


Health-Related Quality of Life of Hematopoietic Stem Cell Transplant Childhood Survivors: State of the Science

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Abstract

The notion of health-related quality of life (HRQoL) holds unique significance in the treatment of patients who have undergone hematopoietic stem cell transplantation (HSCT). Not only is transplant procedure inevitably associated with immediate and late medical effects along with high mortality and morbidity rates, but it can also significantly affect the HRQoL for the patient and family. This review of literature will assist advanced practice nurses and pediatric oncology nurses in distinguishing and targeting interventions for patients and families who are at high risk of encountering distress during and following HSCT. It provides information on the assessment of pre-HSCT variables to identify patient subgroups in need of more aggressive supportive care to improve HRQoL during transplant. Furthermore, it serves as a guideline for developing interventional strategies and the role of the advanced practice nurse and pediatric oncology nurse caring for the patient throughout and following transplant.

Keywords

health-related quality of life, hematopoietic stem cell transplant, survivor, nursing

Background and Significance

Hematopoietic stem cell transplantation (HSCT) is an aggressive therapeutic approach for an assortment of formerly incurable malignancies, hematological disorders, and metabolic storage diseases that have evolved dramatically in the past 25 years, advancing at a rapid pace as scientific discoveries are transformed into the pediatric clinical setting. Unfortunately, despite advances with increased use of alternative donors and stem cell sources, HSCT is a highly risky procedure that carries a high mortality rate 1 year posttransplant (Barrera, Gee, Andrews, Armstrong, & Saunders, 2006). After years of aggressive treatment for a life-threatening illness, many children and adolescents are left with HSCT as the only viable treatment option after disease relapse and failure of conventional treatments. These life-saving or in some cases simply life-extending medical procedures are correlated with many adverse side effects, prolonged hospitalization and isolation, and risk of persistent treatment-related sequelae. Children and families face a future that varies from a cure to chronic graft-versus-host disease (GVHD), relapse, or a relatively high possibility of death (Barrera, Boyd-Pringle, Sumbler, & Saunders, 2000).

As medical advances improve HSCT outcomes, patients and families are still facing compromised health-related quality of life (HRQoL) correlated with the original diagnosis or complications secondary to transplant. Children and families face adverse late effects as a consequence of prior treatments for their disease, disease status such as remission or relapse at time of transplant, pre-transplant comorbidities, medications, chemotherapy, and total body irradiation in conditioning regimens, medications, and infectious complications (Buchsel, 2009). Recognition of this spectrum of both physical and psychosocial late effects has been accompanied by realization that for many HSCT survivors, cure or control of their underlying disease may not be accompanied by a restoration of health. The majority of survivors will experience at least one physical late effect (Skinner & Leiper, 2004). Children who receive HSCT from an allogeneic donor are also at risk for the development of acute (within

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100 days of transplant) and chronic (after 100 days) GVHD in which antigenic disparities between the donor T lymphocytes and recipient cells result in tissue injury, often severe, involving the skin, liver, and gastrointestinal tract (Buchsel, 2009). Suffering from chronic GVHD results in deterioration in physical and social role functioning, increased fatigue, dyspnea, gastrointestinal side effects, anxiety, and skin problems, and consequently those patients are taking more medications (Pallua et al., 2010). Total body irradiation has been well-established as a risk for decline in intelligence, memory, academic achievement, attention, and fine motor skills, causing significant neuropsychological decline (Boulad, Sands, & Sklar, 1998). To reflect the overall value of any therapy, it is crucial to evaluate not only the traditional outcome variables such as overall survival, disease-free survival, morbidity, mortality, and cost but also quality of life.

Numerous HSCT-related stressors have been established, including the life-threatening nature of the procedure itself, prolonged hospitalization in a protected environment, and the enforced isolation that occurs both during and subsequent to hospitalization directly affecting HRQoL during and following transplant. All HSCT recipients experience physical confinement during hospitalization, which may exacerbate feelings of emotional and social isolation. During the first several months of protective isolation, removed from normal role activities, patients are at risk for compromised social and psychological HRQoL. Simultaneously, the disruption and dislocation of the family, the required compliance to aversive daily routines, and the generally high levels of transient treatment-related morbidity create additional burden for all domains of HRQoL (Parsons et al., 2006). Inevitably, HSCT has an impact on how physical, psychological, social, and emotional functioning is perceived by the child and family.

As the number of HSCT survivors increases, the late effects of illness and its consequences of therapy on the patient and families are emerging, and some are life altering. The HRQoL of childhood HSCT survivors has been investigated to define the efficacy of medical treatment of surviving children and adolescents. HRQoL is recognized as an important outcome measure in research. However, it is a poorly understood concept with various definitions existing. The most widespread definition of quality of life provided by the World Health Organization (1993) is defined as a broad, multidimensional concept that focuses on the individual's perception of one's position in life, in the context of the culture and value systems in which one lives and in relationship to goals, expectations, standards, and concerns. Domains of quality of life are those that encompass physical, psychological, social, role functioning, and spiritual issues. In addition, others argue that for children, quality of life measures

should include assessments of cognitive functioning, autonomy, body image, and family relationships (Eiser & Morse, 2001) along with children's expectations and experiences (Carr, Gibson, & Robinson, 2001). However, in the context of health care, treatments may not influence quality of life but rather focus narrowly on medical complaints (Feeny, Furlong, Mulhern, Barr, & Hudson, 1999). As a result, in the health care context, the most restricted concept of quality of life, the notion of HRQoL, refers to the subjective and objective impact of dysfunction on the physical, psychological, and social aspects of quality of life that are influenced by an individual's disease and its treatment (Strand & Russell, 1997).

