



Published in final edited form as:

Support Care Cancer. 2019 April ; 27(4): 1355–1363. doi:10.1007/s00520-018-4411-y.

Fatigue predicts impaired social adjustment in survivors of allogeneic hematopoietic cell transplantation (HCT)

Jumin Park, RN, PhD¹, Leslie Wehrle, RN, MSN, OCN®², Sandra A. Mitchell, PhD, CRNP, FAAN³, Li Yang, MS⁴, Margaret F. Bevens, PhD, RN, AOCN®, FAAN⁵

¹Post-doctoral fellow, National Institutes of Health Clinical Center, Bethesda, MD, USA.

²Nurse Consultant, National Institutes of Health Clinical Center, Bethesda, MD, USA.

³Research Scientist, Outcomes Research Branch, National Cancer Institute, Bethesda, MD, USA.

⁴Statistician, National Institutes of Health Clinical Center, Bethesda, MD, USA.

⁵Nurse Scientist, National Institutes of Health Clinical Center, Bethesda, MD, USA.

Abstract

Purpose—The aim of this study is to examine social adjustment to illness and to identify factors related to social adjustment in allogeneic hematopoietic cell transplantation (HCT) survivors.

Methods—Cross-sectional data were drawn from a longitudinal study of patients 3 years after their first HCT. The five subscales of the Psychosocial Adjustment to Illness Scale (PAIS) that reflect social adjustment, specifically vocational environment (VE); domestic environment (DE); sexual relationships (SEX); extended family relationships (ER); and social environment (SE) were examined in this analysis. Functional Assessment of Cancer Therapy-Fatigue (FACIT-F) measured cancer-related fatigue.

Results—Subjects (N=171) were a median of 5.19 years from HCT (range 3–16). The most impaired dimension of social adjustment was ER with 38% of participants reaching clinically relevant (score ≥ 62) levels of social maladjustment. Unmarried and unemployed participants had lower levels of social adjustment in VE ($p < .001$ and $p < .001$ respectively) and DE ($p = .004$ and $p = .006$ respectively). Survivors with some college had poorer SEX adjustment than those with less or more education ($p < .005$). Hispanics reported lower adjustment with respect to ER adjustment ($p = .002$). Participants with higher fatigue had poorer adjustment in all five dimensions ($p < .001$).

Conclusions—Although the majority of survivors are well adjusted, subgroups may experience significant poor social adjustment. Specifically, survivors with fatigue are at risk to experience lower levels of social adjustment. Development of effective rehabilitation strategies to improve affected areas of social health is warranted, and all HCT survivors should be screened periodically for social maladjustment and provided with resources and referrals.

[†]Corresponding Author: Margaret F. Bevens, PhD, RN, AOCN®, FAAN, National Institutes of Health Clinical Center, 10 Center Drive, Bethesda, MD 20892-1151. Tel: 301-402-9383, Fax: 301-480-9650, Margaret.Bevens@nih.gov.

Declaration of Conflicting interests

The Author(s) declare that they have no conflict of interest.

Keywords

Hematopoietic Stem Cell Transplantation; cancer survivors; social adjustment; fatigue; psychosocial adjustment

Introduction

Allogeneic hematopoietic cell transplantation (HCT) is considered a curative treatment option for individuals suffering from a variety of hematologic, malignant and immunologic conditions. Advances in transplantation techniques and supportive care strategies have resulted in a significant improvement in outcomes and have increased the number of long-term HCT survivors [1]. However, cure or control of the underlying primary disease and effective management of transplant-related late complications, may not be accompanied by a full recovery of health status. Late complications including symptom burden (pain, fatigue, insomnia) and chronic graft-versus-host-disease (cGVHD) associated functional impairments are a major contributor to impairments in quality of life among HCT survivors [2–5]. Given these difficulties, patients may find it challenging to engage in or resume valued activities and daily roles that support higher levels of social well-being including sustaining intimate relationships and participating in activities with friends or family [6]. Accordingly, social adjustment has emerged as a potentially important indicator of recovery after HCT.

Social adjustment refers to a dynamic process, unconscious or conscious, where changes in the life and social environment are made as a result of an individual's chronic illness [7]. Though many late effects of HCT, including cGVHD, have been systematically characterized [4, 8–9], considerably less attention has been focused on social adjustment in HCT survivors [6]. Prior research indicates a majority of HCT survivors report good levels of social adjustment after five years post-transplant [10–12]. When specific aspects of social adjustment are examined, the data reflect enduring negative effects on social adjustment with respect to employment and sexual function [12,13]. Other dimensions, such as connections with family and friends, are not well elucidated.

A recent review highlighted several correlates of social adjustment in HCT survivors [2], including age [14–16], sex [14–16], marital status [17], and education [18]. In addition to socio-demographic factors, existing evidence suggested that fatigue was a common predictor of poor social adjustment, and is a common and persistent symptom in long-term survivors of HCT [19–21]. Compared with the general population of cancer survivors, fatigue remains persistently elevated among long-term HCT survivors compared with the general cancer survivor and healthy-age matched populations [5, 22–25]. Fatigue and lack of energy are negatively related to diverse aspects of daily life, reducing the capacity to perform daily activities, and impairing mental concentration, social functioning, and health-related quality of life [26]. Previous studies reported that fatigue was associated with significant impairments in vocational functioning including performance at work for cancer patients [27] and return to work following autologous or allogeneic HCT [28].

