HHS Public Access

Author manuscript

Biol Blood Marrow Transplant. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

Biol Blood Marrow Transplant. 2015 April ; 21(4): 666–672. doi:10.1016/j.bbmt.2014.12.007.

Health-Related Quality of Life after Allogeneic Hematopoietic Stem Cell Transplantation for Sickle Cell Disease

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Abstract

Sickle cell disease (SCD) is a hereditary hemoglobinopathy that affects over 100,000 people in the United States. Patients with SCD are known to experience suboptimal health-related quality of life (HRQoL). In addition to the physical manifestations of SCD, psychological and social stress, along with academic difficulties, secondary to the chronicity of the disease and its complications often affect patients with SCD. Although medical therapy of SCD has improved, allogeneic hematopoietic cell transplantation (allo-HCT) remains the only curative therapy. The objective of this study was to measure HRQoL before and after allo-HCT by assessing physical, psychological, and social functioning in patients with SCD who have undergone reduced-toxicity conditioning (busulfan/fludarabine/alemtuzumab) followed by allo-HCT. Patients < 21 years of age undergoing allo-HCT (matched siblings and unrelated donors) for SCD and their primary caregiver were enrolled using either the English or Spanish version of the PedsQoL 4.0. Data were collected at 3 time points: before allo-HCT and on days 180 and 365 after allo-HCT. The change in HRQoL from baseline was assessed with unadjusted and adjusted mixed-effects models in which subjects were treated as random effects, and variance component structure was used. Seventeen patients and 23 primary caregivers were enrolled and reported a mean overall HRQoL of 66.05 (SD, 15.62) and 72.20 (SD, 15.50) at baseline, respectively. In the patient-reported analysis with adjusted mixed-effects models, the estimated improvements in overall HRQoL were 4.45 (SE, 4.98; $P = .380$) and 16.58 (SE, 5.06; $P = .003$) at 180 and 365 days, respectively, after allo-HCT. For parent-reported overall HRQoL, the estimated improvements were 1.57 (SE, 4.82; $P = .747$) and 9.28

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Financial disclosure: The authors have nothing to disclose.

Conflict of interest statement: There are no conflicts of interest to report.

(SE, 4.62; $P = .053$) at 180 and 365 days, respectively, after allo-HCT. Similar results were found across the physical, social, and emotional HRQoL domains with mixed-effects models after adjustment of demographic and medical variables. In addition to the alleviation of clinical manifestations of SCD, these patients demonstrated significant improvement in most aspects of HRQoL by 1 year after allo-HCT. These data represent the trajectory of HRQoL during the initial year of follow-up within this population and should be integrated into the decision-making process when considering allo-HCT in patients with SCD.

Keywords

Health-related quality of life; Quality of life; Stem cell transplantation; Sickle cell disease

INTRODUCTION

As of 2011, 1000 children are born with sickle cell disease (SCD) annually in the United States, with over 100,000 people living with the disease [1]. SCD is an hereditary hemoglobinopathy that negatively impacts quality of life and shortens life expectancy in affected individuals [2,3]. Physical complications include painful vaso-occlusive crises (VOC), stroke, acute chest syndrome, splenic sequestration, chronic pulmonary and renal dysfunction, and avascular necrosis of the joints [2,4–7]. In addition to the physical stress, psychological stress of the illness, including the chronicity of complications, limitations in educational and recreational activities due to symptoms, and financial burdens experienced by the family, are experienced by children and adolescents [8]. Such childhood chronic illness can result in poor psychological adjustment, behavioral problems, somatic complaints, lower levels of school and social competence, anxiety, and depression [8,9].

Supportive therapies have greatly improved for patients with SCD, with therapeutic options including chronic blood transfusions, hydroxyurea, and allogeneic hematopoietic cell transplantation (allo-HCT). Recent advancements in the research and application of allo-HCT for pediatric blood disorders have led to increases in survivorship with eradication of SCD symptomatology. To date, allo-HCT is the only established curative option in children with SCD [7]. There are no guidelines as to when allo-HCT should be offered to children with SCD, but historically, it has been reserved for symptomatic patients, such as those with a history of stroke, acute chest syndrome, or recurrent painful VOC, with HLA-matched sibling donors (MSD) [2,7]. As outcomes for sibling donor hematopoietic cell transplantation (HCT) have improved, more children with SCD are being referred for allo-HCT if they meet the definition of highly symptomatic and have a suitably matched unrelated donor.

