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Spiritual Absence and 1-Year Mortality after Hematopoietic Stem Cell Transplant

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Religiosity and spirituality have been associated with better survival in large epidemiologic studies. This study examined the relationship between spiritual absence and 1-year all-cause mortality in allogeneic hematopoietic stem cell transplant (HSCT) recipients. Depression and problematic compliance were examined as possible mediators of a significant spiritual absence-mortality relationship. Eighty-five adults (mean = 46.85 years old, SD = 11.90 years) undergoing evaluation for allogeneic HSCT had routine psychologie evaluation prior to HSCT admission. The Millon Behavioral Medicine Diagnostic was used to assess spiritual absence, depression, and problematic compliance, the psychosocial predictors of interest. Patient status at 1 year and survival time in days were abstracted from medical records. Cox regression analysis was used to examine the relationship between the psychosocial factors of interest and mortality after adjusting for relevant biobehavioral factors. Twenty-nine percent (n = 25) of participants died within 1 year of HSCT. After covarying for disease type, individuals with the highest spiritual absence and problematic compliance scores were significantly more likely to die 1-year post-HSCT (hazard ratio [HR] = 2.49, $P = .043$ and HR = 3.74, $P = .029$, respectively), particularly secondary to infection, sepsis, or graft-versus-host disease (GVHD) (HR = 4.56, $P = .01$ and HR = 5.61, $P = .014$), relative to those without elevations on these scales. Depression was not associated with 1-year mortality, and problematic compliance did not mediate the relationship between spiritual absence and mortality. These preliminary results suggest that both spiritual absence and problematic compliance may be associated with poorer survival following HSCT. Future research should examine these relations in a larger sample using a more comprehensive assessment of spirituality.

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INTRODUCTION

Since the establishment of the National Marrow Donor Program in 1987, over 30,000 unrelated donor hematopoietic stem cell transplants (HSCT) have been facilitated. Over 70% of these recipients have been adults with hematologic malignancies, such as acute myelogenous leukemia (AML) or acquired hematologic conditions, such as severe aplastic anemia. Over the past 20 years, HSCT treatment mortality has significantly declined in tandem with significant improvements in 1- and 2-year survival rates. Nonetheless, between 2003 and 2006, the 1-year mortality rate following HSCT for the acute leukemias and myelodysplastic syndrome (MDS) still approached approximately 50%, suggesting that hematologic malignancies treated with HSCT cause substantial mortality among adults [1].

Over the past 15 years, there has been considerable interest in identifying psychosocial predictors of mortality among HSCT recipients [2]. Although these studies differ in disease inclusion criteria, follow-up period length, and psychosocial assessment methodology, several factors have emerged across these studies as predictors of poorer survival following HSCT. Anxious preoccupation [3], distraction coping [4], problematic social support [5], depressive symptoms [6-9], and poorer functional quality of life [3] have been associated with poorer survival post-HSCT, whereas higher levels of available social support [10]

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and fighting spirit coping [4] have been associated with better survival post-HSCT.

Religiosity and spirituality are 2 common methods by which people cope with stressful life events, such as the diagnosis and treatment of a life-limiting illness [11,12]. Approximately 84% of Americans report affiliation with a religion, and 82% report religion as at least somewhat or very important in their lives [13]. In 2 recent large-scale studies of cancer survivors, 62% reported being "very" or "moderately" religious [14], 69% reported having prayed for their own health [15], and 65% reported being "very" or "moderately" spiritual [14]. Two smaller-scale studies with more homogenous cancer patient populations (ie, malignant melanoma only, breast cancer only) suggest that nearly 85% to 90% of patients report that they are spiritual or that spirituality is important in their lives [16,17]. Despite the fact that religiosity and spirituality have been described as the most commonly used "complementary therapies" by individuals with cancer [14], no published research has examined the relationship between spirituality and health outcomes in HSCT recipients.