For nearly 2 decades, researchers have studied the quality of life following HSCT, including effects on physical function, psychological status, social interaction, economic status, and vocation. There have been 2 reviews of literature of the HRQoL status of childhood transplant survivors. The first review concludes that although there is much evidence to support that children experience a good quality of life following HSCT, methodological issues across studies, timing of assessments after HSCT, and limited longitudinal studies question the validity of the conclusion (Tsimicalis, Stinson, & Stevens, 2005). The more recent review also identified the need to provide more longitudinal study conclusions along with an analysis of the contribution of family factors to HRQoL (Clarke, Eiser, & Skinner, 2008). In this article, all domains of HRQoL following HSCT will be investigated, pre-HSCT and post-HSCT, taking into account baseline HRQoL characteristics of presenting disease. Understanding the significance of HSCT treatment on HRQoL can assist in counseling patients who are considering HSCT. Attention to HRQoL may ultimately change current medical and nursing protocols across all phases of transplant from preadmission to long-term follow-up clinic visits. Awareness of the impact of HSCT on overall HRQoL will allow advanced practice nurses (APNs) and pediatric oncology nurses to isolate particular patients or treatment characteristics that impact HRQoL.

Review of Literature

This review of HRQoL following HSCT is limited to articles published from March 2002 to August 2009. Studies for inclusion in the review were searched using Medline (OVID), PubMed Plus, CINAHL (EBSCO), EMBASE, and PsycINFO using the following terms: *HSCT, bone marrow transplant, child, childhood, children, adolescent, pediatric, survivor, quality of life, and HRQoL*. The literature review included children, adolescents, and adults with any malignancies, hematological disorders, and metabolic storage diseases that were

transplanted during childhood. All studies were included if they measured any dimensions of HRQoL including physical, psychological, social role, and emotional functioning. Finally, articles excluded included literature reviews or case studies, HRQoL not as the primary outcome, and studies published in languages other than English. Table 1 is a descriptive summary of participants and study findings. This article reviews the literature of HSCT recipients' self-reported and parental reported physical well-being, psychological distress, social role, and emotional well-being. Second, clinical implications are explored for immediate incorporation into practice followed by long-term assessment. Finally, conclusions are drawn on future directions of pediatric HSCT survivors to ensure satisfaction in HRQoL.

Health-Related Quality of Life Outcomes

Physical Well-Being

The toxicity and immunosuppression aftermath of HSCT are associated with a variety of long-term challenges with physical function. Late effects such as chronic GVHD, secondary malignancies, organ damage, endocrine dysfunction, infertility, and various physical symptoms, such as pain, nausea, and fatigue, only further aggravate physical dysfunction (Lowe, Bhatia, & Somlo, 2007). In literature, physical functioning has been appraised by examining the ability to conduct a variety of behaviors ranging from self-care to more challenging and vigorous activities requiring strength or endurance along with the assessment of role functioning. Countless patients indicated that they frequently experienced problems with pain, dry skin, and fatigue. Many childhood survivors experience manifestations of pain localized frequently to the head, shoulders, back, knees, and hips (Lof, Winiarski, Giesecke, Ljungman, & Forinder, 2009). Adult survivors of childhood HSCT reported functional limitations in physical performance (Michel et al., 2007).

Clinical factors associated with physical HRQoL over longitudinal studies included age, diagnosis, type of transplant, and GVHD status. Findings across all studies are consistent with clinical impressions that younger children tolerate HSCT with fewer difficulties, whereas older children and adolescents experience relatively higher levels of distress and discomfort. The majority of young HSCT patients felt their physical function and HRQoL to be good (Forinder, Lof, & Winiarski, 2005). The diagnosis of acute lymphoblastic leukemia (ALL) was the best disease factor predictor of worse physical HRQoL outcomes 1 and 2 years post-HSCT than survivors of solid tumors (Barrera, Atenafu, & Hancock, 2009). Children diagnosed with ALL who survive HSCT have endured high-risk medical

regimens before even being considered candidates for transplant and in preparation for their transplant. Phipps, Dunavant, Garvie, Lensing, and Rai (2002) reported significant effects of diagnostic group on somatic distress and physical functioning. Higher levels of somatic distress and lower levels of physical functioning were reported by ALL and other leukemia groups. These effects may to some extent reflect a confounding of diagnostic group with age and type of transplant. In addition, according to Barrera, Atenafu, and Hancock (2009), the cost of their survival is still evident 2 years posttransplant in their poorer HRQoL compared with other HSCT survivors. Children undergoing autologous transplant experienced significantly less somatic distress and loss of physical activity than those undergoing allogeneic transplant, both matched-sibling and matched-unrelated transplants (Phipps, Dunavant, Lensing, & Rai, 2002). Nonetheless, there have been reports of no significant difference between HSCT recipients who have received an allogeneic versus those who have received an autologous transplant (Nuss & Wilson, 2007). However, in the same study, reported HRQoL of individuals who had received a HSCT was significantly lower from that of both a healthy reference group and chronically ill children. According to Barrera, Atenafu, and Hancock (2009) and Forinder, Lof, and Winiarski (2006), potential predictors for physical HRQoL scores were the presence or absence of moderate or severe GVHD and diagnosis. Childhood survivors who did not develop GVHD were reported to have greater improvement in physical HRQoL.