Long-term HCT survivors may not receive their health care at their transplant centers and have often returned to the care of community health care providers [9]. Healthcare providers need to understand factors that place HCT survivors at risk for impaired social adjustment. Although the impact of poor physical and psychological adjustment on recovery is considered in practice [4, 9], in-depth investigations of social adjustment among long-term HCT survivors are limited. The prevailing literature includes survivors less than 2 years from HSCT, autologous or allogeneic (mixed) patients, and often reports on a single dimension of social adjustment (e.g., sexual function). Therefore, the purpose of this analysis was to describe the multiple dimensions of social adjustment to illness and to identify factors that are related to social adjustment in a sample of long-term allogeneic HCT survivors. The research questions were: (1) What areas of social adjustment are impaired (or preserved) in HCT survivors? (2) Do socio-demographic factors (i.e., age, sex, race/ethnicity, marital status, education, employment) and clinical factors (i.e., length of time from HCT, transplantation risk status, conditioning regimen, evidence of underlying disease, intensity of systemic immunosuppression in treatment of cGVHD, level of fatigue) predict social adjustment in HCT survivors?

Methods

Study design and participants

Cross-sectional data (study enrollment time point) were drawn from a longitudinal study of HCT survivors who are three or more years post their first allogeneic HCT [27]. Patients were eligible to participate if they: (1) were at least 18 years old; (2) carried a life expectancy of at least six months; and (3) were able read and speak English or Spanish. All patients provided written informed consent before participation, which was approved by the National Heart, Lung and Blood Institute Intramural Institutional Review Board ().

Measures

Sociodemographic data were obtained directly from the patients including age, sex, race/ethnicity, marital status, education, and employment status. Clinical variables were abstracted from the medical record and included time since HCT, HCT-comorbidity index (HCT-CI) score [30], transplantation risk status, conditioning regimen, evidence of disease, and immunosuppression intensity. Cancer-related fatigue was measured with the Functional Assessment of Cancer Therapy-Fatigue (FACIT-F) scale [31]. The FACIT-F is a 13 item self-administered measure where each item, on a five-point scale (0–4), represents their experience with fatigue during the past week. Lower scores indicate higher levels of fatigue. A cut-score less than 34 points on the FACIT-F scale has been proposed as a criterion for the diagnosis of fatigue [32]. In this study, the internal consistency of FACIT-F was demonstrated by a Cronbach's alpha coefficient of .94.

Social Adjustment—The Psychosocial Adjustment to Illness Scale-Self Report (PAIS-SR) [33] is a 46-item, questionnaire designed for patients with chronic or prolonged illnesses to assess their psychosocial adjustment to illnesses and its sequelae during the past 30 days. Five scales related to social adjustment from PAIS-SR were identified as outcomes for this analysis: (a) vocational environment (e.g., vocational impairment) (6 items); (b)

domestic environment (e.g., family communication) (8 items); (c) sexual relationships (e.g., sexual satisfaction) (6 items); (d) extended family relationships (e.g., interest in interacting) (5 items); and (e) social environment (e.g., individual leisure interest) (6 items). Responses are on a four-point scale (0–3), with higher scores indicating poorer adjustment. A total T-score for each subscale of 62 or greater on any of the PAIS subscales indicates clinically relevant levels of maladjustment in that domain [33]. All five subscales demonstrated acceptable reliability in this sample (Cronbach's alpha values were vocational environment = .70; domestic environment = .76; sexual relationships = .84; extended family relationships = .72; social environment = .89).

Statistical Analysis

Descriptive statistics appropriate for the level of the measurements were computed for all demographic, clinical, and social adjustment variables. Data distribution and normality were checked using the Shapiro-Wilk tests and normal QQ plots for all continuous variables. A priori, based on existing evidence, age, sex, and fatigue were identified as likely predictors and included in all the models. Time since transplant was also included to account for the sample's variability in years following HCT. Parametric (Pearson's correlation, t test, and One-way analysis of variance) or non-parametric tests (Spearman's correlation, Wilcoxon signed-rank test, and Kruskal-Wallis test) were used to examine the relationship between social adjustment and socio-demographic factors (marital status, race/ethnicity, education, employment) and clinical factors (HCT-CI score, transplantation risk status, conditioning regimen, evidence of disease, immunosuppression intensity). Factors related to each PAIS-SR subscale at $p < .20$ were included in the multiple linear regression models to evaluate the potential predictors of each subscale. Normality and homoscedasticity were examined by plotting raw data values and residuals. Transformations were performed if necessary. Multicollinearity was checked by tolerance and VIF. All the statistical analyses were performed with IBM SPSS software package version 21.0 [34].

Results

Socio-demographic and clinical characteristics of the study participants ($N = 171$) have been previously described [3], and summarized in Table 1. Survivors ranged in age from 19 to 76 years (44.5 ± 13.5). The majority of participants were male (62.6%), married (64.7%), graduated from high school or undergraduate/graduate school (71.5%), and working (69.2%). Subjects were an average of 5.2 years \pm 2.9 after HCT, with a range of 3 to 16 years, and reported a mean FACIT-F score of 41.5 ± 9.6 .

Social Adjustment Scales

The PAIS-SR raw subscale scores and subscale T-scores in HCT survivors are presented in Table 2. The participants reported the highest scores, reflecting more difficulties with adjustment, with respect to extended family relationships (55.57 ± 9.39), vocational environment (55.66 ± 5.36), and sexual relationships (54.03 ± 9.31). A subset of respondents (7.6%–38.0%) scored above the clinical cut score ($= 62$) on individual subscales. The domain of extended family relationships had the largest proportion of participants (38%) reporting clinically-relevant levels of social maladjustment. The social environment subscale

had the lowest percentage of survivors meeting the clinical cut score while other subscales were at a similar threshold (13.5–17.0%).