Several systematic reviews of the literature support a relationship between greater religious involvement and lower all-cause mortality [18,19]. In several large-scale studies, less frequent religious attendance [20,21] and participation [22] were associated with greater odds/hazards ratios of mortality, and these relationships were at least partially explained by poorer health status [20], less social integration [20], engagement in unhealthy behaviors [20,21], and greater systemic inflammation [21,22] among individuals low in religiosity. Less is known about whether spirituality (a cognitive schema that organizes one's approach to coping with difficult life circumstances [12]) per se is associated with lower all-cause mortality. Furthermore, few studies have examined the relationship between either religiosity or spirituality and cancer morality, specifically. The few published studies in this area have not supported a robust relationship between religiosity/spirituality and cancer mortality, particularly after controlling for biobehavioral confounding variables [19]. For instance, although Van Ness and colleagues [23] found that women with breast cancer who reported having no religious denomination preference had a greater hazard ratio of breast cancer mortality, other measures of religiosity were unrelated to breast cancer mortality, and spirituality was not assessed. Thus, the possibility exists that lack of documented relationship between religiosity/spirituality and cancer mortality may be partially because of the relative lack of methodologically strong studies that incorporate measures of spirituality in addition to religious participation [19].

The purpose of the present study was to examine the relationship between spirituality and 1-year survival among HSCT recipients. It was hypothesized that individuals high in spiritual absence would have greater hazards of mortality than individuals high in spiritual faith. Gall and Grant [12] posit that a relationship between spirituality and positive health outcome may be mediated by positive affect and engagement in healthy behaviors. Consistent with this theory, high levels of depressed mood and poor medical adherence were examined as mediators of a significant spiritual absence-mortality relationship.

PATIENTS AND METHODS

Data for the present study were collected as part of a larger study [24-26] examining immune status, immune functioning, and clinical outcomes among HSCT recipients (N = 209). The present sample included 85 individuals who underwent routine pre-HSCT diagnostic interviews in the Psychology Clinic at the University of Florida, completed the Millon Behavioral Medicine Diagnostic (MBMD) [27] at that visit, subsequently underwent HSCT between 2002 and 2006, and survived at least 30 days post-HSCT. One hundred twenty-three individuals enrolled in the larger study were not included in the present sample because they were not administered the MBMD. (Prior to 2004, some Psychology Clinic providers administered alternate psychosocial instruments to HSCT candidates.) One individual with MBMD data was excluded, as her post-HSCT survival was <30 days. All study procedures were approved by the institutional review board at the University of Florida Health Science Center in accordance with an assurance filed with and approved by the Department of Health and Human Services, and informed consent was obtained from each participant.

Study Measures

Spirituality and associated factors

The MBMD is a 165-item true/false self-report instrument that assesses psychosocial factors that may influence the course of treatment of medical illness. It has excellent reliability and validity [27]. The MBMD contains 7 domains, including Response Patterns, Negative Health Habits, Psychiatric Indications, Coping Styles, Stress Moderators, Treatment Prognostics, and Management Guides. Spiritual absence versus spiritual faith is a Stress Moderator scale that assesses the degree to which patients lack religious or spiritual personal resources to cope with medical stressors. Individuals scoring high on spiritual absence often endorse the following items "I am not a very spiritual person" and "I have no deep religious beliefs." The spiritual absence scale correlates highly (0.75-0.85) with the most widely used medically

relevant measure of spirituality, the Spiritual Beliefs Inventory (SBI) [28]. As per the theory outlined by Gall and Grant [12], spiritual absence may be associated with negative health outcomes via maladaptive health behaviors and/or maintenance/exacerbation of negative mood. Therefore, the present study also examined the degree to which problematic compliance versus optimal compliance (a Treatment Prognostic scale) and depression (a Psychiatric Indication scale) may have accounted for a possible relationship between Spiritual Absence and HSCT survival. Noncompliant individuals are likely to response False to items such as "I make sure that I'm on time for all my doctor's appointments" and "I would change my lifestyle on my doctor's advice." Individuals scoring high on the depression scale often endorse the following items: "I've lost interest in things that I used to find pleasurable" and "I have been having serious thoughts about suicide." The MBMD Depression scale correlates highly (0.72-0.87) with the widely used Beck Depression Inventory (BDI) [29].