Survivors of pediatric HSCT reported improvement in physical HRQoL at 1 and 2 years post-HSCT, according to mothers in generic and disease-specific instruments (Barrera, Atenafu, & Hancock, 2009). In view of the fact that no significant changes occurred between 1 year and 2 years post-HSCT, it is speculated that critical enhancement arises by 1 year post-HSCT. This too corresponds with study findings from Parsons et al. (2006), which revealed that by the finish of the first year post-HSCT, survivors returned to the level of baseline assessment, which was obtained immediately before having the HSCT. Nevertheless, pretransplant baseline is likely not to reflect a "true" premorbid baseline. Consequently, the return to the level of baseline functioning may still indicate erosion in physical functioning. On the contrary, Phipps, Dunavant, Lensing, et al. (2002) and Felder-Puig et al. (2006) report the worst HRQoL shortly after transplant, and HRQoL thereafter improved steadily until 6 months after HSCT. That same study states that although HSCT survivors were significantly at greater risk for medical adverse effects post-HSCT, there was limited impairment in HRQoL. This might indicate that patients have adapted relatively well in spite of their physical handicap (Michel et al., 2007).

Table 1. Studies Assessing HRQoL in Childhood HSCT Recipients.

Study	Sample Demographics at Baseline	Timing of Assessments	Results	Variables Predicting Outcome
Barrera, Atenafu, and Hancock (2009)	N = 99, 65.6% female, mean age = 8.27 years	Pre-SCT and 1 year and 2 year post-SCT	<ol style="list-style-type: none"> Improvement in physical and psychosocial HRQoL 1 and 2 years post-HSCT Post-SCT for ALL report poorer HRQoL compared with other HSCT survivors Low SES associated with poor HRQoL outcomes Maternal depression associated negatively with physical and psychosocial HRQoL of HSCT survivors 	<p>Disease related</p> <ol style="list-style-type: none"> Diagnosis of ALL <p>Time since diagnosis at SCT</p> <ol style="list-style-type: none"> Longest treatment protocol <p>Demographics</p> <ol style="list-style-type: none"> Younger child age <p>Home environment</p> <ol style="list-style-type: none"> Maternal age and education Maternal depression <p>Demographics</p>
Lof, Winiarski, Giesecke, Ljungman, and Forinder (2009)	N = 53, 57% male, mean age = 10 years	Range 5 to 28 years post-SCT, mean 17 years	<ol style="list-style-type: none"> Post-HSCT, HRQoL poorer than age-matched norm related to physical health, whereas emotional well-being domains on par with norm Post-HSCT, adults report problems with memory and capacity for concentration HSCT group reported poorer HRQoL within sexuality area compared with age-matched norm Clinical levels of depression and/or anxiety among HSCT were higher than in normative populations 	<ol style="list-style-type: none"> Older age Time elapsed post-SCT
Vrijmoet-Wiersma et al. (2009)	N = 21, 85% male, mean age = 11 years	Range 2 to 16 months post-SCT, mean 10 months	<ol style="list-style-type: none"> Post-HSCT, home functioning, physical functioning, and total HRQoL scores were lower than in norm groups Home functioning rate lower post-HSCT than pre-HSCT Parents reported lower HRQoL scores than children pre- and post-HSCT Younger children reported better HRQoL than older children Parenting stress was higher post-HSCT than pre-HSCT 	<p>Demographics</p> <ol style="list-style-type: none"> Younger child age <p>Parenting stress</p> <ol style="list-style-type: none"> Low adaptability Mood swing Parents' own health Parental depressive feelings Marital relationship <p>Demographics</p> <ol style="list-style-type: none"> Younger child age Male gender
Michel et al. (2007)	N = 142, 52% male, mean age = 18.2 years	Range 6 to 18 years post-SCT, mean 11.9 years	<ol style="list-style-type: none"> A higher incidence of physical adverse events in the HSCT group but fewer clinically significant differences in HRQoL compared with age-matched norm No significant difference in reported HRQoL according to parent or adult survivor Significantly poorer physical HRQoL but similar mental health post-HSCT compared with age norm 	

(continued)

Table 1. (continued)