Predictors of Social Adjustment

Table 3 presents the final multiple linear regression models for each outcome including age, sex, time since transplant, and fatigue, as likely predictors based on existing evidence.

Vocational environment—Two factors (marital status, employment) met the bivariate analyses criteria and were added in a standard multiple linear regression model predicting vocational environment. The final model including age, sex, time since transplant, fatigue, marital status and employment was significant, $F(7,145) = 20.850, p < .001$, and accounted for 50.2% of the variance in social adjustment with respect to the vocational environment. Participants who were unmarried ($p < .001$), unemployed ($p < .001$), and experiencing higher levels of fatigue ($p < .001$) reported lower levels of vocational adjustment.

Domestic environment—Two factors (marital status, employment) met the bivariate analyses criteria and were added in a final regression model. The final model including age, sex, time since transplant, fatigue, marital status and employment was significant, $F(6,156) = 17.399, p < .001$, and accounted for 40.1% of the variance in domestic environment. Unmarried ($p = .004$), unemployed ($p = .006$), and participants with more fatigue ($p < .001$) had poorer adjustment in domestic environment.

Sexual relationships—Education was the only factor to meet the bivariate association criteria with sexual relationships and was added in a final regression model. The final model including age, sex, time since transplant, fatigue, and education was significant and the total variance explained by the model was 41.7% ($F(7,138) = 14.128, p < .001$). Survivors with some college had poorer adjustment in sexual relationships compared to those with lower or higher levels of educational attainment ($p = .005$). Older participants, females, and respondents experiencing fatigue all reported lower levels of social adjustment with respect to sexual relationships (all $p < .001$).

Extended family relationships—Race/ethnicity was the only factor to meet the bivariate analyses criteria and was added in a final regression model. The final model including age, sex, time since transplant, fatigue, and race/ethnicity was significant, $F(5,161) = 7.387, p < .001$, and explained 18.7% of the variance in extended family relationships. Hispanics reported more difficulties with extended family relationship adjustment ($p = .002$). Participants with more fatigue had lower levels of adjustment in extended family relationships ($p < .001$).

Social environment—No additional factor met the criterion for inclusion in the final regression model. Therefore only age, sex, time since transplant and fatigue were included. Participants who experienced more fatigue had significantly higher levels of adjustment difficulty in social environment ($p < .001$). The total variance explained by the regression model was 32.9% ($F(4,162) = 19.853, p < .001$).

Fatigue—To further explore associations between social adjustment and fatigue in this sample, the distribution of socio-demographic and clinical factors of the respondents were compared between two groups of respondents, those who were below the established cut-point for fatigue on the FACIT-F (i.e., fatigue ≤ 34 ; no fatigue > 34) (Table 1). The two groups did not differ significantly on clinical variables, including time since HCT, HCT-CI score, transplantation risk status, conditioning regimen, and evidence of disease (all $p > .05$), however, those reporting clinically meaningful levels of fatigue were significantly older (48.4 ± 11.7) than those without clinically meaningful levels of fatigue (43.2 ± 13.8) ($p = .037$). In addition, those who reported clinically meaningful levels of fatigue were significantly more likely to be non-Hispanic ($n=31, 79.5\%$) and employed ($n=19, 48.7\%$) compared to those without fatigue (Table 1).

Discussion

To our knowledge, this is the first study exploring social adjustment and the predictive factors in a sample comprised exclusively of long-term, allogeneic HCT survivors. In this study, the majority of long-term HCT survivors reported good social adjustment. These findings are consistent with previous research indicating that social function was relatively well preserved [10, 11]. In addition, when compared to a published allogeneic/autologous HCT survivor cohort, the allogeneic HCT survivors in this study reported comparable levels of social adjustment except in the area of domestic environment where survivors in this analysis report more problems [35]. Differences may be explained noting that this sample was comprised exclusively of survivors of allogeneic transplantation, compared to a mixed sample where some subjects received an autologous transplant. Late effects, particularly owing to cGVHD, may be greater for those receiving an allogeneic transplant, as opposed to an autologous transplant [36, 37], and these late effects may disproportionately affect those who are older and further out from transplant, when reintegration and a return to normal may be expected. Although the domestic environment is rarely studied in transplant survivors, our findings differ from those in a prior report that found that the dyadic marital adjustment is relatively stable over time [38].

Not all survivors in our sample, however, were socially well adjusted. Consistently across all dimensions of social adjustment, fatigued survivors reported significantly lower levels of social adjustment. Although the majority of survivors did not meet criteria for fatigue, these findings indicate that long-term HCT survivors with fatigue are at particular risk for difficulties with social adjustment. This observation is consistent with previous studies of HCT survivors that found that fatigue was related to lower levels of social well-being [13] and more difficulties with vocational environment [27, 28]. Older survivors and those who reported as non-Hispanic Whites, were more likely to have clinically meaningful levels of fatigue, which has not been previously reported. Recognizing that the impact of transplant on an individual and their family is not static, routine periodic assessment of fatigue and social adjustment during transplant recovery should be incorporated into the delivery of survivorship care for this patient population [39]. Identifying relevant resources to improve affected areas of social adjustment, and tailored to the preferences, needs and resources of the patient and their social network, based on the needs and experiences of the patient and family is imperative for healthcare providers.