The MBMD yields a Prevalence Score (PS) for each subscale. A PS of 75 to 84 suggests that the factor is a moderate or present liability for the health and well-being of the patient, whereas a PS of 85 to 115 suggests that the factor is a marked or prominent liability for the health and well-being of the patient. Thus, spiritual absence, problematic compliance, and depression were coded as "no liability" ("0"), "moderate liability" ("1"), or "marked liability" ("2").

Patient characteristics, health behaviors, and health/treatment status

Patient characteristics, including age and race/ethnicity; health behaviors, including use of psychotropic medications and/or corticosteroids (either of which can influence mood and behavior); and health/treatment status variables, including cancer type, disease risk group (ie, risk for treatment failure based upon disease type and status, see Tables 1 and 2 for a description of these risk groups) [26] and HSCT type (myeloablative or nonmyeloablative) were collected via patient interview and/or medical record review and abstraction.

Survival

Patient survival time and status were abstracted from medical records in January 2010. Survival time was calculated in number of days after HSCT until death (event) or date of last documented visit to the UF Health Science Center (censored). Patient status (censored ["0"] or event ["1"]) at 1-year post-HSCT was then calculated from these data. The primary outcome variable was 1-year all-cause mortality; however, 1-year HSCT-related mortality was examined as a secondary outcome variable. HSCT-related mortality was defined as death due to transplant-associated infection, sepsis, or graft-versus-host disease (GVHD).

Statistical Analyses

Descriptive statistics were first computed on all study variables. Participants from the larger study with complete psychological and MBMD data (n = 85) were compared to those without complete psychological and/or MBMD data (n = 124) on major demographic and health treatment/status variables using one-way analysis of variance (ANOVA) and chi-square analyses. Univariate Cox regression analysis was used to assess the relationship between potential biobehavioral control variables (eg, age, disease risk group, and HSCT type) and 1-year survival. Variables significantly associated with survival at $P \leq .05$ were entered as covariates into subsequent multivariate Cox regression analyses. Multivariate Cox regression analyses were then used to determine the hazards ratio (HR) for survival associated with spiritual absence, problematic compliance, and depression liability groups, respectively, after adjusting for biobehavioral covariates. Survival functions were plotted to illustrate the relationship between liability groups and survival.

RESULTS

The 85 patients in the present study were compared to the 124 patients without a psychosocial evaluation and/or MBMD data from the larger study on major demographic and health status/treatment variables to assess for any systematic differences between the 2 groups. The 85 patients in the present study did not differ from the 124 patients form the larger study on age, sex, HSCT type, disease type, participant relationship to donor, or graft source at $P \leq .05$. A greater proportion of participants from the larger study were classified as having high disease risk compared to those in the present study, χ^2 (1, N = 209) = 4.33, $P = .04$ (Table 1).

Table 1 presents the participants' characteristics. Briefly, participants were 46 adult males (54%) and 39 adult females (46%) with a mean age of 46.85 years (SD = 11.90 years) who were mostly White, non-Hispanic (86%, n = 73), and married (76%, n = 65). The majority of patients were diagnosed with acute leukemia or MDS (63%, n = 54) whose disease was classified as having a high risk of treatment failure (73%, n = 62). Sixty-nine percent (n = 59) of participants underwent peripheral blood stem cell transplant. Twenty-nine percent (n = 25) of participants died within 1 year post-HSCT. The mean number of days survived for patients who died within 1 year was 174 (SD = 124). For the 71% (n = 60) of patients who lived longer than 1-year post-HSCT, the mean number of days survived was 1043 (SD = 406). Percentages of