Study	Sample Demographics at Baseline	Timing of Assessments	Results	Variables Predicting Outcome
Nuss & Wilson (2007)	N = 35, 57% male, mean age = 7 years	Range 1 to 10 years post-SCT	<p>1. Reported HRQoL of individuals who received a HSCT was significantly lower scores from healthy reference group and chronically ill children</p> <p>2. Mothers reported lower QOL compared with children and children's fathers</p> <p>3. No significant differences found between HSCT recipients who received an allogeneic versus autologous HSCT</p> <p>1. Decline in reported HRQoL from pre-HSCT to 10 days post-SCT; overall, improvement in HRQoL by 1 year post-HSCT</p> <p>2. Results suggest that those post-HSCT that do not do well physically suffer from psychosocial problems</p> <p>3. Consider post-HSCT survivor variability</p> <p>4. HRQoL scores of child report were significantly higher than parent reports. Scores of physician reports were generally in between child- and parent-reported scores</p>	<p><i>Demographics</i></p> <p>1. Younger child age</p>
Felder-Pujig et al. (2006)	N = 68, 57.4% male, mean age = 10.35 years	Two assessments pre-SCT and 5 assessments up to 1 year post-SCT	<p>1. Parents reported lower HRQoL on both the psychosocial and physical summary scales than child</p> <p>2. The child's condition had greater impact on parent's emotional situation than in the norm population</p> <p>3. Symptom severity and late effects, including GVHD and cognitive impairment, associated with lower HRQoL with post-HSCT survivors</p>	<p><i>Emotional functioning during acute phase of treatment</i></p> <p>1. High level of worry</p> <p>2. Reduced communication during stay at transplant unit</p>
Forinder, Lof, and Winiarski (2006)	N = 52, 55% male, mean age = 8 years	Range 3 to 20 years post-SCT, mean 8 years	<p>1. Study revealed that functioning by the end of the first year had at least recovered to pre-HSCT assessment (baseline scores lower than age-matched norm)</p> <p>2. Worse functioning at 3 months post-SCT</p> <p>3. Worst functioning and greatest decline in functioning were observed in recipients of unrelated allogeneic transplants at 3 months and most HSCT specific issues at 3 and 6 months</p> <p>4. Older recipient age associated with poorer HRQoL pre-SCT and post-SCT</p>	<p><i>Demographics</i></p> <p>1. Younger child age</p>
Parsons et al. (2006)	N = 160, 57% male, mean age = 12 years	Pre-SCT and 3, 6, and 12 months post-SCT	<p>1. Study revealed that functioning by the end of the first year had at least recovered to pre-HSCT assessment (baseline scores lower than age-matched norm)</p> <p>2. Worse functioning at 3 months post-SCT</p> <p>3. Worst functioning and greatest decline in functioning were observed in recipients of unrelated allogeneic transplants at 3 months and most HSCT specific issues at 3 and 6 months</p> <p>4. Older recipient age associated with poorer HRQoL pre-SCT and post-SCT</p>	<p><i>Disease</i></p> <p>1. Moderate or severe GVHD</p> <p>2. Moderately severe cognitive impairment</p> <p><i>Disease related</i></p> <p>1. Interaction between time and transplant type on physical functioning and body image</p> <p><i>Demographics</i></p> <p>1. Age at time of transplant</p>

(continued)

Table 1. (continued)

Study	Sample Demographics at Baseline	Timing of Assessments	Results	Variables Predicting Outcome
Helder et al. (2004)	N = 22, 54.5% female, mean age = 25 years (range 18-32 years)	Range 6 to 20 years post-SCT, mean 14 years	<ol style="list-style-type: none"> 1. Generic HRQoL measures fell within normal range of functioning 2. Some illness-related impairment was reported on subscales for general and work-related functioning 3. Compared with adults who underwent HSCT during adulthood, pediatric HSCT survivors reported significantly better emotional well being 4. Seeking of social support by survivors as a means of coping with stress was related to better role functioning, whereas passive coping was related to poorer mental health 	<p><i>Demographics</i></p> <ol style="list-style-type: none"> 1. Age at time of transplant <p><i>Emotional functioning</i></p> <ol style="list-style-type: none"> 1. Seeking social support as a means of coping <p><i>Individual</i></p> <ol style="list-style-type: none"> 1. Behavioral, social, and cognitive function pretransplant <p><i>Demographics</i></p> <ol style="list-style-type: none"> 1. Age at time of transplant <p><i>Treatment related</i></p>
Kupst et al. (2002)	N = 153, 55.6% male, mean age = 9.6 years	Pre-SCT and 1 to 2 years post-SCT	<ol style="list-style-type: none"> 1. Stability of IQ over time although younger age at transplant increased risk for later cognitive decline 2. Low prevalence of behavioral or social problems and stability of functioning over time 3. Pre-HSCT functioning strongly predictive of later functioning 	
Phipps, Dunavant, Garvie, Lensing, and Rai (2002)	N = 153, 54.9% male, mean age = 8.9 years	Pre-SCT and 6 months post-SCT	<ol style="list-style-type: none"> 1. Children undergoing HSCT enter hospital with heightened level of distress that increases dramatically following conditioning, reaching a peak approximately 1 week following transplant. It returns to admission levels by week 4 to week 5, followed by further decline to presumed basal levels by 4 to 6 months 2. Moderate to high mood disturbance across different phases of HSCT procedure by parent and child report 3. Younger age at transplant yields higher HRQoL than older age 4. Lower SES children report greater distress and HRQoL disturbances 5. Better HRQoL was reported by autologous transplant patients 	<ol style="list-style-type: none"> 1. Type of transplant <p><i>Demographics</i></p> <ol style="list-style-type: none"> 1. Younger child age <ol style="list-style-type: none"> 2. Lower SES <p><i>Demographic</i></p> <ol style="list-style-type: none"> 1. Younger child age (less than 3 years)
Simms, Kazak, Golomb, Goldwein, and Bunin (2002)	N = 47, 57% male, mean age = 7.6 years	Pre-SCT and 1 and 2 years post-SCT	<ol style="list-style-type: none"> 1. Cognitive, behavioral, and social functioning of children 3 years and older is not affected 2 years post-HSCT 2. Parents of older children reported no cognitive ability problems but lower academic ability 3. Children younger than 3 years are at increased risk of further cognitive functioning problems 2 years post-HSCT 	