In addition, survivors identified the most difficulties in the areas of extended family relationships, vocational environment, and sexual relationships. The participants stated a relational disruption in the extended family constellation that stems from the illness experience. Hispanic survivors were more likely to report poorer adjustment in extended family relationships despite the majority of Hispanic respondents having returned to their home country outside the U.S. This is consistent with previous research demonstrating that cancer survivors experienced reduced interactions and support with family and friends [10, 40] and lack of support from friends [10]. Approximately 90% of transplant recipients reported that people became less supportive overtime and that this was the most distressing factor of long-term survival [10]. Health providers should encourage maintenance of close personal connections such as interventions to enhance social networks of friends and revitalize relationships with relatives, such as support groups or web-based resources [40, 41].

Vocational adjustment is another important factor of financial and role stability in this sample of individuals. The majority (approximately 60–84%) of HCT survivors returned to fulltime work during the first several years following diagnosis [28, 42]. In this study, approximately 70% of the participants were employed, however, those who were unmarried showed poorer adjustment regarding vocational environment. It requires great efforts for them to maintain good performance in their job and to balance their lives within the restrictions imposed by transplantation treatment.

HCT survivors in this study also reported decreases in sexual interest, frequency of sexual activity and sexual satisfaction as well as some degree of sexual dysfunction. Sexual dysfunction and sexual dissatisfaction are highly prevalent after HCT [4]. Despite some recovery, nearly half of men and 80% of women may have long-term sexual problems [15]. Therefore, awareness and the early diagnosis of sexual dysfunction related to HCT treatments are important for their adjustment in long-term survivors of HCT. Similar to what was found in allogeneic BMT patients [14–16], older, women report poorer adjustment in sexual relationships. Survivors with some college had poorer adjustment in sexual relationships than those with less or more education which is consistent with published findings where survivors with less education had more sexual dysfunction [18]. Identifying those at risk, completing an assessment of pre-transplant sexual function, and implementing regular assessment after transplantation, enables the early identification of change warranting treatment [4, 9]. Long-term follow-up after transplant would also be valuable [9], because to the best of knowledge the majority of studies to date have only followed patients for 2 to 3 years [43]. In addition, evidence-based interventions have been well described to address problems with sexual function and satisfaction which should be considered [4].

In contrast to the socio-demographic factors that might identify patients at risk for poor social adjustment, there were no observed associations with clinical factors, including comorbidities, transplantation risk status, conditioning regimen, evidence of disease, or intensity of systemic immunosuppression. We were somewhat surprised to observe the absence of an association between social adjustment and time since transplant suggesting that there is no significant variability in the social adjustment of survivors 3 years or more post HCT, assuming other factors are stable. In addition, few participants in our sample were

dealing with disease recurrence, and although approximately one third were receiving systemic immunosuppression in treatment of cGVHD, only about a third were receiving either moderate (single-agent prednisone 0.5 mg/kg/day and/or any single agent/modality) or high (2 or more agents/modalities) intensity immunosuppression suggesting that cGVHD in this sample was overall mild and/or well-controlled [3].

The strengths of this study include the relatively large sample size and the inclusion of a number of important potential covariates, including cGVHD and comorbidities. Several caveats should be considered in interpreting our findings. First, the design of this analysis was cross-sectional, which prohibits the assessment of time-varying factors that may predict poor social adjustment (e.g., cGVHD). Future research with longitudinal data, including baseline, and qualitative data, are needed to gain in-depth information about social adjustment among long-term, allogeneic HCT survivors. In addition, the effect of additional factors, such as financial burden, health insurance, social support, and cultural factors, on social adjustment should be examined, but were not available for inclusion in this analysis. Further research is needed to evaluate these additional factors as well as symptoms such as sleep disturbance, depression, and pain on social adjustment expanding the predictive model and likely accounting for additional variability in social adjustment.

The results from the current study suggest that socio-demographic factors and concomitant symptomatology, such as fatigue, but generally not clinical factors, place long-term HCT survivors at risk of social adjustment. In particular, as most previous studies partly or exclusively concentrated on autologous HCT survivors, our findings provide valuable information about patterns of social adjustment among allogeneic HCT survivors. This information may help healthcare providers develop and implement strategies to routinely screen, evaluate and manage patients at risk for or experiencing difficulties with social adjustment across the transplant recovery process. With an increasing number of transplant survivors, research will need to continue to monitor the long-term and late consequences of survival beyond the first 5 years post-transplantation. Few studies, however, have documented the social adjustment of survivors who are at least 10 years post-transplantation [12]. Further prospective long-term studies are warranted to confirm and extend our observations. In addition, findings from this study add to the evidence the need for assessing and managing at-risk that included fatigue among HCT survivors. Although there is a large body of empirical evidence to support screening, evaluation, and evidence-based management of fatigue [44], data regarding the prevalence and management fatigue during long-term survivorship (> 5 years), especially in transplant survivors, is more limited [45]. In 2012, Majhail et al. [9] updated the international recommendations for screening and preventive practices for HCT survivors. Syrjala et al. [4] have also reviewed specific suggestions for delivering care to long-term HCT survivors. These recommendations, emphasize the management of late effects but provide comparatively little guidance about evaluation and management of fatigue in long-term HCT survivors. Given that fatigue was strongly associated with social adjustment difficulties in this study, special emphasis should be directed to fatigue management in HCT long-term survivors. These results add to the knowledge base needed to strengthen screening, evaluation and management of social adjustment difficulties in the delivery of survivorship care to transplant survivors. Evaluation and enhancement of survivors' perceived and actual social support might facilitate the

transition between intensive hospital care, long-term outpatient follow-up, and a return to the home community and support reintegration into their normal life.

