Published in final edited form as:

Support Care Cancer. 2013 March ; 21(3): 687–695. doi:10.1007/s00520-012-1566-9.

Parental Emotional Functioning Declines with Occurrence of Clinical Complications in Pediatric Hematopoietic Stem Cell Transplant

Norma Terrin, PhD^{1,2}, Angie Mae Rodday, MS¹, Hocine Tighiouart, MS¹, Grace Chang, MD, MPH³, Susan K. Parsons, MD, MRP^{1,2}, and the Journeys to Recovery Study*

¹Institute for Clinical Research and Health Policy Studies at Tufts Medical Center

²Tufts University School of Medicine, 940 Belmont Street, Brockton, MA 02301

³VA Boston Healthcare System, 940 Belmont Street, Brockton, MA 02301

Abstract

Purpose—Parents' stress levels are high prior to their child's hematopoietic stem cell transplant (HSCT) and during transplant hospitalization, usually abating after discharge. Nevertheless, a subgroup of parents continues to experience frequent anxiety and mood disruption, the causes of which are not well understood. The purpose of this study was to assess whether clinical complications of HSCT could explain variation in parents' recovery of emotional functioning.

Methods—Pediatric HSCT recipients (n=165) aged 5 to 18 and their parents were followed over the first year post-transplant. Health-related quality of life (HRQL) assessments and medical chart reviews were performed at each time period (baseline, 45 days, 3, 6, and 12 months). We tested the association between clinical complications (acute and chronic graft versus host disease - aGVHD and cGVHD, organ toxicity, and infection) and longitudinally measured parental emotional functioning, as assessed by the Child Health-Ratings Inventories (CHRIs). The models used maximum likelihood estimation with repeated measures.

Results—In adjusted analyses covering the early time period (45 days and 3 months), aGVHD grade 2, intermediate or poor organ toxicity, and systemic infection were associated with decreases in mean parental emotional functioning of 5.2 (p=0.086), 5.8 (p=0.052), and 5.1 (p=0.023) points, respectively. In the later time period (6 and 12 months) systemic infection was associated with a decrease of 20 points (p<0.0001). cGVHD was not significantly associated.

Conclusions—When children experience clinical complications after HSCT, parental emotional functioning can be impacted. Intervening at critical junctures could mitigate potential negative consequences for parents and their children.

Keywords

Pediatric hematopoietic stem cell transplant; Parental emotional functioning; Parental distress; Transplant-related toxicity

Correspondence to: Norma Terrin, PhD Institute for Clinical Research and Health Policy Studies Tufts Medical Center 800 Washington Street Box #063 Boston, MA 02111 T 617-636-7245 F 617-636-5560 nterrinn@tuftsmedicalcenter.org.

*See Appendix 2 for full list of participating sites and collaborators

Note to the editor: We have no conflicts of interest to declare. We have full control of all primary data and agree to allow the journal to review the data if requested.

Introduction

Parents of children with life-threatening illnesses are vulnerable to psychological distress that can impair their ability to manage the child's care and result in increased distress for the child [1, 2]. Furthermore, as children suffer serious complications from treatment, parents may experience even greater distress.

HSCT offers potentially life-saving therapy to children with high risk malignancies and other life-threatening diseases of hematologic, immunologic, and metabolic origin. However, the treatment is intense and often produces many acute and delayed sequelae, including infection, acute and chronic graft versus host disease (aGVHD and cGVHD), and organ toxicity [3].

A more complete understanding of how these complications affect parents' mental health could provide opportunities to intervene at critical junctures, and thus prevent potential lapses in the child's care and deterioration in family functioning [4]. A review [5] of parental stress and pediatric HSCT noted the lack of information on HSCT-specific stressors, and the need for disease-specific measures. This report addresses both of those gaps.

The primary objective of this study was to assess the relationship between clinical complications of HSCT and parental emotional functioning over the course of the child's recovery during the first year post-transplant. We also identified demographic and clinical predictors of parents' emotional functioning at baseline.

Methods

Participants

The data are from the Journeys to Recovery study [6] of health-related quality of life (HRQL), which followed 165 pediatric HSCT recipients aged 5 to 18 years over the first year post-transplant at six transplant centers nationwide. For each child enrolled, one parent also participated (self-selected as the one spending more time with the child at the transplant center). Assessments were conducted before the child's transplant (baseline) and at 45 days, 3, 6, and 12 months post-transplant. The study was approved by the Institutional Review Board (IRB) at Tufts Medical Center and at all clinical, recruiting sites before enrollment was commenced in keeping with the 1964 Declaration of Helsinki. Parents provided written consent for their own participation and permission for the participation of the minor child. Age-appropriate assent was obtained from minor children as dictated by the policies of the local IRBs. Children reaching the age of majority (18 years) also provided written consent.

