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ORIGINAL ARTICLE

Cognitive problems following hematopoietic stem cell transplant: relationships with sleep, depression and fatigue

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Cognitive problems are a significant, persistent concern for patients undergoing hematopoietic stem cell transplant (HSCT). Sleep is important for many cognitive tasks; however, the relationship between sleep and cognitive problems for HSCT patients is unknown. This study examined the relationship between sleep and cognitive problems for HSCT patients from pre to post transplant. Patients undergoing HSCT ($N = 138$) completed questionnaires at pre-transplant and during the 12 months following transplant. Questionnaires assessed sleep and cognitive problems as well as commonly co-occurring symptoms: depressive symptoms, fatigue and pain. *Post hoc* analyses examined the relationship of specific sleep problems with cognitive problems. Sleep problems covaried with cognitive problems even after controlling for depressive symptoms, fatigue and pain. Depressive symptoms and fatigue were also uniquely related to cognitive problems. *Post hoc* analyses suggest that sleep somnolence, shortness of breath, snoring and perceptions of inadequate sleep may contribute to the association found between sleep and cognitive problems. Findings suggest that sleep problems are associated with and may contribute to cognitive problems for HSCT patients. However, sleep problems are rarely screened for or discussed during clinic visits. Assessing and treating specific sleep problems in addition to depressive symptoms and fatigue may have implications for improving cognitive problems for HSCT patients.

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INTRODUCTION

Cognitive problems are a significant, though understudied, concern for patients undergoing hematopoietic stem cell transplant (HSCT). More than 50% of HSCT patients report cognitive problems, with over 25% indicating these problems are moderate to severe.[1,2] Cognitive problems following HSCT have been identified in the domains of memory, attention and concentration, executive functioning, mental processing speed, visual memory and motor function.[2–4] These problems are an important quality of life concern for HSCT patients. Patients who report cognitive problems are also likely to report difficulties with emotional, physical and social functioning[2,3,5,6] as well as less confidence in their abilities to manage HSCT-related symptoms.[6]

Sleep is important for many cognitive tasks, including attention and executive functioning, memory consolidation and procedural and visuospatial learning; poor sleep quality is associated with reduced general cognitive functioning.[7–13] Although research from the general population[14] and patients with chronic illnesses (for example, heart failure,[15] Parkinson's disease[11]) has identified a relationship between sleep and cognitive problems, limited work has examined this relationship among cancer patients. What is known comes from cross-sectional studies and suggests that sleep problems are associated with patients' self-reported memory[16] and cognitive problems.[17,18] In one recent study, cancer survivors with sleep disordered symptoms (that is, snoring, frequent gasping during sleep) were nine times more likely to report memory problems.[16] Similarly, breast cancer survivors reporting poorer sleep quality experience worse perceptions of their cognitive functioning and greater cognitive impairments.[17]

The factors that contribute to cognitive problems following HSCT are not well understood yet poor sleep quality is a significant concern that often begins before transplant or during hospitalization.[19–23] In a recent study, more than half of HSCT patients experienced poor sleep quality, with sleep disturbance and sleep onset latency among the most commonly reported problems.[24] Recent research has found the use of sleep medications by HSCT patients to significantly increase during hospitalization; in one study, 8% of those surveyed were using sleep medications before hospitalization, whereas more than half (65.9%) used sleep medications during hospitalization.[23] Other research suggests that sleep problems may peak 1-month following transplant and continue for as long as a year after patients return home.[21,24]

Patients' sleep difficulties may be associated with a variety of factors including, medications provided as part of their pre- and post-transplant treatment regimens. For example, pre- and post-transplant treatment regimens often include high-dose corticosteroids (for example, dexamethasone[25]), which have been linked to reductions in rapid eye movement (REM) sleep, increased REM latency and difficulties staying asleep.[26,27] A better understanding of the connection between sleep and cognitive problems is needed in patients undergoing HSCT and could provide important information for improving the management of these symptoms.

The present study had two aims. First, we examined change from pre- to post transplant for both sleep and cognitive problems. Second, we examined the relationship between sleep and cognitive problems. Because depressive symptoms,

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fatigue and pain co-occur with sleep problems among cancer patients,[28–36] we also examined change in these variables from pre- to post-transplant. Analyses examining the relationship between sleep and cognitive problems included these important co-occurring symptoms. *Post hoc* analyses examined the relationships between specific dimensions of sleep problems (for example, sleep disturbance, snoring and somnolence) and cognitive problems.