To our knowledge, there is only 1 published longitudinal study that has investigated health-related quality of life (HRQoL) in children with SCD after allo-HCT with observational follow-up of 1 year. Kelly et al. [10] compared HRQoL reported by 13 parent-child dyads after allo-HCT for hemoglobinopathies (SCD, 7 dyads; thalassemia, 6 dyads) to that of parent-child dyads receiving allo-HCT for malignant diseases or severe aplastic anemia. The patients in the hemoglobinopathy group reported higher HRQoL at baseline (physical and

emotional functioning scores) than those in the control group and the majority of participants in both groups had returned to baseline levels of functioning at 3 months after transplantation, according to both parent and child report, before essentially reaching a plateau. The 2 groups did not differ in incidence of allo-HCT–related complications (ie, early infection, acute-graft-versus host disease [GVHD], chronic GVHD) [11].

The present quality of life study is a secondary aim of a medical treatment study that showed the efficacy of a reduced-toxicity conditioning (RTC) regimen in patients with SCD undergoing allo-HCT using busulfan, fludarabine, and alemtuzumab [12]. An RTC is defined as a regimen associated with myeloablation but also associated with reduced toxicity secondary to conditioning [13]. The medical treatment study showed improvements in the physical manifestations of SCD in those undergoing RTC allo-HCT. Patients had no VOC, improvements in cardiac, pulmonary, and splenic function, and stabilization of neurologic symptoms. This secondary pilot study aimed to determine whether RTC allo-HCT improved the emotional and social sequelae experienced by many patients with SCD in addition to the physical symptoms.

METHODS

Participants

All patients younger than 21 years of age undergoing allo-HCT for SCD, and their primary caregivers, were enrolled on this HRQoL study as part of their medical treatment protocol to evaluate the efficacy of an RTC regimen followed by allo-HCT from related donors and unrelated cord blood donors in patients with SCD. The protocol was approved by the institutional review board and was in compliance with the Declaration of Helsinki. Informed consent was signed before study initiation and HRQoL data were serially collected as part of the medical protocol using the PedsQL 4.0 Generic Core Scale for patients with SCD before and 1 year after allo-HCT.

Treatment Plan

Twenty-three patients received a conditioning regimen consisting of busulfan, fludarabine, and alemtuzumab, and 1 patient received melphalan, fludarabine, and alemtuzumab as we have previously described [12,14].

Medical Information

As part of the medical treatment study, demographic information, such as indications for HCT, age at HCT, donor source, and conditioning regimen, was collected. After allo-HCT, length of stay and readmissions during the first 100 days after allo-HCT were also recorded. Other assessments after allo-HCT, such as engraftment, transfusion requirements, chimerism studies, presence of GVHD, organ toxicity, and disease status were collected using standard scoring scales [13,15–17].

Measures

HRQoL data were collected using the PedsQL 4.0 Generic Core Scale [18]. To assess all participants enrolled on the medical treatment study, this follow-up study utilized 3 versions

of the PedsQL 4.0: a self-report format for children ages 5 to 18, a self-report format for young adults ages 18 to 25, and a proxy report for parents of children ages 2 to 18. The scale contains 23 items that assess physical (8 items), social (5 items), psychological (5 items), and school functioning (5 items). Overall HRQoL scores and psychosocial health summary scores were calculated as well as 3 individual composite scores (physical, social, and emotional functioning). It is important to note that the school items were not included in the first year analyses because these patients are not allowed to return to school for 1 full year upon completion of their allo-HCT. Consequently, overall HRQoL summary score is a composite of the physical, emotional, and social functioning indices, whereas the psychosocial HRQoL summary score is a composite of items from the emotional and social functioning indices. Scores range from 0 to 100, with higher scores indicating higher HRQoL. Data for the present study were collected from participants and their caregiver at 3 time points: before transplantation and on days 180 and 365 (1 year) after allo-HCT. Participants and their caregivers independently completed either the English or Spanish version of the PedsQL 4.0 at each time point.