Acknowledgement

The authors thank Stephen Klagholz, BS, Lisa Cook, RN, MSN, Eleftheria Koklanaris, RN, BSN, OCN®, Bazetta B. Schuver, RN, BSN, Patricia Prince, MEd, MSW, Kathleen Castro, RN, MS, AOCN®, Michael Krumlauf, RN, BSN, OCN®, Georgie Cusack, MS, RN, AOCNS®, Bipin Savani, MD, Daniel H. Fowler, MD, Richard Childs, MD., John A. Barrett, MD, Gwenyth Wallen, RN, PhD, the NCI and NHLBI Intramural Research Transplant Teams, the NIH Clinical Center staff, and research participants.

Funding

Funding for this study was provided by the NIH Clinical Center Intramural Research Program.

Reference

- Majhail NS, Tao L, Bredeson C, Davies S, Dehn J, Gajewski JL, Hahn T, Jakubowski A, Joffe S, Lazarus HM, Parsons SK, Robien K, Lee SJ, Kuntz KM (2013) Prevalence of hematopoietic cell transplant survivors in the United States. *Biol Blood Marrow Tr* 19:1498–1501
- Bevans M, El-Jawahri A, Tierney DK, Wiener L, Wood WA, Hoodin F, Kent EE, Jacobsen PB, Lee SJ, Hsieh MM, Denzen EM, Syrjala KL (2017) National Institutes of Health hematopoietic cell transplantation late effects initiative: The patient-centered outcomes working group report. *Biol Blood Marrow Transplant* 23:538–551 [PubMed: 27660168]
- Bevans MF, Mitchell SA, Barrett JA, Bishop MR, Childs R, Fowler D, Krumlauf M, Prince P, Shelburne N, Wehrlen L, Yang L (2014) Symptom distress predicts long-term health and well-being in allogeneic stem cell transplantation survivors. *Biol Blood Marrow Tr* 20:387–395
- Syrjala KL, Martin PJ, Lee SJ (2012) Delivering care to long-term adult survivors of hematopoietic cell transplantation. *J Clin Oncol* 30:3746–3751 [PubMed: 23008296]
- Im A, Mitchell SA, Steinberg SM, Curtis L, Berger A, Baird K, Kuzmina Z, Joe G, Comis LE, Juckett M, Avila D, Baruffaldi J, Masuch L, Pirsli F, Pavletic SZ (2016) Prevalence and determinants of fatigue in patient with moderate to severe chronic GvHD. *Bone Marrow Transplant* 51:705–712 [PubMed: 26828906]
- Norkin M, Hsu JW, Wingard JR (2012) Quality of life, social challenges, and psychosocial support for long-term survivors after allogeneic hematopoietic stem-cell transplantation. *Semin Hematol* 49:104–109 [PubMed: 22221790]
- Larsen PD (2016) Psychosocial Adjustment In: Lubkins IM, Larsen PD (ed) *Chronic Illness: Impact and Intervention*. Jones & Bartlett Learning, Burlington, MA, pp 43–62
- Battiwalla M, Hashmi S, Majhail N, Pavletic S, Savani BN, Shelburne N (2017) National Institutes of Health hematopoietic cell transplantation late effects initiative: Developing recommendations to improve survivorship and long-term outcomes. *Biol Blood Marrow Tr* 23:6–9
- Majhail NS, Rizzo JD, Lee S, Aljuttis M, Atsuta Y, Bonfim C, Burns L, Chaudhri N, Davies S, Okamoto S, Seber A, Socie G, Szer J, Van Lint MT, Wingard JR, Tichelli A, Cibmt, Asbmt, Ebmt, Apbmt, Bmstanz, Embmt, Sbtmo (2012) Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Biol Blood Marrow Tr* 18:348–371
- Bush NE, Donaldson GW, Haberman MH, Dacanay R, Sullivan KM (2000) Conditional and unconditional estimation of multidimensional quality of life after hematopoietic stem cell transplantation: A longitudinal follow-up of 415 patients. *Biol Blood Marrow Tr* 6: 576–591.
- Kopp M, Holzner B, Meraner V, Sperner-Unterweger B, Kemmler G, Nguyen-Van-Tam DP, Nachbaur D (2005) Quality of life in adult hematopoietic cell transplant patients at least 5 yr after treatment: A comparison with healthy controls. *European Journal of Haematology* 74:304–308 [PubMed: 15777342]
- Mosher CE, Redd WH, Rini CM, Burkhalter JE, DuHamel KN (2009) Physical, psychological, and social sequelae following hematopoietic stem cell transplantation: a review of the literature. *Psycho-Oncology* 18:113–127 [PubMed: 18677717]