MATERIALS AND METHODS

Participants and procedure

Patients undergoing autologous or allogeneic HSCT were recruited from a bone marrow transplant clinic between August 2011 and January 2014. Patients completed an assessment pre-transplant and at least one assessment in a 3–12 months post transplant. Patients completed questionnaires about their symptoms, daily functioning and quality of life. Given the health status of many HSCT patients, questionnaires were administered in short-format, and subscales were selected from larger questionnaires to reduce overall burden. Exclusion criteria included inability to complete self-report questionnaires due to language or medically documented severe cognitive impairment (for example, Alzheimer's disease, Dementia) and receipt of hospice care. Patients who were diagnosed with chronic, severe GvHD,[37] as indicated by documentation in their medical record, were excluded from the present analyses.

Pre-transplant questionnaires were completed in clinic and returned to clinic staff. Four hundred twenty-seven patients were identified pre-transplant: 61.1% ($n = 261$) completed a pre-transplant assessment, 21.8% ($n = 93$) had begun their preparative regimen or were too ill to complete pre-transplant questionnaires but participated in the study post transplant, and 17.1% ($n = 73$) declined participation. Post-transplant assessments were completed by mail or web-based platform (Qualtrics) after patients returned home. Patients completed at least one questionnaire at 3, 6 and/or 12 months post transplantation. This study was approved by the university Institutional Review Board. All participants completed informed consent.

Data from patients completing questionnaires at both pre- and post transplant were included in the analyses. Of the 261 patients who completed pre-transplant questionnaires, 52.9% ($n = 138$) completed assessments post-transplant, 6.5% were excluded due to a diagnosis of post-transplant chronic, severe GvHD ($n = 17$), 15.7% ($n = 41$) were deceased and 24.9% ($n = 65$) did not return any post-transplant questionnaires. When compared on sociodemographic variables, groups did not differ for race ($P = 0.94$) or gender ($P = 0.20$); however, groups differed on age, with GvHD patients and those who did not return a post-transplant assessment being on average 12 and 5 years younger than those with both pre- and post-transplant assessments, respectively ($P < 0.001$). When compared on pre-transplant variables of interest, there were no significant differences for depressive symptoms, pain, fatigue or cognitive problems. Groups differed for sleep problems ($P = 0.02$), with deceased participants experiencing fewer pre-transplant sleep problems.

Of the 138 participants with pre- and post-transplant assessments, 57% ($n = 78$) completed more than one post-transplant assessment (3 months: $n = 94$; 6 months: $n = 87$; 12 months: $n = 61$).

Measures

Cognitive problems. The 8-item PROMIS Applied Cognitive-General Concerns Scale[38] measured cognitive problems. Patients rated the degree and impact of cognitive difficulties over the past 7 days including mental acuity, concentration, memory, verbal fluency, multi-tasking, interference and functional change. A 5-point response scale ranging from 1 (never) to 5 (very often/several times a day) was used. Items were summed, and possible scores ranged from 5 to 40. Higher scores represent greater cognitive problems. This scale is reliable and valid when used with chronic illness populations.[39] Cronbach's alpha in this sample ranged from 0.96 to 0.97 across assessments.

Sleep problems. The Medical Outcomes Study Sleep Scale[40,41] is a 12-item measure developed for patients with chronic illness. The measure is divided into six dimensions evaluating sleep disturbance, snoring, shortness of breath, perceived adequacy, somnolence and quantity. Patients rate each item over the last 4 weeks. The sleep problems index is derived by creating a composite score for the six dimensions which is transformed to a 0–100 scale; higher scores reflect more sleep problems. This scale is widely used with patients with cancer[42] and is reliable and valid.[43–45] Cronbach's alpha was 0.78–0.85.

Depressive symptoms. The PROMIS 6-item depression scale[46] assessed negative mood (sadness, guilt), views of self (self-criticism, worthlessness), social cognition (loneliness, interpersonal alienation) and decreased positive affect and engagement (loss of interest, meaning and purpose). Items were answered on a 5-point scale ranging from 1 (never) to 5 (always). Items were summed and converted to standardized T-scores; higher T-scores represent more depressive symptoms.[47] Cronbach's alpha was 0.92–0.94.