Statistical Analysis

Descriptive statistics were calculated for all demographic, medical, and HRQoL variables. Specifically, the continuous variables were summarized by mean, standard deviation, median, and range, and the categorical variables were summarized by percentages. The change in HRQoL from baseline was assessed with unadjusted and adjusted mixed-effects models. In the mixed-effects model, the subjects were treated as random effects, and the variance component structure was used. The variance component structure models a different variance component for each random effect. The variables included in the adjusted mixed-effects models were GVHD, insurance type, and donor source. The estimated change of HRQoL from baseline was summarized with mean and standard error (SE) along with its corresponding *P* value. The relationship between proxy and patient HRQoL ratings was examined using intraclass correlation coefficients (ICC), an analysis that incorporates both mean group differences and discrepancies across individual patient/parent dyads, as well as Pearson's product correlation coefficients. The effect of the baseline variables on the missingness of the overall HRQoL at each follow-up time point was assessed with a logistic regression model. In mixed-effects models, all subjects and data were included in the analyses, even if some data were missing. A 2-sided *P* value less than .05 was considered as significant. The analysis was conducted in SAS 9.3 (Cary, NC).

RESULTS

Sample Baseline Characteristics

Seventeen patients and 23 proxies provided serial HRQoL data. Mean age of participants was 8.97 years (SD, 5.28; median, 7.3; range, 2.3 to 20.2). Of the 23 patients, 15 (65%) had Hemoglobin SS (HbSS) disease, 4 (17%) had Hemoglobin SC (HbSC) disease, and 4 (17%) had Hemoglobin Sickle Beta Thalassemia (HbSβThal). Indications for HCT included acute chest syndrome, recurrent VOC, dactylitis, splenic sequestration, retinopathy, and stroke (Table 1). Only 2 of the 23 patients had a history of stroke before HCT (1 with a silent stroke and 1 with an overt stroke causing neurological sequelae). Participants were predominantly

male (n = 19, 83%). The sample was racially divided as follows: Hispanic (n = 13, 56.5%), African American (n = 9, 39.1%), and 1 participant self-identified as “other” (4.4%). The sample was divided closely by insurance type: Medicaid (n = 10, 43.5%) and private insurance (n = 13, 56.5%). Source of hematopoietic cells was MSD bone marrow (n = 16, 70%), MSD cord blood (n = 2, 9%), and unrelated cord blood (n = 5, 21%).

Missingness

The total sample size is 23. Among the 23, self-reported HRQoL was missing from 6 patients at baseline who were too young for self report, from 3 patients at 180 days, and from 6 patients at 365 days. In logistic regression of the missingness as the outcome, none of the baseline characteristics was significant with P values > .10. Among the 23, parent proxy–reported HRQoL was not missing from any at baseline, from 2 patients at day 180, and from 1 patient at day 365. In logistic regression of the missingness of the outcome, none of the baseline characteristics were significant with P values > .10. Therefore, the missingness is considered at random and the missing values were ignored in our data analysis.

Outcomes and Post–allo-HCT Complications

At 1 year after allo-HCT, overall survival was 100% and event-free survival was 100%. The median follow-up was 1346 days, with a range from 364 days to 3306 days. Only 1 patient died, at day 420 after transplantation, and the others were alive. Five patients (22%) developed GVHD and 18 patients (78%) did not. After allo-HCT, 1 patient developed a hemorrhagic stroke in the setting of hypertension and as a possible manifestation of a hemolytic reaction due to ABO incompatibility immediately after transplantation, and another developed a stroke 6 months after transplantation in the setting of uncontrolled hypertension. Follow-up magnetic resonance imaging (MRI) scans showed no progression and no residual neurologic sequelae in either patient. Another patient developed posterior reversible encephalopathic syndrome, both clinically and radiographically on MRI while receiving tacrolimus. After tacrolimus was discontinued, the symptoms resolved and the MRI normalized. No cardiac or pulmonary dysfunction was observed in any patient.

Overall HRQoL

Before allo-HCT, patients reported a mean overall HRQoL of 66.05 (SD, 15.62) (Table 2), which falls below the published at-risk cutoff score (69.7) [19]. The mean HRQoL increased steadily over time to 70.36 (SD, 13.24) at day 180 and 82.34 (SD, 13.86) at 1 year after allo-HCT. Similarly, parent proxies reported a mean overall HRQoL at baseline of 72.20 (SD, 15.50) (Table 3), which increased consistently across time points to 73.82 (SD, 16.20) at day 180 and 81.92 (SD, 15.63) at 1 year after allo-HCT.