Outcome

The primary assessment tool for the Journeys to Recovery study was the Child Health-Ratings Inventories (CHRI), a health-related quality of life (HRQL) questionnaire with versions for both the parent and the patient specific to two patient age groups (5-12 year olds, and 13-18 year olds) [7, 8]. The CHRI contains a General Health Module, a Hematopoietic Stem Cell Transplant (HSCT) Module, and a demographics questionnaire. Parent participants were also invited to complete secondary measures, including selected modules for mood, anxiety, and adjustment disorders of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID).

The outcome for all analyses in this report is the parent's emotional functioning, from the parental CHRI-General Health module. The 7-item self-administered domain is conceptually similar to the five-item mental health domain of the SF-36 [9]. The construct of emotional functioning as measured by the CHRI refers to the past week and contains items

addressing mood, anxiety, and hassles. Item content and response sets of this domain are presented in Table 1. Using the half scale rule, which requires that at least half the items in a scale be completed, the seven items were averaged together to create a summary score, and then transformed to a 100-point scale. The half scale rule was only rarely necessary (< 4% of assessments). The score is not standardized, but is scaled from 0 to 100, with higher scores connoting better functioning. For example, subjects who have been worried, sad, hassled, and stressed some of the time and also happy and calm some of the time would score in the middle.

The score is a good proxy for related modules of the SCID. The area under the receiver operating characteristic (ROC) curve for predicting a threshold or subthreshold disorder using only the CHRIs parental emotional functioning score was 0.75 [10], indicating that the score has good performance in discriminating between subjects with and without a disorder.

Medical Information

Medical Information was collected at each assessment time point, using standardized data collection forms based on validated toxicity scales [11-15]. Information was obtained from the medical record by trained research staff after formal central training and under the supervision of the clinical transplant staff at each of the collaborating sites. All medical chart information was additionally reviewed for accuracy and consistency by Dr. Parsons, who is a transplant physician.

Statistical Analysis

Baseline Analysis—Descriptive analyses were performed for baseline variables including parent characteristics (age, gender, education, race, ethnicity, and threshold and subthreshold Axis I Disorder from the SCID), child characteristics (age, gender, number of siblings, causal diagnosis for transplant (i.e., malignancy yes/no), and duration of illness), type of transplant (autologous, related donor, or unrelated donor), and timing of the baseline assessment (before or during the preparative regimen). T-tests, analysis of variance, and simple linear regression were used to estimate the relation between the baseline variables and parent's emotional functioning at baseline. Linear regression was used for multivariable analysis, which also adjusted for center. Any variable significant at $p < 0.20$ in univariate analyses was a candidate for inclusion in the multivariable regression model. Variables were retained based on backward elimination and significance level $\alpha=0.05$.

Longitudinal Analysis—The independent variables of interest were the clinical complications of HSCT. The time periods were 45 days and 3 months for early clinical complications (aGVHD [13, 14], Bearman maximum overall toxicity [15] (Appendix 1) and infection [11]); and 6 and 12 months for late complications (cGVHD and infection). [11, 12] HRQL assessments and medical chart reviews were performed at each time period. Infection and organ toxicity were recorded if they were present during the week prior to the HRQL assessment. Date of onset, maximum overall grade, and current status of aGVHD and cGVHD were recorded at each relevant time period. We dichotomized aGVHD at grade 2 or higher, as an indicator of severity. We also tested a composite variable for early clinical complications: aGVHD (grade 2 or higher) *or* toxicity (intermediate or poor) *or* systemic infection *or* unplanned subsequent transplant within 100 days. Parent and child characteristics (except for SCID diagnosis), type of transplant, and timing of baseline assessment were tested for association with the outcome in models including all time points. Variables significant at $p=0.20$ were candidates for the models testing clinical complications.

We used maximum likelihood estimation with repeated measures in SAS Proc Mixed to account for within-subject correlation, with an unstructured covariance matrix. Models were adjusted for baseline characteristics and time period. We assessed whether data were missing not at random (MNAR) [16] by plotting mean trajectories of emotional functioning. Separate trajectories were plotted for those who never missed an assessment, those who missed at least once but only for logistical reasons, and those who ever missed an assessment due to distress or the child's medical condition (data not shown). Since the latter group was not consistently lower, we assumed that missing outcome data were missing at random (MAR).

Results

Completion rates ranged from 100% at baseline to a low of 80% at 3 months, averaging 88% over the six time points. The mean (standard deviation) of parent emotional functioning was 49.4 (18.5), 56.8 (18.1), 55.1 (20.4), 58.3 (21.0), and 65.1 (19.4) at baseline, 45 days, 3 months, 6 months, and 12 months, respectively.