Abbreviations: SCT, stem cell transplantation; HSCT, hematopoietic stem cell transplantation; HRQoL, health-related quality of life; ALL, acute lymphoblastic leukemia; SES, socioeconomic status; GVHD, graft-versus-host disease.

A common thread in many of the studies on HRQoL is parental reports rating their children's physical HRQoL significantly lower both pre- and post-HSCT compared with the individual child report as well as compared with a norm group of healthy peers. A potential rationale for such finding is that parent and child reports of HRQoL are formulated on 2 different perspectives: the child reports on his or her subjective condition, whereas parents can only surmise from observations and communication with their child. Second, children tend to focus more on the "here and now," whereas parents express further concern with their child's well-being and HRQoL in the future (Vrijmoet-Wiersma et al., 2009). Likewise, mothers also may compare their child's present well-being with an ideal physical well-being that may not be part of the child's perception. This generates 2 distinct perspectives. With regard to parental versus child reporting of physical functioning, Nuss and Wilson (2007) also found mothers reporting a considerably lower HRQoL compared with their child as well as with the child's fathers. Discordance between the mother/father and child perceptions of HRQoL have been reported in several populations, with mother always perceiving lower HRQoL than the child (Phipps, Dunavant, Garvie, et al., 2002). Nonetheless, despite strong evidence, Michel et al. (2007) reported no significant difference in HRQoL according to the parent or adult survivor. This study did find a higher incidence of physical adverse events in the HSCT group but fewer clinically significant differences in HRQoL compared with the normative age group.

Predictors of physical HRQoL were mother's age and education and child's age. Children of younger mothers with lower education were reported to have poorer physical scores 2 years post-HSCT (Barrera, Atenafu, & Hancock, 2009). These components, in addition to factors related to economic status and level of education, have an interactive and multifactorial effect on the physical HRQoL of HSCT childhood survivors.

Psychological Distress

According to Lof et al. (2009), HSCT survivors experience serious problems with both anxiety and depression compared with normative populations. A critical finding of Phipps, Dunavant, Garvie, et al. (2002) illustrates that children undergoing HSCT enter the hospital with a heightened level of distress—defined by high levels of somatic symptoms, mood disturbance, and low levels of activity—that increases dramatically 1 week following transplant. However, this increased distress is transient, declining rapidly back to admission levels by Week 4 followed by further decline to baseline levels by 6 months post-HSCT. This study found the trajectories of distress depicted by both parent and child report was

astonishingly similar, providing confirmatory support for the soundness of the findings. More important, the findings signify that regardless of an aggressive program of supportive care, with current generation antiemetic medications, narcotic analgesics, and a high level of psychosocial support, a substantial amount of distress is experienced by patients during the acute phase of HSCT (Phipps, Dunavant, Garvie, et al., 2002). The transient psychological distress that occurs in response to demanding therapy was also discovered in results from Felder-Puig et al. (2006). Worse HRQoL shortly after transplant is hardly an unexpected finding. Yet Michel et al. (2007) revealed similar psychological mental health scores post-HSCT compared with a normative age group.

Clinical variables found in literature to have direct causation of psychological HRQoL include child demographics, specifically age, socioeconomic status, and type of transplant. The age of the child at time of transplant influenced specifically procedural anxiety scores (Nuss & Wilson, 2007). Younger children, probably because of their cognitive ability to not recall, report lower procedural anxiety, whereas older children and adolescents at time of HSCT report higher procedural anxiety. This finding supports a previous study by Phipps, Dunavant, Lensing, et al. (2002) but contradicts Helder et al. (2004) who found no significant difference. In connection with future psychological difficulties, there have been studies that indicate that being younger than 3 years at time of HSCT has been associated with being a risk factor for poor psychological HRQoL secondary to greater cognitive impairment (Forinder et al., 2005). On the contrary, Parsons et al. (2006) concluded that older age was a significant variable associated with poorer psychological HRQoL at baseline and posttransplant. Lower socioeconomic status of HSCT recipients reported greater distress and psychological HRQoL disturbances in the study of Phipps, Dunavant, Lensing, et al. (2002).