Results from the adjusted mixed-effect model for patient-reported HRQoL total scores remained significantly higher than baseline in the adjusted analysis, with adjusted mean change of 16.58 (SE, 5.06; P =.003) at 1 year after allo-HCT. Similarly, parent proxy–reported HRQoL revealed higher HRQoL, compared with baseline, 1 year after allo-HCT, with mean changes of 9.28 (SE, 4.62; P = .05) at 1 year (Table 3).

Physical HRQoL

Patients reported a mean physical HRQoL 62.61 (SD, 20.12) at baseline, 66.04 (SD, 17.67) at day 180, and 79.79 (SD, 14.65) at 1 year after allo-HCT. The improvement from baseline was significant in the adjusted mixed-effects model at 1 year, with a mean change of 17.39 (SE, 6.58; $P = .015$) (Table 2). Parent proxy–reported physical HRQoL improved over time as well, with a mean physical HRQoL of 68.61 (SD, 20.52) at the baseline, 69.76 (SD, 21.92) at day 180, and 80.00 (SD, 19.03) at 1 year after allo-HCT. The improvement approached marginal significance at 1 year after allo-HCT in the adjusted model, with an average change of 10.50 (SE, 5.87; $P = .083$) (Table 3).

Social HRQoL

Within the social domain, patients reported a baseline HRQoL of 72.94 (SD, 15.82), which improved to 75.00 (SD, 20.96) at day 180 before increasing to 86.33 (SD, 19.22) at 1 year after allo-HCT, which was significant with a mean change of 14.0 (SE, 6.25; $P = .035$) in the adjusted analysis (Table 2). Within the social domain, baseline parent-reported HRQoL was 81.52 (SD, 15.33). Parent proxy report indicated an improvement over time from 81.52 (SD, 15.33) at baseline to 83.24 (SD, 14.25) at day 180 and 86.50 (SD, 17.93) at 1 year after allo-HCT (Table 2), though improvements were not significant (Table 3).

Emotional HRQoL

Within the emotional domain, the baseline self-reported mean score was 62.94 (SD, 19.85), which increased to 71.88 (SD, 19.31) at day 180 and 82.00 (SD, 17.09) at 1 year after allo-HCT, which was a significant increase of 19.41 points (SE, 6.66; $P = .008$) (Table 2). Additionally, the baseline parent proxy–reported score was 69.57 (SD, 18.70), which improved to 71.62 (16.43) at day 180 and 81.25 (SD, 18.49) at 1 year after allo-HCT—a significant increase of 11.66 points (SE, 5.12; $P = .030$) in the adjusted model (Table 3).

Psychosocial HRQoL

Lastly, both patient-reported and parent proxy–reported psychosocial health summary scores showed improvements over time. Patients reported a mean psychosocial HRQoL of 67.84 (SD, 15.39) at baseline, 74.84 (SD, 18.27) at 180 days, and 84.17 (SD, 16.89) at 1 year after allo-HCT. The improvement from baseline was significant at 1 year in the adjusted model with an increase of 16.78 points (SE, 5.87; $P = .009$) (Table 2). Parent proxy–reported mean psychosocial HRQoL was 75.25 (SD, 14.83) at baseline and improved to 77.08 (SD, 14.02) at day 180 and to 83.88 (SD, 15.97) at 1 year after allo-HCT. The improvement was marginally significant in the adjusted model, with an average change of 8.56 (SE, 4.44; $P = .063$) (Table 3).

Comparisons of composite ratings between groups revealed some significant disparities based on demographic and/or clinical variables. On the basis of insurance type, patients receiving Medicaid reported significantly higher overall ($P = .007$), physical ($P = .025$), and psychosocial ($P = .026$) HRQoL at 1 year compared with patients with private insurance. The presence of GVHD also significantly divided groups for both raters. Specifically, patients who did not have GVHD reported significantly higher psychosocial ($P = .030$), social ($P = .030$), and emotional ($P = .047$) HRQoL at 1 year after allo-HCT than those who

did have GVHD. Additionally, parent reporters at 1 year after allo-HCT whose child did not have GVHD reported significantly higher emotional HRQoL ($P = .031$) and the parent-reported overall HRQoL approached significance ($P = .056$) 1 year after allo-HCT (Table 4).