Baseline analysis

A summary of the baseline variables appears in Table 2. Only Axis I disorder and transplant center were significantly associated with parent's emotional functioning at baseline (Table 3). Mean emotional functioning for those with a threshold mood, anxiety and/or adjustment disorder was almost a full standard deviation (17.5 points) lower than for those who were interviewed and did not meet the criteria for either a threshold or subthreshold diagnosis ($p < 0.001$). Hispanic ethnicity was borderline significant (6 point increase, $p=0.075$). Only transplant center and Axis-I diagnosis were retained in the multivariable model (Table 4).

Longitudinal Analysis

Early Complications—Complication frequencies are in Table 5. AGVHD grade 2, intermediate or poor organ toxicity, and systemic infection were associated with decreases in mean parental emotional functioning of 5.2 ($p=0.09$), 5.8 ($p=0.05$), and 5.1 ($p=0.02$) points, respectively, after adjustment for time period and the parent's emotional functioning at baseline (Table 6). This represents about a quarter to a third of a standard deviation difference. The parent's emotional functioning at baseline was the only baseline variable retained in the models. Of note, transplant type and disease diagnosis were not significant ($p=0.63$ and 0.14). Emotional functioning for parents of children with the early composite was 6.1 points lower ($p=0.01$) than for those without complications (Table 6), which approximates 1/3 of a standard deviation of parental emotional functioning, a clinically important difference.

Late Complications—Complication frequencies are in Table 5. In analyses adjusted for time period and the parent's emotional functioning at baseline, infection was significantly associated with the outcome. Emotional functioning for parents of children with systemic infection was 20.2 points lower than that for parents of children with no infection ($p < 0.0001$, Table 6). CGVHD was not significantly associated with the outcome.

Discussion

Prior studies have established that parental stress is highest prior to transplant and during the transplant hospitalization, decreasing steadily thereafter [5, 17, 18]. These studies revealed that parents with high levels of stress during the acute phase of HSCT were most at risk in the long term. Our data confirm these findings, but also reveal that the trajectory of parental emotional functioning is more nuanced than previously understood. Specifically, we found

that recovery of parental emotional functioning was impeded by clinical complications of HSCT, including aGVHD, organ toxicity, and early-onset infection.

We also found that systemic infection later in the post-HSCT period, at 6 and 12 months, had a strong association with parental emotional functioning, whereas cGVHD did not. Since the numbers with systemic infection at 6 and 12 months were low, the estimated impact of infection may have been exaggerated by a few unusual cases. The strong association between late-onset systemic infection and parental emotional functioning may be explained by the unexpected nature of such infections, the need to return to the hospital, and the experiencing anew of the disruption of hospitalization. Anecdotally, some parents have reported that they “thought they were done,” with this once they had passed the acute transplant period. These explanations, although speculative, may also underlie our failure to detect an association with cGVHD. CGVHD typically does not require emergency rehospitalization and while it represents a serious complication of transplant, it is not completely unexpected, particularly for those with a prior history of aGVHD.

Although our sample size is among the largest in studies of this population, the number of patients who experienced each of the early complications was limited. Defining a composite variable for early complications increased statistical power and was justified by the similar effects of the components on the outcome. Specifically, grade 2 or higher aGVHD, intermediate or poor maximum Bearman toxicity, and systemic infection were each associated with a five to six point decrement in parental emotional functioning.

Since the parent's emotional functioning at baseline was strongly predictive of their emotional functioning at later time points (each one point difference at baseline predicted a half point difference at the other time points, $p < 0.0001$), we performed analyses to assess the determinants of baseline emotional functioning. Among the demographic, clinical, and transplant-related variables we tested, only Axis-I diagnosis and transplant center were statistically significant in univariate and multivariable analyses. In earlier analyses, the timing of the baseline assessment was found to be strongly associated with the parent's ratings of the child's functioning, such that parents who filled out the questionnaires during the preparative regimen rated the children's functioning significantly lower on average than those who filled it out before the regimen began [6]. Thus we were surprised that baseline timing was not associated with parents' ratings of their own emotional functioning. Perhaps this was due to their already high levels of distress, as reported in previous studies during the pre-transplant period [19-21].

Previous research has demonstrated that parenting stress can be high in the post-transplant period for a subset of parents [22]. The collateral impact of the transplant process on parent caregivers [23] may influence their reporting of the child's status. Higher levels of parental stress have been shown to be predictive of poor parental ratings of the child's HRQL[5, 8]. As post-transplant care increasingly shifts away from the transplant center to the local provider and to home-based care, it is imperative that the needs of the parent caregivers are recognized and adequately addressed to ensure their optimum functioning and that of the child, particularly in light of reported associations between high parental stress and child distress[2].