Table 1. Participant Characteristics

Variable	No.	%	Mean	SD
Age*			46.85	11.90
Sex*				
Male	46	54		
Female	39	46		
Married				
Single/never married, divorced, widowed	19	22		
Married	65	76		
Not reported	1	2		
Race/ethnicity				
White, non-Hispanic	73	86		
Black/African-American	4	5		
Hispanic	6	7		
Asian	1	1		
Not reported	1	1		
Tobacco use at pretransplant				
Lifetime nonuser	42	49		
Current user (within Last 90 days)	7	8		
Past user (>90 days abstinence)	36	42		
Alcohol use at pretransplant				
Lifetime nonuser	37	44		
Current user (within last 90 days)	24	28		
Past user (>90 days abstinence)	24	28		
Marijuana use at pretransplant				
Lifetime nonuser	76	89		
Current user (within last 90 days)	0	0		
Past user (>90 days abstinence)	9	11		
Psychotropic medication/steroid use at pretransplant				
No	54	64		
Yes	28	33		
Not reported	3	3		
Caregiver identified at pretransplant				
No	2	2		
Yes	83	98		
HSCT Type*				
Nonmyeloablative	28	33		
Myeloablative	57	67		
Participant relation to donor*				
Related	48	56		
Unrelated	37	44		
Graft Source*				
Bone marrow	23	27		
Peripheral blood stem cell	59	69		
Umbilical cord	3	4		
Disease risk*,†,‡				
Low	23	27		
High	62	73		
Acute leukemia or myelodysplastic syndrome*				
No	31	37		
Yes	54	63		
Developed aGVHD§				
No	63	74		
Yes	21	25		
Developed cGVHD by 1 year§,¶				
No	39	46		
Yes	18	21		
Died within 1 year				
No (censored)	60	71		
Yes (expired)	25	29		
Days survived				
Participants expired at 1 year			173.56	124.02
Participants censored at 1 year			1043.15	406.23
Total sample			787.39	528.36
Primary cause of death at 1 year				
Disease progression	12	46		
GVHD	4	25		
Infection/sepsis	8	35		
New/secondary malignancy	1	4		
Spiritual absence liability group				
No liability	70	82		
Moderate liability	3	4		
Marked liability	12	14		
Problematic compliance liability group				
No liability	62	73		
Moderate liability	16	19		
Marked liability	7	8		
Depression liability group				
No liability	76	89		
Moderate liability	8	10		
Marked liability	1	1		

HSCT indicates hematopoietic stem cell transplant; aGVHD, acute graft-versus-host-disease; cGVHD, chronic graft-versus-host disease.

*Variables on which participants in the present study were compared to nonincluded participants from the larger study.

†A greater proportion of nonincluded participants from the larger study were classified as having high risk for treatment failure (i.e., high-disease risk) compared to those in the present study, χ^2 (1, N = 209) = 4.33, P = .04. There were no other differences between the two groups on any of the other variables examined* at $P \leq .05$.

‡High-disease risk: acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL) other than first complete remission (CR1), primary induction failure; acute leukemia from antecedent hematologic disorder; chronic myelogenous leukemia not in first chronic phase (CML not CP1); chronic lymphocytic leukemia (CLL); acute bilineage leukemia (ABIL); non-Hodgkin lymphoma (NHL); Hodgkin disease (HD); myelodysplastic syndrome (MDS) not refractory anemia (RA) or ringed sideroblasts (RARS); multiple myeloma (MM); eosinophilic leukemia. Low-disease risk: ALL CR1; AML CR1; CML CP1; MDS RA, RARS.

§Does not include 1 participant who developed cGVHD from prior HSCT.

¶Does not include 21 participants who developed aGHVD or 6 participants who died <100 days post-HSCT.

participants scoring in the moderate to marked liability range on the spiritual absence, problematic compliance, and depression subscales were 18% (n = 15), 27% (n = 23), 10% (n = 9), respectively (Table 1).