13. Bartley EJ, Edmond SN, Wren AA, Somers TJ, Teo I, Zhou SC, Rowe KA, Abernethy AP, Keefe FJ, Shelby RA (2014) Holding back moderates the association between health symptoms and social well-being in patients undergoing hematopoietic stem cell transplantation. *J Pain Symptom Manage* 48:374–384 [PubMed: 24529631]
14. Chiodi S, Spinelli S, Ravera G, Petti AR, Van Lint MT, Lamparelli T, Gualandi F, Occhini D, Mordini N, Berisso G, Bregante S, Frassoni F, Bacigalupo A (2000) Quality of life in 244 recipients of allogeneic bone marrow transplantation. *Br J Haematol* 110:614–619 [PubMed: 10997973]
15. Syrjala KL, Kurland BF, Abrams JR, Sanders JE, Heiman JR (2008) Sexual function changes during the 5 years after high-dose treatment and hematopoietic cell transplantation for malignancy, with care-matched controls at 5 years. *Blood* 111: 989–996 [PubMed: 17878404]
16. Wong FL, Francisco L, Togawa K, Kim H, Bosworth A, Atencio L, Hanby C, Grant M, Kandeel F, Forman SJ, Bhatia S (2013) Longitudinal trajectory of sexual functioning after hematopoietic cell transplantation: impact of chronic graft-versus-host disease and total body irradiation. *Blood* 122:3973–3981 [PubMed: 24159171]
17. Andrykowski MA, Bishop MM, Hahn EA, Cella DF, Beaumont JL, Brady MJ, Horowitz MM, Sobocinski KA, Rizzo JD, Wingard JR (2005). Long-term health-related quality of life, growth and spiritual well-being after hematopoietic stem-cell transplantation. *J Clin Oncol* 23:599–608 [PubMed: 15659507]
18. Wingard JR, Vogelsang GB, Deeg HJ (2002) Stem cell transplantation: Supportive care and long-term complications. *Hematology Am Soc Hematol Educ Program* 2002:422–444
19. Danaher EH, Ferrans C, Verlen E, Ravandi F, van Besien K, Gelms J, Dieterle N (2006) Fatigue and physical activity in patients undergoing hematopoietic stem cell transplant. *Oncol Nurs Forum* 33:721–727
20. Hjermstad MJ, Knobel H, Brinch L, Fayers PM, Loge JH, Holte H, Kaasa S (2004) A prospective study of health-related quality of life, fatigue, anxiety and depression 3–5 years after stem cell transplantation. *Bone Marrow Transplant* 34:257–266 [PubMed: 15170167]
21. Jafari H, Jannati Y, Nesheli HM, Hassanpour S (2017) Effects of nonpharmacological interventions on reducing fatigue after hematopoietic stem cell transplantation. *J Res Med Sci* 22:13 [PubMed: 28458705]
22. Bieri S, Roosnek E, Helg C, Verhopen F, Robert D, Chapuis B, Passweg J, Miralbell R, Chalandon Y (2008) Quality of life and social integration after allogeneic hematopoietic SCT. *Bone Marrow Transplant* 42:819–827 [PubMed: 18711345]
23. Esser P, Kuba K, Mehnert A, Schwinn A, Schirmer L, Schulz-Kindermann F, Kruse M, Koch U, Zander AR, Kroger N, Schilling G, Gotze H, Scherwath A (2017) Investigating the temporal course, relevance and risk factors of fatigue over 5 years: a prospective study among patients receiving allogeneic HSCT. *Bone Marrow Transplantation* 52:753–758 [PubMed: 28112750]
24. Gielissen MFM, Schattenberg AVM, Verhagen CAHHVM, Rinkes MJ, Bremmers MEJ, Bleijenberg G (2007) Experience of severe fatigue in long-term survivors of stem cell transplantation. *Bone Marrow Transplantation* 39:595–603 [PubMed: 17369868]
25. Jim HSL, Sutton SK, Jacobsen PB, Martin PJ, Flowers ME, Lee SJ (2016) Risk factors for depression and fatigue among survivors of hematopoietic cell transplantation. *Cancer* 122:1290–1297 [PubMed: 26814442]
26. LaVoy ECP, Fagundes CP, Dantzser R (2016) Exercise, inflammation, and fatigue in cancer survivors. *Exerc Immunol Rev* 22:82–93 [PubMed: 26853557]
27. Munir F, Yarker J, McDermott H (2009) Employment and the common cancers: correlates of work ability during or following cancer treatment. *Occup Med (Lond)* 59: 381–389. [PubMed: 19692524]
28. Morrison EJ, Ehlers SL, Bronars CA, Patten CA, Brockman TA, Cerhan JR, Hogan WJ, Hashmi SK, Gastineau DA (2016) Employment status as an indicator of recovery and function one year after hematopoietic stem cell transplantation. *Biol Blood Marrow Tr* 22:1690–169
29. Bevans MF, Mitchell SA, Barrett AJ, Bishop M, Childs R, Fowler D, Krumlauf M, Prince P, Shelburne N, Wehrlen L (2011) Function, adjustment, quality of life and symptoms (FAQS) in