Pearson correlations were calculated between parent and patient scores across domains and time points. The greatest consistency across raters and domains were observed at 1 year after allo-HCT, with significant correlations in overall HRQoL (r = .53, $P = .05$), in emotional HRQoL (r = .55, $P = .04$), social HRQoL (r = .59, p = .03), and psychosocial HRQoL (r = .66, $P = .01$). The sole exception at 1 year after allo-HCT was in the domain of physical HRQoL (r = .395, $P = .162$).

In terms of consistency between parent and self ratings, ICC were calculated for each scale. ICC values indicated moderate correlations for overall (ICC = .346) and physical (ICC = .386) HRQoL, with slightly lower correlations for emotional (ICC = .296) and psychosocial (ICC = .291) HRQoL. Analyses also revealed markedly lower consistency on ratings of social HRQoL (ICC = .141).

DISCUSSION

This study examined HRQoL in pediatric patients with SCD after allo-HCT. Specifically, the design of this study included 3 serial assessments of patients: before allo-HCT and at 6 months and 12 months after allo-HCT. The mixed design of this study also allowed for demographic, social, and clinical variables to be analyzed as possible contributors to HRQoL ratings, from both self report and parent proxy report.

Self-reported overall baseline HRQoL was lower, falling below the published at-risk cut off scores for chronically ill children [19]. This finding is consistent with prior research [20,21], which indicates a higher level of distress before allo-HCT, likely caused by physical symptoms and anxiety associated with the anticipated treatment. Self-reported HRQoL ratings subsequently exceeded the chronically ill population after allo-HCT and significantly improved over time by 1 year after allo-HCT within the domains of overall, physical, emotional, and psychosocial functioning, reflecting the length of time required to evidence significant improvement. Of note, social HRQoL was the sole domain that did not significantly improve from baseline by 1 year after allo-HCT. Similarly, parent proxy reports indicated overall HRQoL was lower than the population mean for chronically ill children; however, higher HRQoL were reported after allo-HCT, with significant change noted within the domains of overall, emotional, and psychosocial functioning by 1 year after allo-HCT. Of note, physical HRQoL was the only domain that did not significantly improve at 1 year after allo-HCT by parent proxy report. These observed improvements in HRQoL may be related to the emerging trend that children with SCD who receive allo-HCT require significantly fewer inpatient visits by 1 year after allo SCT compared with children with SCD who did not undergo transplantation, as well as requiring fewer outpatient visits after 1 year compared with before alloSCT [22].

With regard to physical HRQoL, patients reported significantly higher scores at 1 year after allo-HCT, whereas parent proxies did not report significantly higher scores, though their

ratings approached significance at 1 year after allo-HCT. It appears that patients are experiencing improved physical functioning that may not be as readily apparent to their caregivers or that the patients are overestimating their physical functioning. Caocci et al. [23] suggests that differences in perception between pediatric patients and parents may be related to parental stress in the post-HCT period, as the child's clinical condition tends to be more guarded in this phase. In contrast, parental perceptions may be supported by prior findings that measurements of physical functioning in survivors years after HCT reveal impairments that are significantly worse than healthy controls, as well as lower than what self report and clinician data indicate [24,25]. Given that the lowest Pearson correlation among the HRQoL areas at 1 year was within the domain of physical functioning, more subjective and objective measurement data are required to better understand the trajectory of physical functioning recovery after transplantation, which can inform opportunities for proactive physical therapy interventions.

Patients and parent proxies reported improvements in emotional HRQoL after transplantation, which is consistent with previous findings of patients reporting satisfactory psychological functioning as far as 2 years after HCT [26], although complications by demographic variables have been reported [27]. Interestingly, the pattern of patient endorsement of higher levels of emotional symptoms than their parents report and the above-mentioned lower correlation between patient and parent on physical functioning are both inconsistent with prior studies indicating higher concordance between patient and proxy reports of HRQoL in observable domains (eg, the presence of somatic symptoms or level of physical functioning) than in more subjective phenomena (eg, psychological distress) [28,29].