Univariate Cox regression analyses (Table 2) examining demographic and biobehavioral covariates on 1-year all-cause mortality indicated that only having acute leukemia or MDS was significantly associated with death at 1 year, HR = 5.00, P = .009. Thus, the presence of acute leukemia or MDS was retained as a covariate in subsequent multivariate Cox regression analyses. There were nonsignificant trends for recipients undergoing (1) myeloablative and (2) unrelated HSCTs to have greater HRs for 1-year all-cause mortality; however, these variables were not covaried, as their 95% confidence intervals (CIs) included a value of "1."

Tables 3 and 4 present the results of multivariate Cox regression analyses examining the relationship between 1-year mortality and spiritual absence and 1-year mortality and problematic compliance, respectively. After covarying for disease type, HSCT recipients with MBMD spiritual absence scores in the marked liability range had a greater hazard of 1-year all-cause mortality (HR = 2.49, P = .043) and 1-year

Table 2. Univariate Cox Regression Analyses for Demographic and Biobehavioral Factors and 1-Year All-Cause Mortality

Variable	*B*	HR*	95% CI	
Age	0.02	1.01	.98 -	1.05
Sex				
Male		1.00		
Female	0.06	1.06	.49 -	2.33
Married				
Single/never married, divorced, widowed		1.00		
Married	0.87	2.38	.71 -	7.99
Race/ethnicity				
White, non-Hispanic		1.00		
Other (Black/African-American, Asian, or Hispanic of any race)	−0.62	.54	.13 -	2.28
Tobacco use at pretransplant				
Lifetime nonuser		1.00		
Current user (within last 90 days)	−0.64	.53	.07 -	4.13
Past user (>90 days abstinence)	0.60	1.82	.81 -	4.10
Alcohol use at pretransplant				
Lifetime nonuser		1.00		
Current user (within last 90 days)	−0.63	.54	.19 -	1.49
Past user (>90 days abstinence)	−0.51	.60	.23 -	1.56
Marijuana use at pretransplant				
Lifetime nonuser		1.00		
Current user (within last 90 days)		n/a		
Past user (>90 days abstinence)	0.26	1.30	.39 -	4.33
Psychotropic medication/steroid use at pretransplant				
No		1.00		
Yes	−0.48	.62	.24 -	1.57
Caregiver Identified at pretransplant				
No	0.56	1.74	.24 -	12.91
Yes		1.00		
HSCT type				
Nonmyeloablative		1.00		
Myeloablative	−0.73	.48‡	.22 -	1.06
Participant relation to donor				
Related		1.00		
Unrelated	0.74	2.10‡	.94 -	4.68
Graft source				
Bone marrow		1.00		
Peripheral blood stem cell	0.41	1.50	.56 -	4.02
Umbilical cord	0.26	1.30	.15 -	11.14
Disease risk†				
Low		1.00		
High	−0.09	.92	.38 -	2.19
Acute leukemia or myelodysplastic syndrome				
No		1.00		
Yes	1.61	5.00¶	1.49 -	16.71
Spiritual absence liability group				
No liability		1.00		
Moderate liability	−12.05	0.00	.00 -	n/a
Marked liability	1.00	2.70§	1.13 -	6.50
Problematic compliance liability group				
No liability		1.00		
Moderate liability	0.46	1.59	.62 -	4.10
Marked liability	1.14	3.13§	1.04 -	9.47
Depression liability group				
No liability		1.00		
Moderate liability	−1.06	.35	.05 -	2.57
Marked liability	−11.12	0.00	.00 -	n/a

HSCT indicates hematopoietic stem cell transplant. aGVHD, acute graft-versus-host-disease; cGVHD, chronic graft-versus-host disease; CI, confidence interval; HR, hazard ratio.

*1.00 Denotes reference category.

†High disease risk: acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL) other than first complete remission (CR1), primary induction failure; acute leukemia from antecedent hematologic disorder; chronic myelogenous leukemia not in first chronic phase (CML not CP1); chronic lymphocytic leukemia (CLL); acute bilineage leukemia (ABIL); non-Hodgkin lymphoma (NHL); Hodgkin disease (HD); myelodysplastic syndrome (MDS) not refractory anemia (RA) or ringed sideroblasts (RARS); multiple myeloma (MM); eosinophilic leukemia. Low disease risk: ALL CR1; AML CR1; CML CP1; MDS RA, RARS.