Our results demonstrate that transplant center was a statistically significant factor in both univariate and multivariate analysis. Although we cannot definitively explain these findings, they may be related to two possible issues. First, transplant centers vary considerably in their requirements and expectations of families as they embark on the transplant process. At one end of the spectrum, some centers require that families arrive at least two weeks before the scheduled admission. All pre-transplant testing and orientation to transplant are performed at

the transplant center. At other centers, families are allowed to arrive essentially the day of admission, bringing with them data from the pre-transplant evaluation. We suspect that parental stress may vary considerably by these different arrangements. Second, although the centers participating in the study offered the full array of transplant options (by conditioning regimen, transplant type, and progenitor source), there may be undetectable differences with respect to diagnosis. Diagnostic mix may influence parental emotional functioning due to prognosis, duration of illness, fear of recurrence, and other factors.

Our results have implications for future intervention. Specifically, parents who report high levels of stress at the time of transplant may warrant formal referral to mental health providers and/or direct interventions to teach parents stress-reduction techniques, as described by Streisand et al.[21] and more recently, by Warner and co-workers [24]. Moreover, the strong association we found between parental emotional functioning and clinical complications during the post transplant period suggests that these clinical complications may serve as important sentinel events, triggering increased parental distress, which in turn, may require direct intervention and/or referral.

Future research is needed to integrate our findings on the impact of clinical complications with other studies, which have highlighted important psychosocial factors associated with parental distress [22]. This combination of factors may help to target at risk parents, which in turn could lead to more timely intervention.

In conclusion, we studied parents of children recovering from HSCT and found that complications of the child's treatment during the first year post-transplant were associated with decrements in the parent's emotional functioning.

Acknowledgments

Funding: Supported by American Cancer Society grant RSGPB-02-186-01-PBP (Parsons, PI) and NIH grant R01 CA119196 (Parsons, PI)

Appendix 1

Bearman Maximum overall toxicity

Regimen-related, non-hematologic toxicity during the first 100 days following HSCT was evaluated for all patients using the Bearman Toxicity Scale, which is widely used in HSCT-related clinical studies. [15] The scale utilizes a four-point scale from 0-3, (range, absent to severe, end-organ damage) for each of eight organ systems (e.g., cardiac, bladder, renal, pulmonary, hepatic, CNS (central nervous system), stomatitis, and GI (gastrointestinal). Maximum overall toxicity is classified as 'good,' 'intermediate,' or 'poor,' based on the combination of toxicity grading for each organ system. 'Good' is defined as grade 1 in all organ systems or maximum toxicity of 2 in 2 organ systems. 'Intermediate' is defined as maximum toxicity of 2 in 3 organ systems, and 'poor' is defined as maximum toxicity of 3 in at least one organ system.

Appendix 2

PARTICIPATING INSTITUTIONS AND SITE INVESTIGATORS IN THE JOURNEYS TO RECOVERY STUDY

Central Project Staff

Tufts Medical Center, Boston, MA: Susan K. Parsons, MD, MRP, Principal Investigator

Site Principal Investigators

Baylor College of Medicine/Texas Children's Hospital, Houston, TX: Lynette Harris, PhD and Robert A. Krance, MD, Principal Investigators

City of Hope, Duarte, CA: Sunita Patel, PhD, Principal Investigator; Joseph Rosenthal, MD, Site Consultant

Dana-Farber Cancer Institute, Boston, MA: Christopher Recklitis, PhD, MPH, Principal Investigator

Fred Hutchinson Cancer Research Center, Seattle, WA: Karen L. Syrjala, PhD, Principal Investigator; Jean Sanders, MD, Co-Principal Investigator

Medical College of Wisconsin, Milwaukee, WI: Mary Jo Kupst, PhD, Principal Investigator; Kristin Bingen, PhD and James Casper, MD, Co-Principal Investigators

University of Pittsburgh/Children's Hospital of Pittsburgh, Pittsburgh, PA: Robert B. Noll, PhD, Principal Investigator; Linda J. Ewing, PhD, RN, Co-Principal Investigator