With regard to social HRQoL, although improvements in mean scores were noted, patient and parent proxies both did not report significantly improved social HRQoL within the first year. In fact, this is the only domain in which patients did not report a significant improvement by 1 year after transplantation. Current research in the field suggests social functioning tends to decline within the first year after transplantation before improving [21,26]. Although patients understandably experience social isolation during and immediately after treatment, the continued feelings of social isolation after allo-HCT represent an important area for intervention by psychosocial clinicians working with this population. This phenomenon is probably best understood in large part by the medical treatment protocol guidelines for 1 year of isolation after transplantation. As mentioned previously, patients were not yet re-enrolled in school by this time, which may contribute to their functioning across domains, particularly for their social HRQoL ratings. Specifically, the development of interventions that assist patients to maintain social connections during and immediately after allo-HCT, perhaps through online or social media including technology to join classrooms and staying connected with peers could be very beneficial. The psychosocial summary score measured HRQoL across the combined social and emotional scales. Similar to the patterns observed in most individual domains, self- and parent proxy–reported psychosocial HRQoL reached significant levels of improvement at 1 year after allo-HCT.

Additional analyses included demographic and medical data, investigating group differences by demographic variables such as insurance type, presence or absence of GVHD, allogeneic type, and hematopoietic cell source. Researchers commonly observe the impact of clinical [23,24,26] and demographic [27] variables, such as GVHD and insurance type on HRQoL. In the current study, the presence of focal significant interactions were observed only at the 1-year follow-up, involving lowered self-reported HRQoL within the domains of overall, physical, and psychosocial HRQoL for those with private insurance, in addition to lowered self-reported HRQoL within the domains of emotional, social, and psychosocial for those who developed GVHD. It is interesting to note that a singular significant interaction by parent report was observed in the domain of emotional HRQoL for children who were diagnosed with GVHD. These findings support the importance of obtaining self-report HRQoL, which can provide a distinct and equally important perspective, as well as the appreciation of the amount of time it can require for significant differences to emerge. Although the findings based upon the presence of GVHD are understandable, given the discomfort and additional medications required, the disparities based upon insurance type raises more questions than answers. Clearly, future studies should explore the impact of socio-economic status on long-term HRQoL within this population, as well as to more fully understand the pretransplantation quality of life and the specific expectations of the transplantation for patients and parents.

Limitations of this study include the small sample size, although it is significantly larger than the only other published study with this population. The sample also has missing values at different points for different subjects, which may significantly affect sample size, depending on how the mixed linear model addresses missing data. Consequently, all nonmissing values were included in mixed-effects model; however, the issue of missing values could remain a limitation because of our limited small sample size. Additionally, all data were collected from a single institution, which may limit the generalizability of the data; however, this perhaps can simultaneously provide the advantage of offering a more uniform study population and treatment regimen. Future studies would benefit from multisite data collection, as there is variation among individual centers' practice guidelines, such as return to school and activity restrictions that could clearly impact HRQoL. Finally, the racial and ethnic composition of this sample, 56.5% Hispanic and 39.1% African American, is incongruent with the distribution of SCD at large. Because the prevalence of SCD is much greater in African American populations compared with Hispanic and other racial/ethnic groups [30], the findings of the current study may be somewhat more generalizable to the Hispanic population.

Future studies into the HRQoL of patients with SCD would also benefit from the inclusion of the PedsQL SCD module [31] to better understand the impact of the disease over time, as well as to detect differences between different levels of severity of SCD and other chronic illnesses. This approach may be particularly informative as it relates to integral demographic variables (eg, socioeconomic status, gender, ethnicity, etc.), as well as medical variables, such as the impact of GVHD and type of transplantation, upon HRQoL in larger samples. Furthermore, given a paramount sequelae of anemia that characterizes SCD includes the experience of fatigue, which has not been systematically assessed or reported in the

literature, the PedsQL Multidimensional Fatigue Scale [32] can add much needed depth to our understanding of the clinical manifestations of the disorder.