Fatigue. The PROMIS 6-item fatigue scale[46] assessed a range of fatigue symptoms, from mild, subjective feelings of tiredness to a sustained sense of exhaustion. This scale measured the experience (that is, frequency, duration and intensity) and impact of fatigue. Items were rated on a 5-point scale ranging from 1 (not at all) to 5 (very much), summed and then converted to standardized T-scores; higher T-scores represent greater fatigue. The PROMIS fatigue scale has good reliability and validity when used with the general population[46] and those with chronic illnesses.[48,49] Cronbach's alpha was 0.95–0.96.

Pain. The Brief Pain Inventory[50] intensity scale assessed pain severity. This measure contains four 0–10 scale ratings corresponding to the patient's pain intensity over the past week. A composite score was created by averaging these items, with higher scores indicating greater pain intensity. Prior studies have shown the measure to have good internal reliability, test-retest reliability and validity.[51] Cronbach's alpha was 0.85–0.92.

Statistical analysis

Longitudinal analyses. Longitudinal linear mixed models were conducted using SPSS v.19 (ref. 52) to examine changes in sleep, cognitive problems, depression and fatigue from pre- to post transplant. Transplant type was included as a covariate in each model given the differences in preparative regimens among patients receiving autologous versus allogeneic transplant (for example, myeloablative versus non-myeloablative preparative regimen).[53] Transplant type was coded as 0 = autologous, 1 = allogeneic transplant. Time was coded as months since transplant. Statistical significance was considered at the level of $P < 0.05$, two-tailed. The data conform to the assumptions of this test.

Multivariate analyses. A multivariate linear mixed model examined the relationship between sleep and cognitive problems using SPSS v.19.[52] This analytic approach uses all available data and allows for randomly missing observations within a participant. Data were nested within participants to address non-independence due to repeated measures and to account for data from participants with more than one post-transplant assessment. The model included sleep, depressive symptoms, fatigue and pain as time-varying covariates and also controlled for time (coded as months from transplant) as well as age and transplant type, two variables known to be associated with cognitive problems. *Post hoc* analyses examined the relationship between specific sleep problems and cognitive problems using multivariate linear mixed models. Statistical significance was considered at the level of $P < 0.05$, two-tailed. The data conform to the assumptions of these tests.

RESULTS

Sample description

Participants ($N = 138$) were primarily male (60.1%) and Caucasian (84.8%) and on average 60.4 years old (Table 1). Approximately 42.8% completed college and/or graduate work, 30.4% were retired, 26.8% were employed and 29.0% were on medical disability. The majority of patients received autologous HSCT (76.5%).

Longitudinal analyses

Longitudinal linear mixed models were run separately with cognitive problems, sleep problems, depression, fatigue and pain as dependent variables. The models estimated time, transplant type (allogeneic versus autologous), and time × transplant type.

Table 1. Sample description ($N = 138$)

Characteristic	*% (n)*	M *(s.d.)*	*Range*
Age		60.4 (9.44)	25–83
Gender (% male)	60.1 (83)		
Race (% Caucasian)	84.8 (117)		
Education (%)			
High school or less	25.3 (35)		
Some college/vocational training	27.5 (38)		
College degree	20.3 (28)		
Graduate or professional training	22.5 (31)		
Unknown	4.3 (6)		
Married or partnered	82.6 (114)		
Employed full or part-time	26.6 (37)		
Type of transplant			
Autologous	77.5 (107)		
Allogeneic	22.5 (31)		
Diagnosis			
Multiple myeloma	55.8 (77)		
Non-Hodgkin's lymphoma	7.2 (10)		
AML	7.2 (10)		
Mantle cell lymphoma	5.8 (8)		
Hodgkin's lymphoma	5.1(7)		
Other	18.9 (26)		

Other diagnosis include: Blackfan-Diamond Anemia, Burkitt's lymphoma, CLL, CML, Diffuse large B-cell lymphoma, follicular lymphoma, MDS, myelofibrosis, myeloproliferative disorder, pancytopenia peripheral T-cell lymphoma, plasmacytoid dendritic cell neoplasm and T-cell NHL.