Reference List

1. Packman W, Weber S, Wallace J, Bugescu N. Psychological effects of hematopoietic SCT on pediatric patients, siblings and parents: a review. *Bone Marrow Transplant*. 2010; 45(7):1134–1146. doi:10.1038/bmt.2010.74. [PubMed: 20383219]
2. Jobe-Shields L, Alderfer M, Barrera M, Vannatta K, Currier J, Phipps S. Parental Depression and Family Environment Predict Distress in Children Prior to Stem-Cell Transplantation. *J Dev Behav Pediatr*. 2009; 30(2):140–146. doi:10.1097/DBP.0b013e3181976a59. [PubMed: 19322103]
3. Copelan EA. Hematopoietic stem cell transplantation. *N Engl J Med*. 2006; 354(17):1813–1826. doi:10.1056/NEJMr052638. [PubMed: 16641398]
4. Downey G, Coyne JC. Children of depressed parents: an integrative review. *Psychol Bull*. 1990; 108(1):50–76. doi:10.1037/0033-2909.108.1.50. [PubMed: 2200073]
5. Vrijmoet-Wiersma CM, Egeler RM, Koopman HM, Norberg AL, Grootenhuis MA. Parental stress before, during, and after pediatric stem cell transplantation: a review article. *Support Care Cancer*. 2009; 17(12):1435–1443. doi: 10.1007/s00520-009-0685-4. [PubMed: 19572154]
6. Parsons, S.; Terrin, N.; Ratichek, S.; Tighiouart, H.; Recklitis, C.; Chang, G. 2009 Trajectories of HRQL following Pediatric Hematopoietic Stem Cell Transplantation (HSCT) [abstract].. International Society for Quality of Life Research Annual Conference; New Orleans: Springer. 2009 October 28-31; p. A-44.Abstract # 1420
7. Parsons SK, Shih MC, Mayer DK, Barlow SE, Supran SE, Levy SL, Greenfield S, Kaplan SH. Preliminary psychometric evaluation of the Child Health Ratings Inventories (CHRI) and Disease-Specific Impairment Inventory-HSCT (DSII-HSCT) in parents and children. *Qual Life Res*. 2005; 14(6):1613–1625. doi:10.1007/s11136-005-1004-2. [PubMed: 16110940]
8. Parsons SK, Shih MC, DuHamel KN, Ostroff J, Mayer DK, Austin J, Martini DR, Williams SE, Mee L, Sexson S, et al. Maternal perspectives on children's health-related quality of life during the first year after pediatric hematopoietic stem cell transplant. *J Pediatr Psychol*. 2006; 31(10):1100–1115. doi:10.1093/jpepsy/jsj078. [PubMed: 16150874]
9. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992; 30(6):473–483. doi: 10.1097/00005650-199206000-00002. [PubMed: 1593914]
10. Rodday A, Terrin N, Chang G, Parsons S. Performance of the parent emotional functioning (PREMO) screener in parents of children undergoing hematopoietic stem cell transplantation. *Qual Life Res*. 2012 DOI 10.1007/s11136-012-0240-5.
11. National Cancer Institute. Common Terminology Criteria for Adverse Events v4.0 (CTCAE). 2009.

12. Shulman H, Sullivan K, Weiden P, McDonald G, Striker G, Sale G, Hackman R, Tsoi M, Storb R, Thomas E. Chronic graft-versus-host disease syndrome in man. A long-term clinicopathologic study of 20 Seattle patients. *Amer J Med.* 1980; 69(1):204–217. doi: 10.1016/0002-9343(80)90380-0. [PubMed: 6996481]
13. Glucksberg H, Storb R, Fefer A, Buckner CD, Neiman PE, Clift RA, Lerner KG, Thomas ED. Clinical manifestations of graft-versus-host disease in human recipients of marrow from HL-A-matched sibling donors. *Transplantation.* 1974; 18(4):295–304. doi: 10.1097/00007890-197410000-00001. [PubMed: 4153799]
14. Przepiorka D, Weisdorf D, Martin P, Klingemann HG, Beatty P, Hows J, Thomas ED. 1994 Consensus Conference on Acute GVHD Grading. *Bone Marrow Transplant.* 1995; 15(6):825–828. [PubMed: 7581076]
15. Bearman SI, Appelbaum FR, Buckner CD, Petersen FB, Fisher LD, Clift RA, Thomas ED. Regimen-related toxicity in patients undergoing bone marrow transplantation. *J Clin Oncol.* 1988; 6(10):1562–1568. [PubMed: 3049951]
16. Hedeker D, Gibbons R. Application of Random-Effects Pattern-Mixture Models for Missing Data in Longitudinal Studies. *Psychol Methods.* 1997; 2(1):64–78. doi:10.1037/1082-989X.2.1.64.
17. Manne S, DuHamel K, Ostroff J, Parsons S, Martini DR, Williams SE, Mee L, Sexson S, Austin J, Winkel G, et al. Coping and the course of mother's depressive symptoms during and after pediatric bone marrow transplantation. *J Am Acad Child Adolesc Psychiatry.* 2003; 42(9):1055–1068. doi: 10.1097/01.CHI.0000070248.24125.CO. [PubMed: 12960705]
18. Nelson AE, Miles MS, Belyea MJ. Coping and support effects on mothers' stress responses to their child's hematopoietic stem cell transplantation. *J Pediatr Oncol Nurs.* 1997; 14(4):202–212. doi: 10.1177/104345429701400404. [PubMed: 9322394]
19. Dermatis H, Lesko LM. Psychological distress in parents consenting to child's bone marrow transplantation. *Bone Marrow Transplant.* 1990; 6(6):411–417. [PubMed: 2097010]
20. Rodrigue JR, MacNaughton K, Hoffmann RG III, Graham-Pole J, Andres JM, Novak DA, Fennell RS. Transplantation in children. A longitudinal assessment of mothers' stress, coping, and perceptions of family functioning. *Psychosomatics.* 1997; 38(5):478–486. doi:10.1016/S0033-3182(97)71425-7. [PubMed: 9314717]
21. Streisand R, Rodrigue JR, Houck C, Graham-Pole J, Berlant N. Brief report: parents of children undergoing bone marrow transplantation: documenting stress and piloting a psychological intervention program. *J Pediatr Psychol.* 2000; 25(5):331–337. doi:10.1093/jpepsy/25.5.331. [PubMed: 10880063]
22. Phipps S, Dunavant M, Lensing S, Rai SN. Psychosocial predictors of distress in parents of children undergoing stem cell or bone marrow transplantation. *J Pediatr Psychol.* 2005; 30(2):139–153. doi: 10.1093/jpepsy/jsi002. [PubMed: 15681309]
23. Manne S, Nereo N, DuHamel K, Ostroff J, Parsons S, Martini R, Williams S, Mee L, Sexson S, Lewis J, et al. Anxiety and depression in mothers of children undergoing bone marrow transplant: symptom prevalence and use of the Beck depression and Beck anxiety inventories as screening instruments. *J Consult Clin Psychol.* 2001; 69(6):1037–1047. doi:10.1037/0022-006X.69.6.1037. [PubMed: 11777107]
24. Warner CM, Ludwig K, Sweeney C, Spillane C, Hogan L, Ryan J, Carroll W. Treating Persistent Distress and Anxiety in Parents of Children With Cancer. *J Pediatr Oncol Nurs.* 2011; 28(4):224–230. doi:10.1177/1043454211408105. [PubMed: 21646637]

Table 1

Content of the CHRIs-General parental emotional functioning domain

Question	Please select the one response that is most applicable
During the past week, how nervous, worried, or fidgety have <i>you</i> felt?	Not at all A little Some A lot A whole lot
During the past week, how happy or sad have <i>you</i> been?	Really happy Pretty happy Happy A little sad Sad
During the past week, how often: ^a	All of the time
a. have <i>you</i> felt calm and peaceful	Most of the time
b. have <i>you</i> felt sad, down hearted, and blue	Some of the time
c. have <i>you</i> been a happy person	A little of the time
d. have <i>you</i> felt hassled	None of the time
e. have <i>you</i> felt stressed	

^aThese five questions were asked in a matrix form with a separate response elicited for each question.

Table 2

Descriptive statistics for baseline variables (N=165)

	<u>Mean (SD), median (25th to 75th), or n (%)</u>
Parent Characteristics	
Parent age in years, mean (SD)	38.9 (6.9)
Parent gender, n (%)	
Female	139 (84.2%)
Male	26 (15.8%)
Parent race, n (%)	
White	133 (83.1%)
Black or African American	7 (4.4%)
Asian	4 (2.5%)
Native Hawaiian/Pacific Islander	3 (1.9%)
American Indian/Alaska Native	6 (3.8%)
Other, Refused, Mixed	7 (4.4%)
Parent ethnicity, n (%)	
Non-Hispanic	129 (79.1%)
Hispanic	34 (20.9%)
Parent education, n (%)	
Less than high school	13 (7.9%)
High school graduate	45 (27.3%)
Some college	47 (28.5%)
College or more	60 (36.4%)
Parental Axis-I diagnosis, n (%)	
No	49 (29.7%)
Subthreshold	20 (12.1%)
Threshold	34 (20.6%)
Not done or inevaluable	62 (37.6%)
Child Characteristics	
Child age in years, mean (SD)	10.8 (3.9)
Child gender, n (%)	
Female	82 (49.7%)
Male	83 (50.3%)
Number of siblings, n (%)	
None	14 (8.5%)
One	60 (36.4%)
Two or more	91 (55.2%)
Causal malignancy, n (%)	
Yes	141 (85.5%)
No	24 (14.6%)
Transplant type, n (%)	
Autologous	32 (19.4%)

	<u>Mean (SD), median (25th to 75th), or n (%)</u>
Related allogenic	51 (30.9%)
Unrelated allogenic	82 (49.7%)
Duration of illness in months, median (25 th to 75 th)	10.0 (5.0, 31.0)
Prior Treatment, n (%)	
Yes	125 (75.8%)
No	40 (24.2%)
Timing of baseline measures, n (%)	
Before preparative regimen	69 (41.8%)
During preparative regimen	96 (58.2%)
Transplant center, n (%)	
Center 1	65 (39.4%)
Center 2	21 (12.7%)
Center 3	29 (17.6%)
Center 4	28 (17.0%)
Center 5	4 (2.4%)
Center 6	18 (10.9%)

Notes: 5 missing race, 2 missing parent ethnicity.

The mean time of Axis-I diagnosis relative to the transplant date was -2.5 days (SD, 7.3 days).

Of the 62 Axis-I interviews "not done or inevaluable," 5 interviews were inevaluable.

Fifty-seven subjects declined to be interviewed.

Table 3

Univariate analyses of relation between parent emotional functioning at baseline and baseline variables (N=165)

	Mean baseline parent emotional functioning (SD) * or β (SE) **	p-value
Parent Characteristics		
Parent age in years, β (SE)	0.14 (0.22)	0.528
Parent gender, mean (SD)		0.168
Female	48.6 (18.7)	
Male	54.0 (17.2)	
Parent race, mean (SD)		0.184
White	48.6 (17.6)	
Black or African American	63.9 (19.7)	
Asian	38.5 (7.9)	
Native Hawaiian/Pacific Islander	59.7 (2.4)	
American Indian/Alaska Native	45.8 (24.9)	
Other, Refused, Mixed	51.8 (23.8)	
Parent ethnicity, mean (SD)		0.075
Non-Hispanic	48.1 (17.3)	
Hispanic	54.4 (21.9)	
Parent education, mean (SD)		0.671
Less than high school	48.4 (19.9)	
High school graduate	46.7 (14.5)	
Some college	51.2 (19.6)	
College or more	50.2 (20.1)	
Parent Axis-I diagnosis, mean (SD)		<0.001
No	55.0 (15.3)	
Subthreshold	52.5 (17.5)	
Threshold	37.5 (14.5)	
Not done or inevaluable	50.5 (20.5)	
Child Characteristics		
Child age in years, β (SE)	0.22 (0.37)	0.549
Child gender, mean (SD)		0.293
Female	47.9 (18.3)	
Male	50.9 (18.7)	
Number of siblings, mean (SD)		0.781
None	49.1 (15.4)	
One	48.1 (18.2)	
Two or more	50.3 (19.2)	
Causal malignancy, mean (SD)		0.975
Yes	49.4 (18.7)	
No	49.3 (17.5)	
Transplant type, mean (SD)		0.930

	Mean baseline parent emotional functioning (SD) [*] or β (SE) ^{**}	p-value
Autologous	49.4 (20.8)	
Related allogenic	48.6 (20.5)	
Unrelated allogenic	49.9 (16.3)	
Log duration of illness in months, β (SE)	1.0 (1.2)	0.441
Prior treatment, mean (SD)		0.489
Yes	50.0 (19.0)	
No	47.6 (16.8)	
Timing of baseline measures, mean (SD)		0.569
Before preparative regimen	48.4 (18.7)	
During preparative regimen	50.1 (18.4)	
Transplant center, mean (SD)		0.012
Center 1	44.4 (17.1)	
Center 2	46.3 (16.2)	
Center 3	58.0 (19.8)	
Center 4	51.6 (19.6)	
Center 5	43.8 (13.0)	
Center 6	55.3 (17.8)	

Notes:

Higher scores correspond to higher functioning

p-value from: t-test (binary), ANOVA (categorical), or linear regression (continuous)

* Mean (SD) displayed for binary or categorical variables

** Beta coefficient (SE) displayed for continuous variables

Table 4

Multivariable baseline model (N=165)

	β (SE)	p-value
Intercept	50.0 (2.9)	<0.0001
Transplant center, n (%)		
Center 1	reference	
Center 2	6.5 (4.5)	0.149
Center 3	16.1 (4.3)	<0.001
Center 4	9.9 (3.9)	0.011
Center 5	-1.7 (8.8)	0.848
Center 6	10.8 (4.6)	0.020
Parental Axis-I diagnosis		
No	reference	
Subthreshold	0.1 (4.7)	0.982
Threshold	-17.7 (3.9)	<0.001
Not done or inevaluable	-9.0 (3.6)	0.014

Global p-value for transplant center: p=0.002 and parental Axis-I diagnosis p=0.001

Table 5

Complications (frequency and percent)

	45 days	3 months	6 months	12 months
Early Complications	n=139	n=125		
aGVHD, n (%)				
Autologous ^I	24 (17.3%)	24 (19.2%)		
None, grade 1	95 (68.3%)	83 (66.4%)		
grade 2	20 (14.4%)	18 (14.4%)		
Bearman toxicity, n (%)				
Good	112 (80.6%)	100 (80.0%)		
Intermediate/poor	27 (19.4%)	25 (20.0%)		
Infection, n (%)				
None	93 (67.4%)	80 (64.5%)		
Localized	7 (5.1%)	15 (12.1%)		
Systemic	38 (27.5%)	29 (23.4%)		
Unplanned subsequent transplant, n (%)				
No	139 (100.0%)	124 (99.2%)		
Yes	0 (0.0%)	1 (0.8%)		
Early complications composite, n (%)				
No	97 (69.8%)	89 (71.2%)		
Yes	42 (30.2%)	36 (28.8%)		
Late Complications		n=123	n=109	
cGVHD, n (%)				
Autologous ^I		25 (20.3%)	21 (19.3%)	
None		57 (46.3%)	44 (40.4%)	
Limited		22 (17.9%)	30 (27.5%)	
Extensive		19 (15.4%)	13 (11.9%)	
Infection, n (%)				
None		100 (82.0%)	90 (84.1%)	
Localized		9 (7.4%)	11 (10.3%)	
Systemic		13 (10.7%)	6 (5.6%)	

Abbreviations: aGVHD= acute graft versus host disease; cGVHD=chronic graft versus host disease

Early composite: aGVHD>=grade 2, Bearman>=intermediate, infection=systemic, unplanned subsequent transplant within 100 days

Not tabulated because outcome missing: 1 infection at 45 days; 1 infection at 3 months; 1 infection at 6 months; 1 cGVHD at 12 months; 2 infection at 12 months

At 3 months, 8 subjects had limited and 3 had extensive cGVHD. These were included in a model covering the 3, 6, and 12 month time points (data not shown).

^IPatients with autologous transplants are not eligible for GVHD and were therefore excluded from the GVHD models.

Table 6

Relation between HSCT complications and parent's emotional functioning.

	β (SE)	p-value
Early (45 days and 3 months)		
Model 1: aGVHD		
Intercept	32.0 (3.7)	<0.0001
45 days	reference	
3 months	-1.6 (1.4)	0.258
aGVHD		
None, grade 1	reference	
grade 2	-5.2 (3.0)	0.086
Baseline parent emotional functioning	0.5 (0.1)	<0.0001
Model 2: Bearman		
Intercept	31.9 (3.6)	<0.0001
45 days	reference	
3 months	-1.4 (1.4)	0.317
Bearman		
Good	reference	
Intermediate/poor	-5.8 (3.0)	0.052
Baseline parent emotional functioning	0.5 (0.1)	<0.0001
Model 3: Infection		
Intercept	31.7 (3.7)	<0.0001
45 days	reference	
3 months	-1.3 (1.4)	0.363
Infection *		
None	reference	
Localized	-2.8 (3.5)	0.430
Systemic	-5.1 (2.2)	0.023
Baseline parent emotional functioning	0.5 (0.1)	<0.0001
Model 4: Early Composite		
Intercept	33.1 (3.7)	<0.0001
45 days	reference	
3 months	-1.6 (1.4)	0.263
Early composite		
No	reference	
Yes	-6.1 (2.4)	0.013
Baseline parent emotional functioning	0.5 (0.1)	<0.0001
Late (6 and 12 months)		
Model 5: cGVHD		
Intercept	34.9 (4.2)	<0.0001
6 months	reference	
12 months	6.0 (1.8)	0.001

	β (SE)	p-value
cGVHD **		
None	reference	
Limited	0.7 (3.3)	0.824
Extensive	2.5 (4.0)	0.534
Baseline parent emotional functioning	0.5 (0.1)	<0.0001
Model 6: Infection		
Intercept	36.2 (3.9)	<0.0001
6 months	reference	
12 months	5.3 (1.6)	0.002
Infection *		
None	reference	
Localized	3.2 (3.6)	0.364
Systemic	-20.2 (3.9)	<0.0001
Baseline parent emotional functioning	0.5 (0.1)	<0.0001

* global p-values for infection: $p = 0.072$ early; $p < 0.0001$ late

** global p-value for cGVHD: 0.823