CONCLUSIONS

These results suggest that, in addition to the improvement in physical symptoms seen in patients with SSD after allo-HCT, the general improvement in HRQoL over time is encouraging and represents another factor for families and caregivers to consider before deciding upon stem cell transplantation in select patients with SCD. These findings may simultaneously guide the development of proactive interventions, particularly within the acute post-transplantation phase, to assist children in adjusting to their newly emerging medical identities (ie, fewer emergent visits to the hospital, fewer opportunities for interaction with supportive clinic staff, while at the same time not being allowed to return to school or social activities for up to 1 year after allo-HCT). Overall, this study highlights the significant improvement in the overall, psychosocial, and emotional HRQoL by both self and parent report, along with significant improvement in the physical HRQoL by self report. These results may assist families when considering allo-HCT as a treatment for SCD [33].

Acknowledgments

Funding source: No external funding was secured for this study.

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Table 1

Patient Characteristics

ID	Indications for HCT	Age at HCT, yr	Donor Source	Initial HCT LOS, d	% Whole Blood Chimerism (Days 100, 180, 365 after HCT)	No. of Transfusions through Day 100 after HCT (Platelet/ PRBC)	GVHD	Disease Status at 1 Year	No. of Readmissions in First 100 Days after HCT	Post-HCT Complications	Lansky/ Karnofsky Performance Scores (Before HCT, 1 Year after HCT)
1	Dactylitis, ACS, VOC	5.3	RCB	78	95,97,94	17/10	No	NED	1	None	90/no note
2	ACS	7.3	RBM	38	91,93,93	12/6	No	NED	3	None	100/90
3	VOC	9.9	UCB	57	99,99,98	23/10	Yes-acute	NED	2	None	100/90
4	VOC	5.3	RBM	43	98,96,93	6/1	No	NED	0	None	100/90
5	VOC	7.0	RBM	42	90,88,80	0/0	No	NED	1	None	100/100
6	Abnormal TCD, ACS	6.3	UCB	66	60,94,93	14/7	Yes-acute and chronic	NED	0	Stroke	90/100
7	Splenic sequestration, dactylitis	2.7	RCB	105	65,88,89	43/14	No	NED	4	None	100/no note
8	ACS	6.3	UCB	114	0, not evaluable, not evaluable	95/19	Yes-acute	NR	0	None	90/90
9	VOC, splenic sequestration	2.4	UCB	162	99,96,99	40/12	No	NED	0	None	100/100
10	VOC, ACS	2.3	RBM	37	96,95,94	9/3	No	NED	0	None	100/100
11	Sickle retinopathy, VOC, ACS, splenic sequestration	18.3	RBM	37	99,96,94	3/3	No	NED	1	None	100/90
12	VOC, ACS, splenic sequestration	9.4	RBM	57	92,94,78	31/10	Yes-acute	NED	1	None	100/80
13	Abnormal TCD	5.4	RBM	44	89,79,75	15/8	No	NED	1	None	100/100
14	Stroke, splenic sequestration	20.2	RBM	37	98,90,83	2/1	No	NED	1	None	80/90
15	VOC, ACS	14.7	RBM	46	98,89,86	4/1	No	NED	0	None	90/100
16	ACS, VOC	13.8	RBM	65	99,98,94	24/6	Yes-acute	NED	1	None	100/no note
17	VOC	12.4	RBM	70	99,98,97	2/4	No	NED	0	None	100/100
18	Splenic sequestration	4.5	UCB	57	85,91,91	19/11	No	NED	1	None	100/no note
19	Splenic sequestration, ACS, VOC	16.3	RBM	30	99,98,92	1/4	No	NED	1	None	100/100
20	Abnormal TCD, Silent stroke, ACS, VOC	8.3	RBM	30	38,58,68	16/5	No	NED	2	Stroke	100/100
21	ACS	12.4	RBM	29	89,87,93	2/1	No	NED	0	PRES	100/100
22	ACS, splenic sequestration	13.3	RBM	55	99,83,77	11/7	No	NED	0	Diarrhea, hypomagnesia, grade II mucositis, E. Cloace sepsis, Acinetobactor line infection, VZV	100/80
23 *	Had no SCD-related complications, had matched sibling	2.7	Sibling bone marrow	40	100	16/7	No		0	Diarrhea, hypomagnesia, grade II mucositis, E. Cloace sepsis, Acinetobactor line infection, VZV	100

LOS indicates length of stay; ACS, acute chest syndrome; RCB, related cord blood; NED, no evidence of disease; RBM, related bone marrow; UCB, unrelated cord blood; NR, no response; TCD, transcranial Doppler; PRES, posterior reversible encephalopathic syndrome; VZV, varicella zoster virus.