Autologous transplant consistently demonstrates higher levels of reported HRQoL during the first 6 months after the HSCT procedure, including less somatic disturbances and higher activity levels, rather than transplant with an allogeneic donor. The recovery is much faster and more pronounced among autologous patients, whose somatic distress declined to preadmission levels by Week 4, in contrast to the allogeneic groups who did not reach preadmission levels until Month 3 according to Phipps, Dunavant, Garvie, et al. (2002). In the same study, there was a large tendency for patients undergoing unrelated-donor transplants to experience greater distress than those undergoing matched-sibling transplants.

Childhood cancer survivors report poor psychological HRQoL secondary to problems with memory and the capacity for concentration (Lof et al., 2009). Nonetheless, IQ index scores were inclined to remain stable between

baseline and both 1 year and 2 years post-HSCT indicating stability in global cognitive functioning according to Kupst et al. (2002). However, lower arithmetic scores was the exception to the results of stable global cognitive functioning. These results support many studies that have found that survivors of ALL and central nervous system lymphoma treatment experience this late effect. With regard to Kupst et al. (2002), many of the children were diagnosed with ALL coupled with intensive systematic and intrathecal chemotherapy, which has been identified as a risk factor for neurocognitive problems. However, in this study by Kupst et al. (2002), there was no relationship between young age at time of transplant to later cognitive difficulties. A possible explanation is the rather small sample size of young children. Simms, Kazak, Golomb, Goldwein, and Bunin (2002) reported children younger than 3 years at risk for increased cognitive functioning problems 2 years post-HSCT. Furthermore, pre-existent moderate to severe cognitive impairment was identified as a variable to place post-HSCT survivors at higher risk for lower psychological HRQoL scores (Forinder et al., 2006).

Maternal distress and total parenting stress levels were 2 predictive variables explored in a small number of studies. According to Barrera, Atenafu, and Pinto (2009), although maternal distress, measured by symptoms of depression, emerged as a risk factor negatively associated with physical and psychosocial HRQoL of HSCT survivors, its strength and validity is questionable. Possibly, a mother battling with more symptoms of depression reported more negatively about her child's HRQoL as a reflection of her psychological well-being rather than her child's. Clinical levels of anxiety and depression were associated with low socioeconomic status and a poorer HRQoL in most psychological HRQoL areas. When considering total parenting stress levels, studies found higher post-HSCT parenting stress than at admission baseline levels. An important predictor of HRQoL was found in the child's demandingness perceived by the parents, assessed before and after admittance for HSCT (Vrijmoet-Wiersma et al., 2009). A potential predictor of psychological outcome is family cohesion (Barrera, Atenafu, & Pinto, 2009)

Social Well-Being

As the process and supportive care aspects of HSCT are improving, recipients are living longer but often with long-term consequences. Often, there is a strong relationship between physical and social function, suggesting that those who do not do well physically also suffer from social problems as a predictive variable (Felder-Puig et al., 2006). Significant predictors were found across studies for social HRQoL including age, pre-HSCT functioning,

and type of transplant. Age at HSCT was a predictor of social competence at 1 year, indicating that older children may return to school and social activities more quickly than do younger children. According to Kupst et al. (2002), the strongest predictor of social well-being was pre-HSCT functioning including behavioral and cognitive capacities. Children and adolescents with higher cognitive and behavioral competence tended to fare better in terms of social functioning. Kupst et al. examined resiliency among and its impact on social functioning. Factors that tended to strength social functioning included academic ability, pre-HSCT behavioral and social functioning, a relatively higher socioeconomic status, and older age at 1 year post-HSCT. Overall, there was a low prevalence of behavioral or social difficulties and stability of functioning over time post-HSCT.

HRQoL social well-being scores included ratings of body image, satisfaction with family life, relationship to spouse, and sexual function and satisfaction. The adult survivors after childhood HSCT considered themselves less attractive and reported poorer self-image because of their treatment and illness compared with the normative group. Both men and women are frequently found well below general population height and weight affecting self-image and physical appearance reports leading to poorer well-being and social outcome among adult survivors. Other poor areas of social HRQoL reported for adult survivors of childhood HSCT according to Lof et al. (2009) include satisfaction with family life, relationship to spouse, and sexual function and satisfaction compared with the age-matched norm. Predictive variables to social outcome were older age and the length of time elapsed since transplant. Parsons et al. (2006) found an interaction between time and transplant type on reported body image. Worst functioning and greatest decline of reported body image was observed in recipients of unrelated allogeneic transplants at 3 months post-transplant (Parsons et al., 2006). This may reflect clinical differences in medication regimens for recipients of unrelated-donor transplants, such as the use of corticosteroids for GVHD prophylaxis. Older age at time of transplant was also identified as a demographic predictive variable of poorer social HRQoL both pre- and post-HSCT. This study did reveal that social functioning had at least recovered to pre-HSCT assessment. However, these baseline scores are still lower than the age norm. Compared with a chronically ill reference group, the HSCT recipients in Nuss and Wilson's (2007) study reported comparable significantly lower scores for the social functioning subscale of HRQoL. The group with chronic GVHD also had lower HRQoL when rating general health and self-esteem. In the same study, in areas of general behavior and role behavioral difficulties, the HSCT patients scored higher compared with the normative group. There is also a

negative association between HRQoL and increasing age at time of assessment in that self-esteem tends to decline with age.