The time effect tested whether the variables changed from pre- to post transplant and across the post-transplant assessments. Results of the fixed effects are presented in Table 2. There was no significant effect of time for cognitive problems, sleep problems, depressive symptoms, or pain (Ps > 0.05). The magnitudes of the slopes suggest that these variables remained stable over time. The time effect for fatigue bordered on significance ($B = -0.21$, s.e. $= 0.11$, $t = -2.08$, $P = 0.06$), suggesting that fatigue decreased over time in this sample. Transplant type was significantly associated with pain and fatigue, with patients who received autologous transplants reporting greater pre-transplant pain ($B = -3.23$, s.e. $= 1.55$, $t = -2.08$, $P < 0.04$) and fatigue ($B = -0.81$, s.e. $= 0.39$, $t = -2.07$, $P = 0.04$). The time × transplant type effects were not significant (Ps > 0.05), indicating that the rate of change in the variables of interest did not differ by transplant type.

Multivariate analysis

Table 3 reports fixed effects for the multivariate model examining the covariation of sleep and cognitive problems controlling for months since transplant, age and transplant type. Sleep problems were significantly associated with cognitive problems ($B = 0.07$, $P = 0.002$) after accounting for depressive symptoms, fatigue and pain. This suggests that sleep problems are associated with cognitive problems above and beyond the effect of these other symptoms. Depressive symptoms ($B = 0.31$, $P < 0.01$) and fatigue ($B = 0.18$, $P < 0.01$) were also uniquely related to cognitive problems such that patients who experienced more depressive symptoms and/or greater fatigue experienced more cognitive problems. Pain was not associated with cognitive problems.

Post hoc analyses

Post hoc analyses examined the relationship between specific dimensions of sleep problems (that is, somnolence, shortness of breath, snoring, sleep adequacy, sleep disturbance, quantity) and cognitive problems after controlling for months since transplant, depressive symptoms, fatigue, pain, age and transplant type. Separate models were conducted for each sleep problem. Sleep somnolence ($B = 0.06$, s.e. $= 0.02$, $t = 3.09$, $P = 0.002$), shortness of breath ($B = 0.04$, s.e. $= 0.02$, $t = 2.38$, $P = 0.02$), snoring ($B = 0.03$, *s.e.* $= 0.01$, $t = 2.42$, $P = 0.02$) and sleep adequacy ($B = -0.03$, *s.e.* $= 0.01$, $t = -2.04$, $P = 0.04$) significantly covaried with cognitive problems. Sleep disturbance and number of hours of sleep were not significantly associated with cognitive problems (P's > 0.05).

Table 2. Fixed effects for linear mixed models examining change in study variables from pre- to post transplant

	B	*S.e.*	t	P-*value*	*95% CI*
Cognitive problems					
Intercept	18.22	0.78	23.27	< 0.01**	16.68, 19.77
Time	0.01	0.10	0.14	0.89	−0.18, 0.21
Transplant type	−0.64	1.65	−0.39	0.70	−3.91, 2.62
Transplant type × time	−0.27	0.233	−1.17	0.25	−0.73, 0.19
Sleep problems					
Intercept	31.27	1.52	20.56	< 0.01**	28.26, 34.28
Time	−0.10	0.24	−0.41	0.69	−0.58, 0.38
Transplant type	−1.23	3.21	−0.38	0.70	−7.58, 5.13
Transplant type × time	−0.66	0.56	−1.18	0.24	−1.77, 0.45
Depressive symptoms					
Intercept	47.51	0.80	59.03	< 0.01**	45.92, 49.10
Time	0.04	0.11	0.34	0.74	−0.18, 0.25
Transplant type	−1.61	1.70	−0.95	0.34	−4.97, 1.74
Transplant type × time	0.06	0.25	0.22	0.83	−0.44, 0.55
Fatigue					
Intercept	54.51	0.74	73.95	< 0.01**	53.05, 55.97
Time	−0.22	0.11	−1.91	0.06	−0.44, 0.01
Transplant type	−3.23	1.55	−2.08	0.04*	−6.31, −0.16
Transplant type × time	−0.14	0.27	−0.52	0.61	−0.68, 0.40
Pain					
Intercept	2.20	0.19	11.853	< 0.01**	1.83, 2.57
Time	−0.19	0.02	−0.89	0.37	−0.06, 0.02
Transplant type	−0.81	0.39	−2.07	0.04*	−1.59, −0.04
Transplant type × time	−0.01	0.05	−0.27	0.79	−0.11, 0.08

Abbreviation: CI = confidence interval. Transplant type coded as 0 = autologous transplant, 1 = allogeneic transplant. *$P < 0.05$. **$P < 0.01$.