‡$P < .10$

§$P < .05$

¶$P < .01$.

Table 3. Multivariate Cox Regression Analyses Examining the Relationship Between Spiritual Absence and 1-Year Mortality

	β	HR*	95% CI		
Outcome no. 1: 1-Year mortality, all-cause					
Acute leukemia or myelodysplastic syndrome					
No		1.00			
Yes	1.64	5.15§	1.54	-	17.26
Spiritual absence liability group					
No liability		1.00			
Moderate liability	−12.64	.00	.00	-	n/a
Marked liability	0.91	2.49‡	1.03	-	6.01
Outcome no. 2: 1-Year mortality, HSCT-related (infection/ sepsis, GVHD)					
Acute leukemia or myelodysplastic syndrome					
No		1.00			
Yes	1.19	3.28	.72	-	15.07
Spiritual absence liability group					
No liability		1.00			
Moderate liability	−12.93	.00	0.00	-	n/a
Marked liability	1.52	4.56§	1.43	-	14.53

GVHD indicates graft-versus-host disease; CI confidence interval; HR, hazard ratio.
*1.00 denotes reference category.
†$P < .10$
‡$P < .05$
§$P < .01$.

Table 4. Multivariate Cox Regression Analyses Examining the Relationship Between Problematic Compliance and 1-Year Mortality

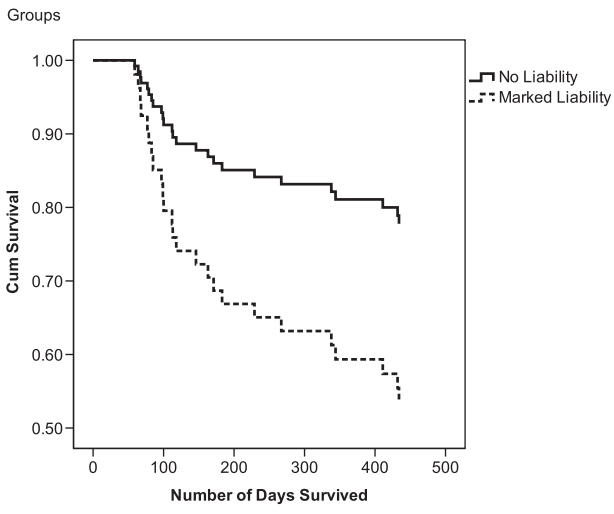
	β	HR*	95% CI		
Outcome no. 1: 1-Year mortality, all-cause					
Acute leukemia or myelodysplastic syndrome					
No		1.00			
Yes	1.70	5.46§	1.62	-	18.39
Problematic compliance liability group					
No lability		1.00			
Moderate liability	0.66	1.93	.74	-	5.02
Marked liability	1.25	3.47‡	1.14	-	10.60
Outcome no. 2: 1-Year mortality, HSCT-related (infection/sepsis, GVHD)					
Acute leukemia or myelodysplastic syndrome					
No		1.00			
Yes	1.27	3.55	.77	-	16.36
Problematic compliance liability group					
No liability		1.00			
Moderate liability	.23	1.26	.26	-	6.09
Marked Liability	1.73	5.61‡	1.42	-	22.21

GVHD indicates graft-versus-host disease; HR, hazard ratio; CI, confidence interval.
*1.00 denotes reference category.
†$P < .10$
‡$P < .05$
§$P < .01$.

HSCT-related mortality (HR = 4.56, $P = .01$), in particular, than those with scores in the no liability range. Similarly, HSCT recipients with MBMD problematic compliance scores in the marked liability range had greater hazard of 1-year all-cause mortality (HR = 3.47, $P = .029$) and 1-year HSCT-related mortality (HR = 5.61, $P = .014$), in particular, than those in the no liability range. However, in contrast to hypotheses, depression liability group was not associated with 1-year all-cause or HSCT-related mortality (*Ps* = ns for moderate and marked liability group HRs). (Spiritual absence, problematic compliance, and depression liability groups were not associated with 1-year mortality secondary to disease progression or new/secondary malignancy.)