In regard to work-related functioning, Helder et al. (2004) reported adult survivors who had undergone HSCT in childhood suffered from some illness-related impairment. Examples of illness-related impairment included working fewer hours per week because of illness-related complaints, only being able to perform easy or light chores because of illness-related impairment, and only being able to work continuously for a short period of time or having to take regular, scheduled breaks. Childhood HSCT survivors who sought social support as a means of coping with stress correlated with better role functioning, whereas passive coping was related to poorer social HRQoL outcomes. These findings are consistent with Barrera, Atenafu, and Pinto (2009) who reported that young adults who underwent HSCT during childhood experience more problems, compared with their peers, with regard to their studies and work possibilities.

Emotional Well-Being

Moderate to high mood disturbances across different phases of HSCT procedure are evidence in parent and child report (Phipps, Dunavant, Garvie, et al., 2002). However, this contradicts reports by Lof et al. (2009) who found that emotional well-being domains were on par with the norm age comparative group. Clinical variables identified by Barrera, Atenafu, and Hancock (2009) as predictive of emotional HRQoL scores include younger child age, a diagnosis of ALL, time since diagnosis, maternal depression, and lower socioeconomic status. Higher maternal depression scores were associated with lower psychosocial scores along with survivors of ALL rated as having significantly worse emotional HRQoL than survivors of blood disorders and solid tumors. The longest treatment protocols associated with years of uncertainty about the future and fear of disease recurrence or relapse makes these children with ALL at increased risk of poor emotional well-being. The worst emotional HRQoL scores were of survivors who had the longest time since diagnosis at transplant. A possible explanation for such findings, suggested by Barrera, Atenafu, and Hancock (2009), about those survivors who have been under a treatment protocol the longest, and likely had disease recurrence, is that the cumulative chronicity of compromised health is a risk factor for emotional well-being of childhood HSCT survivors.

Felder-Puig et al. (2006), in an attempt to find out which HRQoL problems during the acute phase of treatment were associated with HRQoL 1 year post-HSCT, identified 3 major predictor variables: emotional functioning, worry, and communication. Not only do compromised emotional

functioning, a high level of worry, and reduced communication during the stay at the transplant unit have an immediate adverse effect of the patient's emotional status, but they may also negatively affect outcome in additional HRQoL domains for up to 1 year post-HSCT. In this study, other related variables, such as age, gender, and total body irradiation dose were evaluated for a relationship with emotional outcome. No correlation was reported between these variables and measures of patient's emotional HRQoL. Social support as a means of coping with stress was related to better role functioning (emotional part), whereas passive coping was related to poorer mental health according to Felder-Puig et al. (2006).

Protective factors reported for emotional HRQoL at 2 years post-HSCT according to Barrera, Atenafu, and Hancock (2009) is younger age at pre-HSCT. This finding may reflect the fact that younger children may have less recollection of their difficult experience before and particularly during the difficult weeks following HSCT procedures. This was also consistent with Phipps, Dunavant, Lensing, et al. (2002) that younger children tolerate HSCT with fewer difficulties, whereas older children and adolescents experience relatively higher levels of emotional distress and discomfort.

Clinical Implications

Throughout the course of treatment, APNs and pediatric oncology nurses must maintain a focus on not only survival but also the patient's quality of life going forward. APNs and pediatric oncology nurses can better facilitate an improved HRQoL for the patient through anticipatory guidance, communication, and early identification and intervention.

One way APNs foster health coping during the HSCT process is by providing anticipatory guidance to the patient and family. Beginning at diagnosis, APNs must encourage the maintenance or development of protective factors that can maximize HRQoL during transplantation and survivorship years. During the active treatment phase, APNs should continue to discuss preexisting and newly occurring risk factors and to promote realistic expectations for post-HSCT functioning. Open communication during active treatment is necessary because a full restoration of health is unlikely for the majority of HSCT recipients. APNs' anticipatory guidance increases the patient's awareness of HRQoL issues. Armed with an accurate depiction of attainable quality of life, patients are more likely to report a satisfactory survivorship.

It is important for APNs and pediatric oncology nurses to communicate not only with patients and families but also with the transplant team. Since the pediatric oncology nurse spends the most time at the bedside, they are more likely to recognize quality of life issues. Therefore,

Table 2. Risk Factors for Poor Health-Related Quality of Life

Risk Factor	Who Are at High Risk?
Age	Older children and adolescents
Diagnosis	Acute lymphoblastic leukemia
Type of transplant	Allogeneic transplant
Donor source	Unrelated donor
Graft-versus-host disease	Presence of acute or chronic graft-versus-host disease
Socioeconomic status	Lower socioeconomic status
Cognitive functioning	Preexistent moderate to severe cognitive dysfunction
Family functioning	Preexistent maternal distress and/or elevated total parenting stress levels
Psychosocial functioning	Preexistent anxiety and/or depression, reduced communication

pediatric oncology nurses must communicate with other members of the bone marrow transplantation team early to formulate intervention strategy. Team communication also develops broader nurse awareness in identifying risks for poor HRQoL and evaluating the effectiveness of intervention techniques. APNs and pediatric oncology nurses contributing to that knowledge base will help identify future childhood HSCT survivors at risk for jeopardized HRQoL.