Table 3. Fixed effects of model predicting cognitive functioning

	Beta	*S.e.*	t	P-*value*
Intercept	−8.63	2.65	−3.253	< 0.01**
Age	0.06	0.05	1.20	0.23
Transplant—allogenic	0.17	1.11	0.16	0.88
Time	0.02	0.07	0.34	0.74
Depressive symptoms	0.31	0.05	6.41	< 0.01**
Fatigue	0.18	0.05	3.84	< 0.01**
Pain	0.05	0.20	0.30	0.77
Sleep problems	0.07	0.02	3.07	< 0.01**

Transplant type coded as 0 = autologous transplant, 1 = allogeneic transplant. **$P < 0.01$.

Significant associations remained between depressive symptoms and fatigue and cognitive problems in all models.

DISCUSSION

This study examined the relationship between sleep and cognitive problems in patients who have undergone HSCT. Overall, sleep and cognitive problems remained stable pre- to post transplant, and the trajectories of change did not differ by transplant type. Mean levels of cognitive problems were similar to those experienced by patients with chronic diseases associated with cognitive decline and impairment (that is, multiple sclerosis).[39] The sample average for sleep problems was approximately half a standard deviation higher than the mean for the general population,[45] suggesting HSCT patients experience more sleep problems than the general population.

Sleep problems covaried with cognitive problems such that patients with more sleep problems also had more cognitive concerns. The relationship between sleep and cognitive problems was found after controlling for depressive symptoms, fatigue and pain, symptoms known to cluster with sleep problems among cancer patients.[34,54] This suggests that sleep problems endorsed by HSCT patients may independently contribute to cognitive problems above and beyond the effect of commonly co-occurring symptoms. Specific dimensions of sleep difficulties including sleep somnolence, shortness of breath, snoring and sleep adequacy may account for the unique relationship between sleep and cognitive problems. Depressive symptoms and fatigue were also significantly associated with cognitive problems in multivariate and *post hoc* models, which is consistent with prior research[55] showing HSCT patients with more depressive symptoms or greater fatigue experience more cognitive problems.[1,56]

The presence of sleep problems can contribute to the diagnosis of depression;[57] however, the relationship between depressive symptoms and cognitive problems occurred independent of the relationship between sleep and cognitive problems. This finding suggests many of the sleep problems associated with cognitive problems among HSCT patients may be distinct from those commonly found among individuals with depressive symptoms. Two domains of sleep difficulties that commonly co-occur with depressive symptoms (that is, sleep disturbance, numbers of hours slept) were no longer associated with cognitive problems after accounting for depressive symptoms.

Cancer-related fatigue is a common and persistent concern for cancer survivors,[58] including HSCT patients.[59] Although sleep problems and fatigue are correlated,[35,36,59] cancer-related fatigue often does not improve following sleep[36] suggesting that fatigue and sleep problems may be distinct symptoms. This study provides support for the distinction between sleep problems and fatigue, as each independently contributed to cognitive problems for HSCT patients.

Although sleep problems affect many HSCT patients, a recent survey of 180 HSCT physicians revealed that patients and physicians rarely discussed sleep disruption during clinic visits.[60] Only 17% of physicians reported having discussions about sleep during at least half of patient visits. A first step to addressing sleep problems among HSCT patients is to routinely assess these symptoms. This can be done in a variety of ways including a nurse-led assessment or via electronic assessment prior to clinic appointments. Information obtained from actigraphs[61] or patients' personal activity trackers (for example, Fitbit) may also provide objective sleep data to guide sleep discussions.

The results of the present study have important clinical implications for treating cognitive problems reported by HSCT patients. Specifically, three types of symptoms should be considered: sleep problems, depressive symptoms and fatigue. The use of symptom-specific techniques may assist with improving cognitive functioning.

First, specific sleep difficulties (that is, somnolence, shortness of breath, snoring, sleep adequacy) significantly associated with cognitive problems may occur in the context of sleep apnea syndrome (SAS). SAS is often worsened or complicated by chemotherapy, radiation, and other cancer therapies.[62,63] There are many possible treatments for SAS, the most prevalent being Continuous Positive Airway Pressure (CPAP) therapy.[64] CPAP therapy may alleviate the respiratory-related sleep problems that likely contribute to cognitive problems for some HSCT patients. A clinical workup of sleep problems (for example, sleep study) is recommended for patients with suspected SAS.