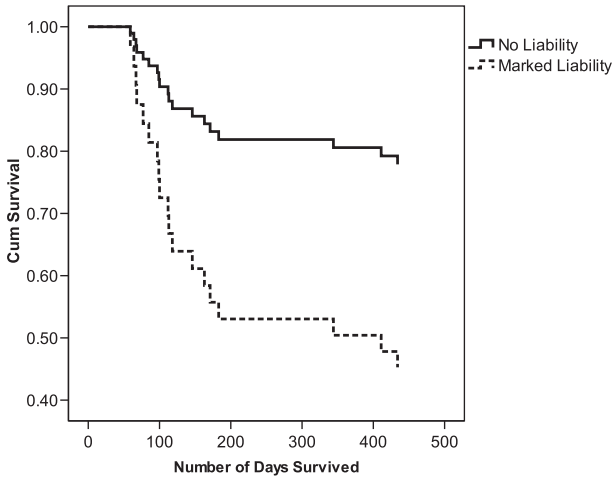
Figures 1 and 2 present the unadjusted Kaplan-Meier survival curves for the spiritual absence and problematic compliance liability groups, respectively, using 1-year all-cause mortality as the outcome. Mean survival time for individuals with marked liability in spiritual absence was 680 days (SE = 172 days, 95% CI = 343-1017 days), whereas mean survival for those with no liability in spiritual absence was 1848 days (SE = 119 days, 95% CI = 1616-2081 days), log rank χ^2 (1, N = 82) = 5.37, $P = .021$. In addition, mean survival time for individuals with marked liability in problematic compliance was 685 days (SE = 250 days, 95% CI = 195-1175 days), whereas mean survival time for those with no liability in problematic compliance was 1881 days (SE = 124 days, 95% CI = 1684-2124 days), log rank χ^2 (1, N = 69) = 4.19, $P = .041$.

To examine whether problematic compliance mediated the relationship between spiritual absence and 1-year all-cause mortality, the direct effect of Problematic Compliance on mortality was assessed after covarying for the presence of acute leukemia/MDS and Spiritual Absence. There was no direct effect of



Note. log rank X^2 (1, N = 82) = 5.37, p = .021.

Figure 1. Unadjusted Kaplan-Meier survival curve for spiritual absence liability groups. Note: log rank χ^2 (1, N = 82) = 5.37, $P = .021$.



Note. log rank $X^2(1, N = 69) = 4.19$, $p = .041$.

Figure 2. Unadjusted Kaplan-Meier survival curve function for problematic compliance liability groups. *Note:* log rank χ^2 (1, N = 69) = 4.19, $P = .041$.

problematic compliance liability group on 1-year all-cause mortality after covarying for the presence of acute leukemia/MDS and spiritual absence liability group (HR = 2.00, $P = .32$, 95% CI = 0.52-7.70, not shown). Thus, problematic compliance was not supported as a mediator of the relationship between spiritual absence and mortality. Likewise, spiritual absence liability group was not associated with 1-year all-cause mortality after covarying for the presence of acute leukemia/MDS and the problematic compliance liability group (HR = 2.32, $P = .23$, 95% CI = 0.60-8.92, not shown).

DISCUSSION

The present study suggests that allogeneic HSCT recipients identified prior to transplant as having marked liabilities or elevations in spiritual absence and problematic compliance had greater hazards of 1-year all-cause mortality, in general, and 1-year HSCT-related mortality due to infection, sepsis, or GVHD, in particular, following HSCT than those without liabilities in this areas. Individuals identified as having marked elevations in depressive symptomatology, however, did not have greater hazard of 1-year all-cause or HSCT-related mortality. Furthermore, problematic compliance did not mediate the relationship between spiritual absence and mortality, suggesting that both spiritual absence and noncompliance may be individually associated with mortality in this sample.