To improve post-HSCT quality of life, APNs and pediatric oncology nurses must be aware of patient subgroups in need of more intensive supportive care before HSCT. For example, a higher level of supportive care and earlier and more aggressive intervention is necessary for those undergoing allogeneic HSCT, older children and adolescents, and those from lower socio-economic backgrounds. A summary of clinical variables predicting poor HRQoL can be found in Table 2. Beyond predictive clinical variables, APNs and pediatric oncology nurses must also be aware of specific components of HSCT and complications, such as GVHD, that place this unique population of childhood cancer survivors for risk of compromised HRQoL.

Collaboration among members of the bone marrow transplantation team can develop early interventions to reduce patient distress during the acute phase of transplant among patients with established risk factors of poor HRQoL. Strategies may include improving existing services and offering professional support in anticipation of crucial periods of transition and adjustment to enhance HRQoL of these children (Tsimicalis et al., 2005). Childhood cancer survivors have demonstrated enhanced quality of life while participating in a variety of interventions, including cognitive-existential group psychotherapy, cognitive-behavioral stress management, and expressive writing. Pediatric oncology nursing interventions assess the level of uncertainty experienced by HSCT survivors and, depending on the level and cause of uncertainty,

intervene by providing information, encouraging expression of feelings, normalizing the experience, and enhancing personal control (Saleh & Brockopp, 2001). APNs must prescribe early interventions and collaborate with psychologists and other health care providers to reduce high levels of patient distress, which can slow healing and increase medical complications. Pediatric oncology nurses play key roles in providing education and risk-based monitoring along with clinical assessment for children throughout HSCT and for their families across the illness trajectory along with the APNs.

APNs should begin to implement standardized HRQoL assessments in order to better conduct interventions. The APN is the pivotal force in the implementation of, and in education promoting, standardized HRQoL assessments in the clinical setting. Using an instrument specifically designed to assess HRQoL unique to HSCT patients and families is critical to identify deficits in need of remediation. Moreover, given the current inconsistencies in clinical findings because of the use of various measurement tools, standardizing HRQoL assessments would help formulate new interventional strategies to benefit the HSCT population.

Ultimately, HSCT recipients will have improved survivorship years and require less intervention throughout adulthood because of anticipatory guidance, communication, and early identification and intervention. APNs and pediatric oncology nurses play critical roles in working at survivorship clinics. By recognizing the subtle onset of late effects, APNs and pediatric oncology nurses can help survivors experience a positive HRQoL that would otherwise not exist. Surveillance and long-term follow-up should include monitoring of children and adults treated during childhood who are at risk for functional loss so that they can be referred for intervention to restore function. APNs and pediatric oncology nurses may provide compensatory strategies for function restoration or adapt the survivor's environment to allow optimal participation in

home and social settings. APNs and the clinic nurse may use rehabilitation and counseling experts who will be able to enhance or improve survivors' functioning. The APN and pediatric oncology nurse who implement regular, structured assessments of HRQoL post-HSCT will help develop interventional strategies and future evidence-based protocols specific to childhood HSCT survivors.

Continuing to identify HRQoL predictors is necessary to guide decision making, counsel and support recipients and their families, educate health care providers, and guide the development of interventions to ameliorate the impact of HSCT on patients and families.

Conclusions

Children who have undergone HSCT are particularly at high risk for altered HRQoL. This is in part because of the paradox of HSCT: The intense treatment that offers patients and their families hope against fairly certain death from disease may actually result in death itself and invariably leads to acute and delayed sequelae (Eilers & King, 1998). To optimally support the post-HSCT patient, it is essential to consider not only medical but also physical, social, emotional, and psychological aspects during follow-up (Lof et al., 2009). As HSCT recipients attempt to resume age-appropriate activities, many discover that their developmental trajectory and future potential have been permanently altered. Likewise, this enormous stress of the underlying disease and its treatment coupled with the fear of complications, relapse, and death has the potential to disrupt HRQoL for the child and family.

Pediatric HSCT survivors may have decades to live without transplant. Consequently, providing interventions to ensure survivor HRQoL is crucial. Current literature provides helpful knowledge regarding the target of interventions and supportive care. Despite the fact that all patients undertaking HSCT require elevated levels of supportive care, earlier and more aggressive intervention must be concentrated on those undergoing allogeneic HSCT, older children and adolescents, and those from lower socioeconomic backgrounds. Rather than waiting for HSCT recipients who are at high risk to present themselves, interventions must begin early and be administered in a preventive, or proactive, manner for those patients prior to transplant. APNs and pediatric oncology nurses must identify risk factors leading to impaired functioning for particularly vulnerable patients and families. This knowledge will facilitate the development of appropriate intervention programs to alleviate the long-term effects of HSCT on pediatric HRQoL.

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