- allogeneic hematopoietic stem cell transplantation (HSCT) survivors: a study protocol, *Health Qual Life Outcomes* 9:24 [PubMed: 21496339]
30. Sorror ML, Maris MB, Storb R, Baron F, Sandmaier BM, Maloney DG, Storer B (2005) Hematopoietic cell transplantation (HCT)-specific comorbidity index: A new tool for risk assessment before allogeneic HCT. *Blood* 106:2912–2919 [PubMed: 15994282]
 31. Cella D (2004) Manual of the Functional Assessment of Chronic Illness Therapy (FACIT) measurement system, Version 4.1. Center of Outcomes, Research, and Education (CORE), Evanston Northwestern Healthcare and Northwestern University, Evanston, IL
 32. Van Belle S, Paridaens R, Evers G, Kerger J, Bron D, Foubert J, Ponnet G, Steichel DV, Heremans C, Rosillon D (2005) Comparison of proposed diagnostic criteria with FACT-F and VAS for cancer-related fatigue: proposal for use as a screening tool. *Support Care Cancer* 13:246–254 [PubMed: 15549424]
 33. Derogatis LR (1986) The psychosocial adjustment to illness scale (PAIS). *J Psychosom Res* 30:77–91 [PubMed: 3701670]
 34. IBM Corp. (2012) IBM SPSS Statistics for Windows, Version 21.0. IBM Corp.: Armonk, NY
 35. Molassiotis A, vandenAkker OBA, Milligan DW, Goldman JM, Boughton BJ, Holmes JA, Thomas S (1996) Quality of life in long-term survivors of marrow transplantation: Comparison with a matched group receiving maintenance chemotherapy. *Bone Marrow Transplantation* 17:249–258 [PubMed: 8640175]
 36. Khera N, Zeliadt SB, Lee SJ (2012) Economics of hematopoietic cell transplantation. *Blood* 120:1545–1551 [PubMed: 22700725]
 37. Majhail NS (2017) Long-term complications after hematopoietic cell transplantation. *Hematol Oncol Stem Cell Ther.* doi.org/10.1016/j.hemonc.2017.05.009
 38. Langer SL, Yi JC, Storer BE, Syrjala KL (2010) Marital adjustment, satisfaction and dissolution among hematopoietic stem cell transplant patients and spouses: a prospective, five-year longitudinal investigation. *Psycho-Oncology* 19:190–200 [PubMed: 19189319]
 39. Hashmi SK, Srivastava A, Rasheed W, Adil S, Wu T, Jagasia M, Nassar A, Hwang WYK, Hamidieh AA, Greinix HT, Pasquini MC, Apperley JF, Aljurf M (2017) Cost and quality issues in establishing hematopoietic cell transplant program in developing countries. *Hematol Oncol Stem Cell Ther.* doi.org/10.1016/j.hemonc.2017.05.017
 40. Bloom JR, Stewart SL, Chang S, Banks PJ (2004) Then and now: Quality of life of young breast cancer survivors. *Psycho-Oncology* 13:147–160 [PubMed: 15022150]
 41. Helgeson VS, Reynolds KA, Tomich PL (2006) A meta-analytic review of benefit finding and growth. *J Consult Clin Psychol* 74:797–816 [PubMed: 17032085]
 42. Kirchoff AC, Leisenring W, Syrjala KL (2010) Prospective predictors of return to work in the 5 years after hematopoietic cell transplantation. *J Cancer Surviv* 4:33–44 [PubMed: 19936935]
 43. Duncan CN, Majhail NS, Brazauskas R, Wang Z, Cahn JY, Frangoul HA, Hayashi RJ, Hsu JW, Kamble RT, Kasow KA, Khera N, Lazarus HM, Loren AW, Marks DI, Maziarz RT, Mehta P, Myers KC, Norkin M, Pidala JA, Porter DL, Reddy V, Saber W, Savani BN, Schouten HC, Steinberg A, Wall DA, Warwick AB, Wood WA, Yu LC, Jacobsohn DA, Sorror ML (2015) Long-term survival and late effects among one-year survivors of second allogeneic hematopoietic cell transplantation for relapsed acute leukemia and myelodysplastic syndromes. *Biol Blood Marrow Tr* 21:151–158
 44. Berger AM, Mitchell SA, Jacobsen PB, Pirl WF (2015) Screening, evaluation, and management of cancer-related fatigue: Ready for implementation to practice? *CA Cancer J Clin* 65:190–211 [PubMed: 25760293]
 45. Denlinger CS, Ligibel JA, Are M, Baker KS, Broderick G, Demark-Wahnefried W, Friedman DL, Goldman M, Jones LW, King A, Ku GH, Kvale E, Langbaum TS, McCabe MS, Melisko M, Montoya JG, Mooney K, Morgan MA, Moslehi JJ, O'Connor T, Overholser L, Paskett ED, Peppercorn J, Rodriguez MA, Ruddy KJ, Sanft T, Silverman P, Smith S, Syrjala KL, Urba SG, Wakabayashi MT, Zee P, McMillian NR, Freedman-Cass DA (2016) NCCN Guidelines (R) Insights Survivorship, Version 1.2016 Featured Updates to the NCCN Guidelines *J Natl Compr Canc Netw* 14:715–724 [PubMed: 27283164]

Table1.