Although based on a modest sample size, these preliminary results add to the growing bodies of literature demonstrating (1) relationships between psychosocial factors and survival in HSCT recipients, and (2) relationships between religiosity/spirituality and health outcomes. Furthermore, it is one of the only published studies, to our knowledge, to suggest a relationship between religiosity/spirituality and survival in cancer.

There are several noteworthy limitations of this study. First, the study's sample size was modest (N = 85), and a small sample size may contribute to inaccurate inference. However, the study's sample size was within the range (N = 42 [3] to N = 199 [9]) of other published studies demonstrating similar effect sizes for the relationship between psychosocial factors and survival in HSCT. Regardless, only tentative conclusions may be drawn until replication with a larger sample has been performed.

Second, the study's assessment of spirituality was limited to only 1 instrument, the MBMD, as this was the only psychological instrument routinely administered to each HSCT candidate during pretransplant evaluation from 2002 to 2005. This poses several potential problems. Although the correlation between the MBMD Spiritual Absence scale and the more widely used SBI [28] is high, the degree to which they may be correlated in an HSCT sample is unknown. Furthermore, because only the MBMD was used, potentially important mediators of a significant spiritual absence-mortality relationship, such as social support and integration, could not be examined. Finally, the prevalence of clinically significant depressive symptomatology (10%) in the present sample was on the lower end of the range reported in other HSCT samples (9%-17%) [9,30]. This suggests that the sensitivity of the MBMD's Depression subscale may be low in the present sample, which could account for the lack of relationship between depression and mortality in the present study.

A third limitation is that although disease type was controlled for in statistical analyses, all of the known medical factors that predict survival in this population could not be covaried. The possibility exists that controlling for one of these medical factors could reduce or eliminate the statistically significant relationship between spirituality and survival in this sample. It is also possible that pre-HSCT biobehavioral factors, such as prior treatment experiences, may influence spirituality and compliance scores at the time of HSCT.

Overall, the findings of the present study suggest that future research should examine these relationships in larger scale research using more comprehensive psychosocial measures. Specifically, this research should include more comprehensive assessments of spirituality, depression, and social support quantity and quality. The SBI-54 [16] may be an appropriate spirituality assessment instrument, given that it has been validated in cancer samples. Furthermore, this area of research may benefit from more comprehensive assessments of depression using semistructured diagnostic interviews (eg, Structured Clinical Interview for the Diagnostic

and Statistical Manual of Mental Disorders—Fourth Edition [DSM-IV]) [31] and self-report depression instruments (eg, the Beck Depression Inventory—Second Edition [BDI-II]) [32]. In addition, this research should examine the possible pre-HSCT biopsychosocial factors that may influence spirituality and compliance at the time of transplant.

If a relationship emerges between spirituality and survival in this larger scale and more comprehensive research, it may provide support for initiating research to explore the feasibility and acceptability of delivering psychospiritual interventions among HSCT recipients. Although spirituality is a burgeoning area of research in the field of psycho-oncology [33], little is still known about how to translate this research into practical interventions with patients [34]. Broadly speaking, spirituality based psychological interventions aim to improve mind-body-spirit well-being via exploration of constructs such as sense of meaning and purpose, peace, faith, hope, altruism, gratitude, and forgiveness [34]. These facets of spiritual well-being may be enhanced through the use of cognitive-behavioral therapy techniques, creative arts interventions, life review interviews, and mindfulness/mantram meditation techniques [19,35-41]. There is emerging evidence for the feasibility and acceptability of delivering psychospiritual interventions among coronary artery bypass graft (CABG) inpatients [42], a population with similarities to the HSCT inpatients in terms of treatment intensity, treatment-induced functional impairment, and length of hospitalization. If feasibility and acceptability of psychospiritual interventions are demonstrated in HSCT recipients, as well, research may then examine the effects of psychospiritual interventions on quality of life and clinical outcomes in this population using a methodologically rigorous, randomized clinical trial design.

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