Second, psychosocial interventions may benefit patients who do not exhibit clear breathing-related sleep problems. Given that sleep disturbances are often related to depressive symptoms and fatigue, managing these symptoms concurrently may be beneficial for also addressing cognitive problems. Cognitive-behavioral therapy for insomnia (CBTi) has been shown to not only improve sleep but also result in generalized improvements in depression and fatigue in cancer patients with insomnia.[65–67] In one study, when compared to usual care, patients receiving CBTi saw a greater reduction in clinically significant insomnia (17.5% reduction versus 52% reduction), fatigue (2.5% increase versus 10.9% reduction) and depression (5% increase versus 5.5% decrease).[65]

Sleep hygiene recommendations (for example, reducing caffeine intake, keeping consistent sleep/wake times) are an important component of CBTi protocols.[68] A sleep hygiene intervention offered to patients prior to transplantation may assist them with maintaining good sleep during hospitalization and following their return home. Assistance with improving the sleep environment during hospitalization is also important. Aspects of the hospital environment may leave patients vulnerable to sleep problems.[69] Several strategies have been suggested to address barriers to sleep during hospitalization[69] including those that address noise (for example, offering earplugs), lighting (that is, offering eye masks), and the effects of treatment (for example, reducing the frequency of overnight monitoring).

Third, patients may benefit from exercise-based interventions. A recent review[70] found that participating in aerobic exercise (for example, home-based walking, bed cycle ergometer), resistance training, and mindfulness-based exercise (that is, yoga) designed for cancer survivors produced improvements in sleep, depressive symptoms, fatigue, and cognitive problems. In one study, HSCT patients who began using a cycle ergometer 6 days before transplant and continued post transplant saw significant improvements in emotional state while those in the control group saw worsening of fatigue.[71] In another study, HSCT patients randomized to participate in endurance-based exercises and strength training experienced reductions in fatigue and distress over time.[72] Jarden and colleagues[73] found that, when compared to a control group, HSCT patients randomized to a multimodal exercise intervention (that is, stationary cycling, dynamic and stretching exercises, and resistance training) experienced fewer cognitive symptoms (that is, diminished concentration, memory problems) at 6-month follow-up.

Sleep and cognitive problems were stable over time, from pre- to post-transplant, suggesting that the contribution of transplant to these variables may be unclear. It appears that for many patients, their prior treatments and pre-transplant preparative regimens may contribute to pre-transplant sleep[21] and cognitive problems.[74] Regardless of the direct impact of transplant on these variables, sleep and cognitive problems continue to be important quality of life concerns for HSCT patients throughout the disease trajectory and are important intervention targets. The interventions (for example, psychosocial, cognitive-behavioral, exercise-based, and so on) described previously can help to improve quality of life and outcomes for transplant patients, and

the results of the present study suggest that early intervention may be beneficial.

In the present study, sleep and cognitive problems were assessed via self-report questionnaires rather than objective measures. The self-report measures used in the present study have been well validated, and self-reported measures of sleep and cognitive problems have been associated with objective measures. For example, self-reported perceptions of cognitive decline have been correlated with underlying neurodegenerative changes even in the absence of measurable cognitive changes on a neuropsychological assessment.[75] Further, self-report measures of sleep may tap into sleep-related phenomena that cannot be assessed via objective measures.[76] Future studies utilizing objective measures of sleep and cognitive problems in addition to self-reported measures with HSCT patients are necessary to confirm the results of the present study.

The present study has several strengths including a longitudinal design, controlling for symptoms (depression, fatigue, pain) that often cluster with sleep problems, *post hoc* analyses examining the relationship of specific sleep problems to cognitive problems, and the use of a robust analytic strategy to ensure inclusion of cases with missing data. The study has limitations that merit acknowledgment. First, the relatively small sample size and the fact that the HSCT patients accrued were primarily Caucasian and received autologous transplants due to the nature of their disease (primarily multiple myeloma[77]) may limit the generalizability of the results to other racial/ethnic groups and patient populations. Second, sleep and cognitive problems were assessed concurrently therefore causality cannot be ascertained. Additional longitudinal studies are necessary to determine the direction of the relationship between sleep and cognitive problems. Future studies should also examine whether interventions targeting sleep problems, depressive symptoms, and fatigue result in improvements in cognitive problems among HSCT patients.

In sum, this study suggests that sleep problems, depressive symptoms, and fatigue may independently contribute to cognitive problems experienced by HSCT patients. Knowledge of these three domains underscores the importance of developing targeted screening measures and interventions to address the cognitive concerns of HSCT patients.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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