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* Patient not yet 1 year after HCT.

Table 2

Self-Reported HRQoL Scores

Time	Overall HRQoL	Physical HRQoL	Social HRQoL	Emotional HRQoL	Psychosocial HRQoL
T1: Before HCT * (n = 17 of 17, 100%)	66.05 (15.62)	62.61 (20.12) (n = 16)	72.94 (15.82)	62.94 (19.85)	67.84 (15.39)
T2: 180 Days * (n = 16 of 17, 94%)	70.36 (13.24)	66.04 (17.67) (n = 15)	75.00 (20.96) (n = 15)	71.88 (19.31)	74.84 (18.27)
T3: 365 Days * (n = 15 of 17, 88%)	82.34 (13.86)	79.79 (14.65)	86.33 (19.22)	82.00 (17.09)	84.17 (16.89)
Change over time					
T2-T1 †	4.45 (4.98)	3.23 (6.57)	1.95 (6.26)	9.10 (6.54)	7.22 (5.77)
Day 180-baseline	.380	.627	.758	.177	.223
T3-T1 †	16.58 (5.06)	17.39 (6.58)	14.00 (6.25)	19.41 (6.66)	16.78 (5.87)
Day 365-baseline	.003‡	.015‡	.035‡	.008‡	.009‡

*Data presented are mean (SD). Result from adjusted mixed-effect model self-reported QOL (adjusted by GVHD, insurance type, and donor source).

†Data presented are mean (SE); *P* value.

‡Indicates statistical significance.

Table 3

Parent-Reported HRQoL Scores

Time	Overall HRQoL	Physical HRQoL	Social HRQoL	Emotional HRQoL	Psychosocial HRQoL
T1: Before HCT [*] (n = 23 of 23, 100%)	72.20 (15.50)	68.61 (20.52)	81.52 (15.33)	69.57 (18.70)	75.25 (14.83)
T2: 180 Days [*] (n = 17 of 23, 74%)	73.82 (16.20)	69.76 (21.92)	83.24 (14.25)	71.62 (16.43)	77.08 (14.02)
T3: 365 Days [*] (n = 20 of 23, 87%)	81.92 (15.63)	80.00 (19.03)	86.50 (17.93)	81.25 (18.49)	83.88 (15.97)
Change over time					
T2-T1 [†]	1.57 (4.82)	.69 (6.13)	1.77 (5.14)	2.56 (5.34)	2.12 (4.63)
Day 180-baseline	.747	.912	.732	.635	.650
T3-T1 [†]	9.28 (4.62)	10.50 (5.87)	4.91 (4.93)	11.66 (5.12)	8.56 (4.44)
Day 365-baseline	.053	.083	.326	.030[‡]	.063

[*] Data presented are mean (SD). Result from adjusted mixed-effect model parent-reported QOL (adjusted by GVHD, insurance type, and donor source).

[†] Data presented are mean (SE) and *P* value.

[‡] Indicates statistical significance.

Table 4

Selected Results from Group Comparisons at One Year Follow-Up

	Insurance				
	Medicaid		Private		*P* Value
	n	Mean (SD)	n	Mean (SD)	
Self-reported					
Overall	4	95.6 (5.7)	11	77.5 (12.8)	.007*
Physical	4	93.0 (8.2)	11	75.0 (13.6)	.025*
Psychosocial	4	96.9 (6.3)	11	79.5 (17.3)	.026*

	GVHD				
	Yes		No		*P* Value
	n	Mean (SD)	n	Mean (SD)	
Self-reported					
Emotional	4	65.0 (20.8)	11	88.2 (11.0)	.047*
Social	4	67.5 (27.2)	11	93.2 (10.1)	.026*
Psychosocial	4	66.3 (23.3)	11	90.7 (7.8)	.030*
Parent-reported					
Emotional	4	61.3 (22.5)	16	86.3 (14.1)	.031*
Psychosocial	4	69.4 (17.1)	16	87.5 (13.9)	.056

*Indicates statistical significance.