed)

for, CG-distress was unrelated to their patient's emotional, social, and functional well-being as measured by subscales of the FACT-BMT. This suggests that the shared measures in the distress composite score capture the majority of the distress within dyads that contribute to patients' QoL. These findings are important in conjunction with emerging literature highlighting the contribution of pre-transplant quality of life to important clinical outcomes.

In the current study, we sought to describe overlap in measures of caregiver/patient well-being, distress, and QoL. Understanding these specific interrelationships in patient caregiver dyad is vital for informing supportive interventions. We focused on separate subscales of the FACT-BMT to explore this overlap. The results, in both bivariate comparisons as well as a simultaneous model removing the shared variance of PT and CG-distress, demonstrated that social, emotional, and functional well-being of the patients' QoL were unrelated to CG-distress. However, relations of patient physical well-being and FACT-BMT approached significance such that BMT-specific physical symptoms were still related to patient and caregiver distress, suggesting that physical symptoms specific to the BMT process may be particularly salient in relating to the shared distress within dyads. In our prior work, quality of life was significantly related in caregivers and patients [5]. In non-HSCT cancer populations, patient and spouse psychological well-being was the strongest predictor of patient QoL, while the distress of their partner remained a significant predictor of the patients' QoL. [36] Results replicate these findings, such that patients' distress was the strongest predictor of their own QoL, while building on this work in that caregiver well-being remained a significant predictor after controlling for this relationship. This finding is supported by a cross-sectional analysis of caregivers about to care for HSCT patients finding that QoL was related to family support that
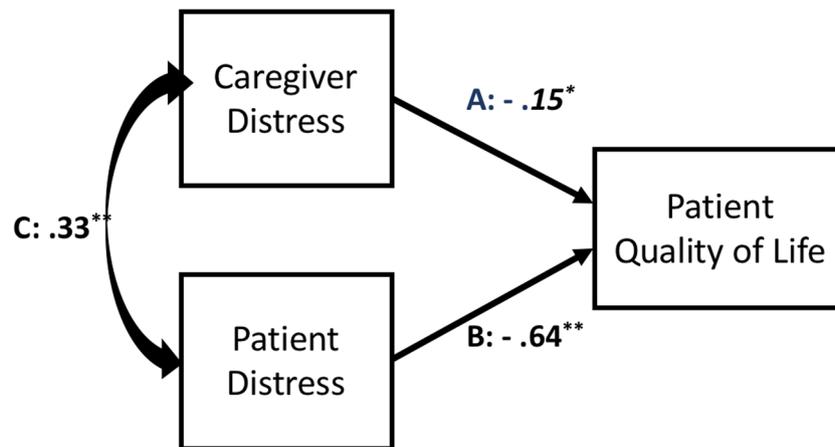
Fact Subscale	A. Beta estimate of *caregiver* distress predicting patients' domains of QOL	SE	B. Beta estimate of *patient* distress predicting patients' domains of QOL	SE	C. Shared distress (correlation) among patient and caregiver distress
Emotional Well-being	-.053	.093	-.22*	.094	.33**
Physical Well-being	-.18*	.078	-.41**	.074	.34**
Social Well-being	-.053	.093	-.22*	.094	.33**
Functional Well-being	-.068	.080	-.47**	.072	.33**
BMT-specific subscale	-.13	.069	-.61**	.057	.34**

*p ≤ .05 (2-tailed); **p ≤ .01 (2-tailed).

Fig. 1 Path diagram accounting for shared variance of PT/CG-distress in the prediction of patient quality of life. *p ≤ .05 (2-tailed); **p ≤ .01 (2-tailed). Figure presented demonstrates simultaneous estimation of shared correlation between patient and caregiver distress composite score, in addition to predicting patients' quality of life (overall FACT-BMT score). Separate models are then presented for each FACT-BMT subscale, with respective path coefficients (A, B, C) outlined in the figure corresponding to values in the table below

further was a significant predictor of objective burden [37]. Cancer and the transplant process affects the dyad as a unit—they cope together with a reciprocal influence on each other [38]. The present results support the importance of approaching each patient-caregiver dyad as the unit of intervention in the transplant process at an early stage.

In addition to shared distress within dyads, caregiver level of distress deserves a comment. Indeed, caregivers had poor levels of well-being in this study in the month preceding transplant. This highlights the challenges caregivers face even before the transplant process begins. Caregiver well-being and ability to provide attentive support for Allo-HSCT patients is an important component of a successful transplant. For example, pre-transplant caregiver's perceived emotional support predicts patient pre-transplant anxiety, depression, and post-transplant distress; in addition to being associated with longer survival in Allo-HSCT patients [39]. Further, patients' pre-transplant anxiety and depression predict worse QoL throughout the early

post-transplant hospitalization [5], an increase in GvHD, and lower overall survival [40]. Transplant programs require caregivers, but screening for caregiver distress is not necessarily a standard of care. Identifying and intervening with distressed caregivers would not only lower their distress [41] but may have a positive effect on patient outcome. Screening prior to transplant, using abbreviated formats, such as PROMIS measures [42] or distress screening [43], could identify patients as well as caregivers with elevated depression and low QoL to target interventions for vulnerable dyads. Expanding pre-transplant screening in Allo-HSCT to caregivers is an important direction given the roles caregivers play in maintaining patient well-being during the transplant process.

Study limitations

A study limitation includes lack of diversity in the patient/caregiver population (most caregivers were Caucasian and

well educated). As such, subgroup analyses were not possible. Future studies should strive to recruit diverse groups of patients and caregivers to further parse out for whom psychological services are most needed and how psychological presentation may differ across demographic groups. Another limitation is the cross-sectional design. The present participants were part of a study in which both members of the dyad were followed longitudinally as part of a randomized control study (currently under review). Finally, it is worth noting that the analytic model presented here—an application of the APIM [34]—was unable to test separate variables measured in both patients and caregivers, as QoL was only operationalized in patients. As new analytic approaches continue to emerge, we can better understand caregivers' needs as they change over time and then plan long-term follow-up interventions as a priority [44] in care of HSCT patients and their families.

Clinical implications

Due to distress noted in this study, the pre-transplant period is important in predicting later well-being in Allo-HSCT patients, which may affect transplant outcome [45]. After accounting for their overlapping distress, patients' physical well-being appears to drive shared influences on quality of life within dyads. Thus, the importance of screening for psychological distress in both patients and caregivers is important. Future research should assess the relationship between caregiver well-being and patient outcome, and whether caregiver or dyadic interventions improve patient QoL.

Compliance with ethical standards

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

Ethics statement All subjects provided informed consent and were given monetary reimbursement for participation. The Colorado Multiple Institutional Review Board approved this study (COMIRB#13-2639) and the randomized trial was registered at ClinicalTrials.gov (NCT02037568).

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