Demographics and Clinical Characteristics

Demographic characteristics	FACIT-F cut off 34 ^a n (%)		p-value
	No n= 130	Yes n= 39	
Age, Mean (SD), year	43.2 (13.8)	48.4 (11.7)	.037*
Sex			.450
Male	84 (64.6)	22 (56.4)	
Female	46 (35.4)	17 (43.6)	
Marital status			.570
Married	82 (63.6)	27 (69.2)	
Not married	47 (36.4)	12 (30.8)	
Race/Ethnicity			.008*
Non-Hispanic	71 (54.6)	31 (79.5)	
Hispanic	59 (45.4)	8 (20.5)	
Education			.602
High school graduate	35 (27.3)	11 (28.2)	
Associate's degree/ some college	32 (25.0)	11 (28.2)	
Bachelor's degree	25 (19.5)	10 (25.6)	
Graduate degree	36 (28.1)	7 (17.9)	
Employment			.006*
Not working	96 (75.0)	20 (51.3)	
Working (full-time, part-time, student)	32 (25.0)	19 (48.7)	
Clinical characteristics			
Time since HCT, Mean (SD), year Range	5.1 (2.9)	5.5 (3.0)	.509
HCT-CI Score			.605
0 score	44 (33.8)	10 (25.6)	
1 or 2 score	41 (31.5)	13 (33.3)	
3 score	45 (34.6)	16 (41.0)	
Transplantation risk status			.533
Low	70 (53.8)	21 (53.8)	
Intermediate	29 (22.3)	6 (15.4)	
High/very high	31 (23.8)	12 (30.8)	
Conditioning regimen			.799
RIC	57 (43.8)	18 (46.2)	
Myeloablative	73 (56.2)	21 (53.8)	
Evidence of disease			.151
No ^b	107 (82.3)	28 (71.8)	
Yes	23 (17.7)	11 (28.2)	
Immunosuppression intensity			.055
None	92 (70.8)	21 (53.8)	

Demographic characteristics	FACT-F cut off 34 ^a n (%)		p-value
	No n= 130	Yes n= 39	
Mild/Moderate/High	38 (29.2)	18 (46.2)	

Numbers may not sum to total due to missing data (n=169).

CR, complete remission; FACT, functional assessment of cancer therapy; HCT, hematopoietic stem cell transplantation; HCT-CI, hematopoietic stem cell transplantation-comorbidity index; MRD, minimal residual disease; PD, progressive disease; PR, partial remission; SD, standard deviation.

^aA total score of 34 or less indicates a clinically meaningful levels of fatigue.

^bSubjects in complete remission and who had not received treatment for their primary disease in the past year.

* $p < .05$.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Social adjustment subscale scores in HCT survivors

Social adjustment	Mean (SD)		PAIS-SR T-score cut off	62 ^a n (%)	
	Raw scores	T-scores		No	Yes
Vocational environment	3.99 (3.21)	55.66 (5.36)	134 (85.4)	23 (14.6)	
Domestic environment	5.15 (3.87)	51.07 (10.72)	139 (82.7)	29 (17.3)	
Sexual relationships	5.15 (4.16)	54.03 (9.31)	121 (81.2)	28 (35.8)	
Extended family relationships	1.59 (2.18)	55.57 (9.39)	104 (61.5)	65 (38.5)	
Social environment	4.09 (4.11)	46.59 (12.67)	156 (92.3)	13 (7.7)	

HCT, hematopoietic stem cell transplantation; SD, standard deviation.

^aA total t-score of 34 or less indicates a clinically relevant levels of maladjustment.

Table 3.

Socio-demographic and clinical predictors of social adjustment

Characteristics	Vocational environment		Domestic environment ^a		Sexual relationships		Extended family relationships ^a		Social environment	
	<i>B</i> (<i>SE</i>)	95% CI	<i>B</i> (<i>SE</i>)	95% CI	<i>B</i> (<i>SE</i>)	95% CI	<i>B</i> (<i>SE</i>)	95% CI	<i>B</i> (<i>SE</i>)	95% CI
Age	.029 (.017)	(-.004, .062)	-.008 (.005)	(-.018, .002)	.088 (.022)*	(.044, .132)	-.001 (.005)	(-.011, .009)	.006 (.020)	(-.034, .045)
Sex (ref: male)	-.492 (.405)	(-1.293, .308)	-.044 (.130)	(-.301, .214)	2.609 (.579)*	(1.465, 3.754)	-.025 (.136)	(-.293, .243)	-.023 (.550)	(-1.108, 1.063)
Marital status (ref: married)										
Not married	1.823 (.426)*	(.980, 2.665)	.394 (.135)†	(.126, .661)						
Race/Ethnicity (ref: non-Hispanic)										
Hispanic	-	-	-	-			.441 (.141)†	(.163, .719)	-	-
Education (ref: graduate degree)										
High school graduate	-	-	-	-	.007 (.994)	(-1.495, 1.506)	-	-	-	-
Associate's degree/ some college	-	-	-	-	2.223 (.777)†	(.687, 3.759)	-	-	-	-
Bachelor's degree	-	-	-	-	-.693 (.805)	(-2.284, .898)	-	-	-	-
Employment status (ref: not working)										
Working	-2.298(.452)*	(-3.191, -1.404)	-.402(.144)†	(-.686, -.119)	-	-	-	-	-	-
Conditioning regimen (ref: myeloablative)										
RIC	.762 (.449)	(-.125, 1.649)	-	-	-	-	-	-	-	-
Time Since HCT	.000 (.006)	(-.003, .004)	.001 (.002)	(-.003, .004)	-.007 (.008)	(-.022, .009)	-.002 (.002)	(-.006, .001)	.005 (.007)	(-.010, .019)
FACTT-Fatigue	-.171 (.021)*	(-.212, -.130)	-.057 (.007)*	(-.070, -.044)	-1.76 (.030)*	(-2.35, -1.117)	-.038 (.007)*	(-.051, -.024)	-.241 (.028)*	(-.296, -.186)
<i>R</i> ²	.502		.401		.417		.187		.329	
<i>F</i>	20.850*		17.399*		14.128*		7.387*		19.853*	

CI, confidence interval; FACTT, functional assessment of cancer therapy; ref, reference; SE, standard error.

^aSquare root transformed variable

* p < .001.

$10^{\circ} < \theta < 10^{\circ}$
 $50^{\circ} < \theta < 50^{\circ}$

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript