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# The Quality of Life of Adult Survivors of Childhood Hematopoietic Cell Transplant

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## Abstract

Survival rates following myeloablative hematopoietic cell transplantation (HCT) in childhood have improved. We conducted a cross-sectional study evaluating the quality of life (QOL) of 214 adult survivors of a childhood HCT compared to controls using standardized self report measures with strong psychometric properties to evaluate physical function, psychological function, and cognitive symptoms. From these results we conducted a multivariate analysis of risk factors. This analysis for physical functioning showed poorer function among myeloid disease survivors compared to patients with all other diagnoses (p=0.02), males functioned better than females (p=0.05) and those >18 years after transplant functioned more poorly than those <18 years after transplant (p=0.05). Psychological functioning showed those who received more therapy and females were more likely to be depressed (p=0.03) and (p=0.005). Perceived cognitive symptoms demonstrated that female survivors had more symptoms than male survivors (p=0.01), and those receiving more preceding therapy compared to those with less preceding therapy (p=0.001) or cranial irradiation compared to those without cranial irradiation (p=0.002) had more perceived cognitive symptoms. Overall, these data indicate the majority of adult survivors of a childhood transplant are functioning well, but some have problems which need to be addressed.

### Keywords

Quality of Life; Pediatric long term survivors; Quality of life of adult pediatric survivors

## INTRODUCTION

Survival rates after myeloablative hematopoietic cell transplantation (HCT) have improved considerably during the past 30 years. There is a growing population of survivors, and in particular individuals who received their HCT when they were children. These patients make up a unique group about whom few previous studies have been performed evaluating their health related quality of life (QOL) as they are surviving into adulthood. QOL is



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defined as a multi-dimensional construct encompassing physical, mental and social well-being.1 Improved understanding of these individuals' QOL will facilitate more accurate informed consent, permit better planning by parents, patients, and medical providers, and enable the design of interventions to improve outcome for future patients.

The late effect medical complications of HCT have been well described and for children include chronic graft-versus-host disease (GVHD), recurrent infection, diabetes mellitus, pulmonary function abnormalities, growth and development issues, recurrent malignancy and development of secondary malignancy.2–9

Studies conducted on the QOL of adult survivors of adult transplants have yielded contradictory results. While some studies of adult transplant survivors indicate that these individuals are relatively unaffected at late follow-up, others report a wide variety of problems, including low energy levels and sleep difficulties, physical limitations, sexual difficulties, psychological distress and impaired social relationships.10–12 Some have attributed this disparity in findings to differences in methodology and sampling.13 Some of these studies, however, show that age at transplant is important with younger adult transplant recipients doing better. Higher total body irradiation (TBI) dose seems to be related to poorer sexual, cognitive, and physical functioning. After the first year time post transplant does not seem to influence psychosocial status, functional QOL and affective status. Fatigue, psychological distress and sexual dysfunction are the most frequently reported symptoms after transplant.10,14

The purpose of the present study was to evaluate the quality of life of a large number of adults who received their transplant as a child 5 or more years previously. Based on previous research the hypotheses were that a) the majority would not have physical limitations that disrupted their activities of daily living, and, b) these individuals would report impaired social function, but the majority would be psychologically without major impairments, and c) the majority of these adults would not self-report cognitive difficulties. Therefore, we conducted a cross-sectional study evaluating the QOL of all available adult survivors of transplants that took place at the Fred Hutchinson Cancer Research Center when the individual was less than 18 years old. The objective was to determine the extent to which these individuals are at risk for ongoing issues with physical limitations, psychosocial issues, and cognitive symptoms based on demographic or treatment factors. Results were compared to a gender and age matched control cohort.

## METHODS

### Participants and Procedures

All 334 potentially eligible participants had to be able to speak, read, or write English adequate to complete patient reported outcome questionnaires. Eligible patients were 5 years or more after HCT, were less than 18 years of age at the time of HCT and were now more than 18 years of age and without any evidence of their original disease. All diagnoses, all preparative regimens and all donor types were included. Diagnosis categories were considered based on the similarity of the treatment received prior to transplant and the type of transplant preparative regimen received. Lymphoid disease category included patients

with acute lymphoblastic leukemia (ALL), non-Hodgkin lymphoma (NHL) and Hodgkin Disease (HD) because the majority of these patients were beyond first remission at the time of transplant and had similar transplant preparative regimens. Myeloid disease category recipients were grouped together because the majority of patients were early in the course of their disease, including patients with acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS). Chronic Myelogenous Leukemia (CML) was considered separately because the disease is treated differently from acute leukemia prior to transplant. Similarly, the majority of the non-malignant disease category patients had aplastic anemia and all received similar or the same preparative regimen. Patients were further categorized by relatively how much disease specific therapy had been administered prior to transplant. Those categorized as “less” therapy included non-malignant disease patients, CML in chronic phase, and those with acute leukemia in first remission. Those patients categorized as “more” therapy included all of those patients beyond first remission or beyond chronic phase. Among the 334 eligible patients, 13 were lost to follow-up or were living overseas and contact was prohibited for one patient. A total of 320 eligible survivors were contacted of whom 289 indicated they were willing to participate. Among these 67 did not return data leaving a population of 222 who participated in the study.

The control subjects were gender matched with the survivors and were within 5 years of the survivors’ age. The controls were a sibling or friend of the survivor who met the age and gender criteria. Use of siblings as controls is the standard control also used by the Childhood Cancer Survivorship Study.15 Since they are not ideal in that influences of the HCT experience cannot be ruled out, when available, population norms are also reported and compared. The protocol and questionnaires were approved by the Institutional Review Board prior to initiation of the study. The survivors and controls were contacted by phone by the study coordinator who explained the study and asked if the packet of questionnaires could be mailed to them. Implied consent was obtained by the survivors’ and controls’ completion of the questionnaires and returning them to the study coordinator in the provided self-addressed envelopes. Medical records provided details regarding the survivor diagnosis, treatment regimens, type of HCT donor, history of acute and chronic GVHD and survival.

## Measures

Patient-reported outcomes have established reliability in medical and non-medical populations including HCT survivors. Standard self-report questions asked about age, gender, ethnicity, race, education, and income. Respondents indicated whether specific diseases had been diagnosed and how severe the specific health problem was using ratings of none, mild, moderate or severe. Active diseases and problems were noted and reported.

Three aspects of QOL were investigated: physical functioning, psychosocial functioning, and cognitive symptoms. Standardized scales or measures with strong psychometric properties were used to measure QOL. **Physical functioning** was measured using the Medical Outcome Study Short Form 36 Health Survey (SF36). **Psychosocial functioning** was evaluated using the depression and anxiety subscales of the Symptoms Checklist 90-R, 16 the Satisfaction with Life Roles,17 the Family Relations Index (FRI),17 and Social Support Questionnaire Short Form (SSQSR).18 **Cognitive symptoms** were measured using

the Neurobehavioral Rating Scale (NBRS)19 and the Modified Memory Questionnaire (MMQ).20

**Physical Capability—**The SF-36 is a widely used QOL measure that provides a non-disease-specific measure of adult functioning and well being, allowing for comparison with a broad range of same-aged norm groups including those of an age and gender-matched healthy population.21 The eight subscales measure the physical functioning, role limitations due to physical health problems, bodily pain, general health, vitality, mental health, social functioning, and role limitations due to emotional health. Two summary scores are also calculated from the subscales, a physical component score (PCS) and a mental component score (MCS).

**Psychosocial functioning—**The SCL-90-R is a standardized, multidimensional self-report inventory of psychological symptoms with norms available for a large sample of nonpsychiatric adults. The scale has extensive reliability and validity testing and has been used in HCT survivors.10 FRI17 measures the quality of social relationships in the family. It includes subscales that comprise the relationship domains of Cohesion, Expressiveness, and Conflict along with the total score. This is a widely used, reliable and valid measure used in oncology as well as non-medical research. The Life Satisfaction scale was developed to assess the impact of HCT on roles such as family, home, and work. Respondents are asked to rate their satisfaction from 0 = not at all to 10 = extremely well for 10 aspects of family, home, and work roles, including parent, spouse, homecare, worker, and student as well as appreciation of life and religious or spiritual participation. The score is the mean response of those items that are applicable to the individual. Internal consistency reliability with the full cohort in this study is alpha = .86. Validity is supported by correlations with the SF-36 mental health subscale of r = .57 and with the FRI total score of r = .40. The SSQSR18 inventory of social support is one of the most broadly used brief measures of social support designed to measure perceived social supports and satisfaction with available support.

**Cognitive symptoms—**The NBRS measures self-observed alertness, distractibility, intrusion of irrelevant thoughts, coherence of conversion, anxiety, tension, disinhibitory behavior, motor behavior and expressive/receptive language ability. The MMQ is a self-report test of everyday memory. The measures provide assessment of perceived deficiencies verbal recall and learning and provide an assessment of memory deficiencies.

## Analysis

Statistical analysis was performed using SPSS 12.0 and SAS Version 8. Scores were examined for outliers and normality of distribution. No transformations were performed. Chi-square tests and Student’s t-tests were used to compare demographic and clinical variables as well as QOL scores between the survivor and control groups and survivors vs QOL score population norms where available. Analysis of variance (ANOVA) was used to adjust the latter comparisons for age and gender, and to perform multivariate analysis (MANOVA) of factors influencing QOL outcomes among survivors. Demographic and treatment variables considered in the analyses included diagnosis group lymphoid malignancy [acute lymphoblastic leukemia (ALL), Hodgkin Disease (HD), non-Hodgkin

Lymphoma (NHL)] vs. myeloid malignancy [acute myelogenous leukemia (AML), myelodysplastic syndrome (MDS) juvenile myelomonocytic leukemia (JMML)] vs. chronic myelogenous leukemia (CML) vs non-malignant disorders [aplastic anemia (AA), red cell aplasia, Wiskott Aldrich Syndrome], preparative regimen TBI vs no TBI, pre-transplant cranial irradiation, clinical extensive chronic GVHD, scleroderma and/or contractures, age at transplant, age at study participation, time post-transplant, gender, prior therapy (more vs less), donor type (autologous, matched vs mismatched), and second transplant.

## RESULTS

Among the 222 participating survivors transplanted April 1972 through November 1994 (69% of eligible, approached participants), eight were excluded because of unusual preparative regimens or diagnoses, leaving a total population of 214 included in the analysis. The population included was similar in distribution to the total number of patients transplanted during this time period. The survivors were a mean of 28.7 years of age (range 18.8–45.9 years). Ninety-six were female and 118 were male. There were 194 who were Caucasian and 20 who were non-Caucasian. There were no differences between participants and non-participants with respect to gender, diagnosis, cranial irradiation, having received TBI, race and time post-transplant. Participant's age at transplant was 11.9 (range: 1.8–17.9) years of age compared to non-participant age at transplant of 10.4 (range: 1.5–17.9) years of age ($p = 0.005$). Among the participant's there were more females (47%) than males compared to non-participant's where females were 32% compared to males ($p = 0.01$). Among the participants there were fewer non-white race individuals (9%) than among the non-participants (19%) ($p = 0.01$). For all other comparisons between the participants and non-participants there were no differences in age at diagnosis, time from diagnosis to transplant, diagnosis at transplant, cranial irradiation, transplant preparative regimen, acute and chronic GVHD and donor type as well as age at study.

Among the 197 controls, the mean age was 28 years (range 18–51 years). There were 105 females and 92 males and 178 Caucasians and 19 non-Caucasians. Among controls, the 120 siblings were not statistically different from the 77 non-siblings in terms of gender, ethnicity, race, educational status, full time work or school, financial situation or marital status. The control siblings were a mean of 29 years of age and the control non-siblings were 26.4 years of age ($p = 0.005$). Siblings did not differ from non-sibling controls in any of the outcomes reported. Transplant characteristics of the survivors are shown in Table 1. Among these survivors, 148 (69%) received HCT for a type of leukemia and 31% had a non-malignant disease. Prior to transplant, 21% of survivors had received 18.0–24.0 Gy cranial irradiation. The time between the survivor's diagnosis and the HCT was a mean of 1.4 (range: 0.1–11.4) years. The transplant preparative regimen included 12.0–15.75 Gy fractionated TBI for 51% of the survivors. Acute and chronic GVHD were problems for 48% and 28% of the survivors respectively. The average time after transplant patients were studied was 16.2 (range: 5.2–28.9) years, and the average age when the patients were studied was 28.7 (range: 18.8–45.9) years.

## Comparisons between survivors and controls

**Physical Function—**This was measured by SF-36 PCS. Higher scores indicate better functioning with a population mean of 50 and a standard deviation of 10. In all instances the control participants had significantly better functioning as indicated by higher scores (Table 2). Although survivors did not differ from population norms (50.0 vs 51.1) when comparing the survivors with the controls, the controls functioned significantly better than the transplanted survivors on the PCS as indicated by higher scores (55.1 vs. 51.1, p = 0.001). With respect to the physical sub-scales of the SF-36 including physical function, role physical, bodily pain and general health, the transplant recipients were significantly worse than the control groups (Table 2).

**Psychological Function—**This was measured by the SF-36 mental component score (MCS) and mental health sub-scales, Life Satisfaction as well as SCL-90-R depression and anxiety sub-scales. For the SCL-90-R scale, higher scores indicate worse functioning, but for the SF-36 and Life Satisfaction scales, higher scores indicate better functioning. In overall MCS survivors did not differ from controls or from population norms. On the SF-36 MCS sub-scales (mental health, vitality, social function, and role emotional), the control subjects had higher scores than the survivors, but none were statistically significant (Table 2). For the SCL-90-R scales for depression, the survivors were more likely to be depressed (p = 0.03) than the control subjects and trended toward having more anxiety (p = 0.07). However, survivors were more likely to have greater satisfaction with their role in life (p = 0.01) than controls.

**Family Relationships—**This was measured by the Family Relations Index (FRI) looking at the subscales of cohesion, expression, conflict and total relationship. In no instance was there a significant difference between the transplant recipients and the controls (data not shown).

**Cognitive Symptoms—**This was assessed by the NBRS and MMQ. On the NBRS and MMQ scales, higher scores indicate more symptoms, and on the RS cognitive scale, higher scores indicate fewer symptoms. When transplant survivors were compared with controls, the MMQ (0.55 vs 0.53) overall were not significantly different from each other (p = NS and p = NS) (Table 2). The NBRS patient scores indicated more cognitive symptoms than controls (1.64 vs. 1.28, p = 0.01).

**Overall Comparison of Quality of Life—**The data for this evaluation is shown in Table 2 in the QOL domain and number of QOL problems. Overall, 70% of the transplant survivors had no QOL problems compared to 74% of controls (p = 0.04).

## Risk Factor Analysis among Survivors

**Physical Functioning—**Table 3 shows the results of multivariate analysis for demographic and treatment risk factors which had an apparent association with either outcome. Other factors included in the analysis but not significant include preparative regimen, cranial irradiation, chronic GVHD, age at transplant, age at study participation, and second transplant (data not shown). There were differences in physical function based on

patient diagnosis with patients with Lymphoid Malignancy and CML functioning the best and those with myeloid malignancy having the poorest physical functioning. All other measures of physical function were not significant

**Psychological Function—**Table 4 shows the results of the multivariate analysis for psychological function risk factors which had an apparent association with any of the outcomes. Other factors included in the analysis but are not significant include preparative regimen, cranial irradiation, chronic GVHD, age at transplant, age at study participation, donor type and second transplant (data not shown). In this analysis, the diagnosis did not play a role in psychological functioning. Patients receiving more therapy before transplant were more likely to be depressed after transplant and less satisfied with life roles as measured by the depression scale and the life satisfaction with life scales ($p = 0.03$ and 0.005 respectively). Females were more likely to have psychological dysfunction MCS ($p = 0.01$) and depression ($p = 0.005$) scales and more anxious as measured by the anxiety scale ($p = 0.02$) compared to males. The number of years after transplant did not have an effect on development of anxiety or depression.

**Cognitive Symptoms—**Table 5 shows the results of multivariate analysis for risk factors which had an apparent association with any of the outcomes. Other factors included in the analysis, but were not significant include preparative regimen, chronic GVHD, age at study participation, donor type and second transplant (data not shown). There were no differences in perceived cognitive symptoms with respect to diagnosis for the MMQ or NBRS measures. Among patients receiving more therapy MMQ and NBRS were all significantly impacted among those who had received more therapy. Among those who had received cranial irradiation prior to transplant only self reported memory as measured by the MMQ was significantly impacted, but self reported cognitive function as measured by NBRS was not significantly impacted. Females had more symptoms than males on both the MMQ and transplant age of <13 years appeared to result in more cognitive symptoms with the MMQ only.

## Social Relationships, Education and Insurance

More survivors than controls reported that they were living with their parents (25% of patients and 12% of controls, $p = 0.001$). Few in both groups, but more survivors, reported that they had never dated (5% of survivors and <1% of controls, $p = 0.007$). More patients than controls indicated that they had never married or had a live-in partner (43% of patients and 32% of controls, $p = 0.04$). A majority of both groups were married or cohabitating. There were 57% of patients and 54% of controls who were currently married or cohabiting ($p = NS$).

In considering education, 14% of patients and 4% of controls noted that they were in special education classes during school ($p = 0.001$). The reasons for the special education classes were not explored. In school achievement, however, a grade point average of less than 3.0 was earned by 41% of patients and 40% of controls ($p = NS$) and 52% of patients and 58% of controls completed 2-year college or trade school or further education ($p = NS$). At the time of assessment, 82% of the patients and 91% of the controls were working fulltime,

were in school full time or were full time homemakers (p = 0.001). More survivors than controls depended upon family or the government for financial support (15% of survivors and 6% of controls, p = 0.002), with the remainder being self sufficient.

Health insurance had been denied to 18% of transplant patients and 2% of controls (p = 0.001), but 12% and 14% respectively did not have health insurance (p = NS). The source of health insurance was mainly from the employer (46% transplant patient, 50% control, p = NS) and from spouse or parent (24% transplant patient, 27% control, p = NS). Life insurance was obtained by 57% of patients and 60% of controls (p = NS).

## DISCUSSION

This study provides information about the largest cohort of adults reported to date who received an HCT as a child with a median follow-up of 16 years. The transplant patients report functioning as well as non-transplant controls on various aspects of QOL, although survivors were more likely than controls to report continuing difficulties in physical functioning and depression. Reasons for greater functional difficulties in some survivors are not entirely clear and cannot be entirely related to the degree of transplant complications, especially chronic graft-versus-host disease (GVHD) or prior therapy received by this population. Consistent with findings of adult survivors of HCT, female survivors of pediatric transplants had more psychological difficulties.22

The participants and non-participant transplanted recipient groups were similar in most aspects, but differed significantly with respect to the age at transplant (mean 11.9 years vs 10.4 years), gender (females 47% vs 32%) and race (non-white 9% vs 19%). Participant bias may have been a factor in the risk factor analysis where gender was a significant factor with respect to physical functioning, psychosocial functioning, and cognitive symptoms. This difference in gender distribution with more female participants than male participants may have influenced the risk factor analysis where more females than males had more cognitive symptoms, had poorer physical functioning and were more likely to be depressed. If equal number of males and females had participated, the results of this analysis could have been impacted. It is unlikely that the mean difference in age at transplant between participants and non-participants of 1.5 years had any influence on the outcomes measured since age was not a significant factor in the risk factor analysis. Similarly, it is unlikely that the imbalance between race of the participants and non-participants was a factor since race was also not a significant factor.

Physical functioning after transplant was significantly worse in the transplant patients compared to the controls. The risk factor analysis showed that diagnosis of myeloid malignancy was a significant risk factor as was having received an autologous transplant. This suggests that chronic GVHD per se was not a major factor in long term physical functioning although a few patients with scleroderma reported worse physical function. This differs from what was observed by others where there was no reported physical impairment, 23 but similar to another study where physical adverse events were seen in the HCT group. 24 A recent Swedish study showed poor satisfaction with physical health.25 Duration of time after transplant did not predict better or poorer function, but this could be because the

median follow-up time was 16 years and our study was not designed to be sensitive to early post-transplant changes in physical stamina and return to regular life activities. Syrjala, et al. observed in adults that it took as long as five years before patients were fully functioning at near pre-transplant levels.14 One study evaluated patient's physical activity and found that transplant patients had more restrictions in sports activities and mobility reported and attributed to disease or treatment sequelae. The transplant patients were more likely to spend free time in passive activities that required no physical activities.1,23,26,27

As has been observed in the adult transplant population, females were more likely to be depressed after transplant than males, and patients on average were more depressed than controls. This may be an extension of the observations that post-transplant teenagers had more difficulties in coping with themselves and significant others than a control group of healthy girls.28 Nespoli et al showed that adolescent patients had slightly increased levels of depression.29 Ness also found more psychosocial difficulties reported by adult survivors of pediatric transplantation.30 On the other hand, Kupst, et al, found a relative lack of psychosocial problems,26 and Lof et al found emotional well being and satisfaction with family similar to norms.25 In our study, patients who had received more leukemia therapy pre-transplant were subsequently more likely to be depressed. This observation bears watching in future studies, especially among patients who come to transplant heavily pre-treated.

In the present study there was no difference among the patients compared to controls in self-reported symptoms of memory difficulty (MMQ) or in areas of alertness, or ease of distractibility, but there was poorer expressive/receptive language function (NBRS) among the transplant recipients compared to the controls. More of the transplant patients needed to have special education compared to controls, consistent with other reports.30 But ultimately the patients had grade point averages comparable to the controls and completed trade school or higher education in similar proportions. More than 80% of patients and 90% of controls were gainfully employed. In addition, survivors indicated higher levels of life satisfaction than controls. These findings suggest that overall a large majority of childhood HCT recipients will function well in school and work-related roles.

Several studies have measured cognitive function. Four studies have shown that either the pre and post-transplant IQ was stable26 or there were no differences in cognitive functioning after HCT.31,32 Some studies measured declines in cognitive function for subgroups of pediatric transplant survivors after transplant out to five years.31,33 While this study did not test objective neuropsychological function, the results of these patient-reported outcomes suggest that most patients function as well as controls with respect to cognitive function.

It is gratifying to learn that the majority of pediatric transplant survivors are self-sufficient adults who are contributing to society. The results documenting a high rate of employment among the transplanted patients is similar to the observations of others who have found that up to 95% of transplant survivors were attending school or employed.28

There are several limitations of the current study that may affect the generalization of findings. First, this was a cross-sectional study in a population of patients accrued over

nearly three decades. During that time the approaches to chemotherapy, the drugs used and the duration of therapy have changed. Similarly, the approaches to transplantation have changed including the transplant preparative regimens, the way donors are selected, and the extent of psychosocial and learning support available to pediatric transplant recipients. All of these factors may influence the long-term post-transplant QOL among survivors.

Questions can be raised about whether the control cohort is appropriately matched to the survivors. Bias could have been introduced if patients had multiple eligible candidate controls and consistently selected a more or less healthy case-match or if siblings introduced negative psychosocial health bias as a result of having experienced the HCT in a sibling. In the pediatric situation, the sibling may not yet have been born when the transplant took place. One could argue that although siblings are excellent controls for biologic outcomes, their experience of transplant could influence their psychosocial outcomes in a manner not detected. Other methods of selecting controls include random-digit dialing, not including siblings in recruitment or having survivors nominate many possible case matched controls and randomly selecting controls from this sample. We note that the Childhood Cancer Survivor Study also uses siblings as controls for their survivors.15 We have compared our results to both matched controls and population norms, where available, and find that siblings are as healthy as population norms.

In summary, these data suggest that in general adult survivors of a childhood transplant have a reasonable QOL. Some have physical, psychosocial, and cognitive problems which may be able to be addressed with survivorship programs that target rehabilitation and education interventions, and are increasingly accessible to those with unmet needs.34 Most all are gainfully employed and have insurance. Future studies should address following these transplanted patients prospectively to learn the pace at which these survivors return to normal physical and mental health after transplant, to address the problems observed in the AML patients and to address the depression and anxiety observed among the female patients. Understanding of these individuals' QOL needs, based on results of this study and similar research, will facilitate more detailed informed consent, permit better planning by parents, patients, and medical providers, and enable the design of interventions to improve outcomes for future patients.

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**Author Contribution Statement**

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## Table 1

Characteristics of Transplant Survivors Studied

| Diagnosis | Non-Malignant | Lymphoid Malignancy | Myeloid Malignancy | CML |
|---|---|---|---|---|
| No. Patients | 53 | 69 | 68 | 24 |
| Age at Tx – yrs Mean (range) | 11.5 (1.7–17.9) | 11.3 (3.4–17.4) | 12.4 (1.9–17.9) | 13.7 (3.9–17.8) |
| Study Age – Yrs Mean (range) | 32.1 | 27.3 | 27.1 | 24.9 |
| Gender M:F | 24:29 | 49:20 | 34:34 | 11:13 |
| Regimen S-TBI | 2 | 29 | 17 | 2 |
| Fx-TBI | 4 | 40 | 44 | 21 |
| BUCY | 4 | 0 | 7 | 1 |
| CY | 43 | 0 | 0 | 0 |
| Prior Treatment Less: More | 53:0 | 18:51 | 59:9 | 24:0 |
| Donor – Auto | 0 | 4 | 8 | 0 |
| Match | 53 | 53 | 48 | 16 |
| Mismatch | 0 | 12 | 12 | 8 |
| GVHD – Acute | 13 | 39 | 35 | 15 |
| Chronic | 10 | 16 | 22 | 12 |
| Severe Chronic | 1 | 3 | 4 | 1 |

Non-Malignant – includes aplastic anemia, immune deficiency, red cell aplasia Lymphoid Malignancy – includes acute lymphoblastic leukemia, Hodgkin Disease, Non-Hodgkin lymphoma, Myeloid Malignancy – includes acute myelogenous leukemia, myelodysplastic syndrome, juvenile myelomonocytic leukemia

CML – chronic myelogenous leukemia, TX – transplant, S-TBI is single fraction total body irradiation, FX TBI is fractionated total body irradiation, BUCY is busulfan plus cyclophosphamide, CY is cyclophosphamide only. Less treatment includes no cytotoxic therapy, first remission, untreated first relapse. More treatment includes second or greater remission, relapse, cranial irradiation. Auto is autologous, match is HLA matched related or unrelated donor, mismatch is HLA mismatched related or unrelated donor. GVHD = graft versus host disease

## Table 2

Overall Quality of Life Comparison with Controls

| QOL measure | BMT | Control | p-value* |
|---|---|---|---|
| Number of patients | 214 | 186 | |
| Physical | Mean Score | Mean Score | |
| Physical Component (PCS) | 51.1 | 55.1 | <0.001 |
| Physical Function | 89.1 | 94.5 | <0.001 |
| Role Physical | 84.5 | 91.0 | 0.02 |
| Bodily Pain | 79.2 | 82.9 | 0.05 |
| General Health | 70.1 | 81.4 | <0.001 |
| Psychological | | | |
| Mental Component (MCS) | 50.4 | 48.5 | NS |
| Depression | 0.57 | 0.53 | NS |
| Anxiety | 0.30 | 0.30 | NS |
| Cognitive | | | |
| MMQ | 0.55 | 0.53 | NS |
| NBRS | 1.64 | 1.28 | 0.01 |
| QOL domains | N | N | |
| PCS <40 | 25 (12%) | 6 (3%) | 0.001 |
| MCS <40 | 34 (16%) | 36 (18%) | NS |
| Cognitive <−1 | 46 (21%) | 27 (14%) | 0.04 |
| Number of QOL problems | | | |
| 0 | 149 (70%) | 146 (74%) | 0.04 |
| 1 | 29 (14%) | 33 (17%) | |
| 2 | 29 (14%) | 18 (9%) | |
| 3 | 6 (3%) | 0 | |

Abbreviations: QOL = quality of life, BMT = bone marrow transplant patient group, PCS = physical component score of SF 36 <40 = abnormal functioning, MCS = mental component score of SF 36 <40 = abnormal symptoms. MMQ = modified memory questionnaire, NBRS = neurobehavioral rating scale.

* Student's t test. On the NBRS and MMD higher scores indicate more symptoms. On the RS cognitive, higher scores indicate fewer symptoms.

## Table 3

Multivariate Analysis of Risk Factors for Physical Function

| Variable | No. of Pts | SF-PCS* | SEE | p-value |
|---|---|---|---|---|
| Diagnosis | | | | |
| Myeloid | 68 | −2.0 | (2.64) | 0.02 |
| Lymphoid | 69 | 3.9 | (3.24) | |
| CML | 24 | 1.0 | (3.19) | |
| NM | 53 | --- | | |
| Donor type | | | | |
| Matched | 171 | -- | | |
| Mismatched | 31 | −3.2 | (1.79) | NS |
| Autologous | 12 | −7.4 | (2.75) | 0.008 |
| Gender | | | | |
| Female | 170 | | | |
| Male | 44 | 0.90 | (1.25) | NS |
| Prior Therapy | | | | |
| Less | 143 | | | |
| More | 71 | −3.5 | (2.24) | NS |
| Time post BMT | | | | |
| <18 years | 129 | | | |
| >18 years | 85 | −2.0 | (1.42) | NS |

**Abbreviations:** SF-PCS = Short Form 36 physical scale where higher scores indicate better functioning, Myeloid = acute myelogenous leukemia, myelodysplastic syndrome, juvenile myelomonocytic leukemia, Lymphoid = Acute lymphoblastic leukemia, Hodgkin Disease, Non-Hodgkin Lymphoma, CML = chronic myelogenous leukemia, NM = non-malignant includes aplastic anemia, immune deficiency, red cell aplasia. Matched = HLA identical siblings or unrelated donors, mismatched = HLA non-identical family members or unrelated donors. Prior therapy less = first remission therapy or no therapy, prior therapy more = second or subsequent remission or relapse therapy or cranial irradiation. SEE = Standard Error of the Estimate

*Numbers reflect mean differences relative to reference group.

--- = reference group.

**Table 4**

Multivariate Analysis of Risk Factors for Psychological Function

| Variable | No. of Pts | CMS* | SEE | p-value | Depression* | SEE | p-value | Anxiety* | SEE | p-value | Satis* | SEE | p-value |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Diagnosis | | | | | | | | | | | | | |
| Myeloid | 68 | −2.30 | (2.72) | NS | 0.25 | (0.17) | NS | 0.21 | (0.14) | NS | −0.09 | (0.48) | NS |
| Lymphoid | 69 | 1.68 | (3.33) | | −0.03 | (0.21) | | 0.10 | (0.17) | | 0.87 | (0.59) | |
| CML | 24 | 0.47 | (3.28) | | 0.06 | (0.20) | | 0.18 | (0.17) | | 0.42 | (0.58) | |
| NM | 53 | --- | | | --- | | | --- | | | | | |
| Prior therapy | | | | | | | | | | | | | |
| Less | 143 | -- | | | -- | | | -- | | | -- | | 0.005 |
| More | 71 | −2.9 | (2.31) | NS | 0.31 | (0.14) | 0.03 | 0.17 | (0.12) | NS | −1.15 | (0.41) | |
| Gender | | | | | | | | | | | | | |
| Female | 96 | -- | | | -- | | | -- | | | | | |
| Male | 118 | 3.3 | (1.28) | 0.01 | −0.23 | (0.08) | 0.005 | −0.16 | (0.06) | 0.02 | 0.38 | (0.23) | 0.10 |
| Scleroderma | | | | | | | | | | | | | |
| No | 205 | -- | | | -- | | | -- | | | -- | | |
| Yes | 9 | 7.6 | (2.31) | 0.02 | −0.19 | (0.20) | NS | −0.34 | (0.17) | 0.04 | 0.55 | (0.59) | NS |
| Time post BMT | | | | | | | | | | | | | |
| <18 years | 129 | -- | | | -- | | | -- | | | -- | | |
| >18 years | 85 | −0.5 | (1.46) | NS | 0.17 | (0.09) | 0.07 | 0.08 | (0.07) | NS | −0.43 | (0.26) | 0.10 |

Abbreviations

CMS = composite mental score where higher values are better, depression where lower scores are better, anxiety where lower scores are better. Satis = satisfaction with life. Less prior therapy = first remission or no therapy and more therapy = second or subsequent remission therapy or relapse or cranial irradiation. Myeloid includes acute myelogenous leukemia, myelodysplastic syndrome, juvenile myelomonocytic leukemia. Lymphoid includes acute lymphoblastic leukemia, Hodgkin Disease, Non-Hodgkin lymphoma, CML = Chronic Mylogenous Leukemia, NM = non-malignant includes aplastic anemia, immune deficiency, red cell aplasia SEE = Standard Error of the Estimate

*Numbers reflect mean differences relative to reference group.

---- = reference group

**Table 5**

Multivariate Analysis of Risk Factors for Cognitive Symptoms

| Variable | No. of Pts | MMQ* | SEE | p-value | NBRS* | SEE | p-value |
|---|---|---|---|---|---|---|---|
| Diagnosis | | | | | | | |
| Myeloid | 68 | 0.12 | (0.14) | NS | 0.31 | (0.44) | NS |
| Lymphoid | 69 | −0.08 | (0.18) | | −0.38 | (0.54) | |
| CML | 24 | −0.04 | (0.17) | | −0.39 | (0.53) | |
| NM | 53 | --- | | | --- | | |
| Prior Therapy | | | | | | | |
| Less | 143 | --- | | | --- | | |
| More | 71 | 0.43 | (0.12) | 0.001 | 0.74 | (0.37) | 0.05 |
| Cranial Rads | | | | | | | |
| No | 170 | -- | | | --- | | |
| Yes | 44 | −0.40 | (0.13) | 0.002 | −0.50 | (0.38) | NS |
| Gender | | | | | | | |
| Female | 96 | --- | | | --- | | |
| Male | 118 | −0.11 | (0.07) | NS | −0.53 | (0.21) | 0.01 |
| Age at BMT | | | | | | | |
| <13 years | 110 | --- | | | --- | | |
| >13 years | 104 | −0.14 | (0.07) | 0.04 | −0.32 | (0.21) | NS |

**Abbreviations:** MMQ = Modified Memory Questionnaire where higher values worse, NBRS = Neurobehavioral Rating Scale where higher values worse, Lymphoid = Acute lymphoblastic leukemia, Hodgkin Disease, Non-Hodgkin lymphoma, Myeloid = Acute Myelogenous Leukemia myelodysplastic syndrome, juvenile myelomonocytic leukemia, CML = Chronic Myelogenous Leukemia, NM= non-malignant includes Aplastic Anemia, immune deficiency, red cell aplasia, Less Therapy = first remission therapy only or no therapy, more therapy = second or subsequent remission therapy or relapse or cranial irradiation, Cranial rads = cranial irradiation. SEE = Standard Error of the Estimate

*Numbers reflect mean differences relative to reference group

--- = reference group.