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Health-Related Quality of Life in Adolescents at the time of Diagnosis with Osteosarcoma or Acute Myeloid Leukemia

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Abstract

Although measuring health-related quality of life (HRQoL) in adolescents with cancer helps clinicians to personalize care for their patients, no previous studies have included HRQoL measurement at the time of diagnosis of osteosarcoma (OS) or acute myeloid leukemia (AML). The purpose of this study was to evaluate the feasibility of measuring adolescents' HRQoL at the time of their diagnosis of OS or AML, and to compare their ratings with those of their parents and of similarly diagnosed but younger patients aged 8- to 12- years. Participants included 126 patients (79 adolescents) and 130 parents (78 parents of adolescents); most completed the HRQoL instrument/s within 48 hours of the first chemotherapy cycle. Ninety-three percent of adolescents diagnosed with OS and 93% of those diagnosed with AML completed the HRQoL instruments. Agreement between the adolescents and their parents ranged from 0.29 to 0.71 (OS) and 0.44 to 0.62 (AML). In all domains, OS adolescents had significantly lower PedsQL v.4.0 scores than adolescents with AML. Our findings demonstrates the feasibility of measuring HRQoL in adolescents with OS or AML (and their parents) at the time of diagnosis, and thus their HRQoL ratings can be used to inform their cancer care from diagnosis forward.

Measuring health-related quality of life in adolescents at the time of their diagnosis with cancer makes it possible for clinicians to incorporate into their care what matters to individual adolescents from the moment of diagnosis forward. Incorporating health-related

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quality of life (HRQoL) considerations into care is theorized to a) establish effective patient and family communication with physicians and other members of the health care team, b) improve overall patient and family satisfaction with care, c) identify otherwise hidden morbidities of treatment, and d) facilitate treatment decision-making (Eiser & Jenney, 2007; Varni, et al., 2006a). In addition, measuring adolescents' HRQoL from the point of diagnosis forward aids in assessing the impact of different therapies or courses of treatment on adolescents, including their symptom experience and functional outcomes. Measuring and addressing adolescents' self-reported HRQoL at the time of diagnosis and during treatment conveys the clinicians' concerns to the adolescents about them as persons as well as about their disease and this may affect treatment outcomes for the adolescents.

The benefits of soliciting adolescents' HRQoL reports are augmented by adding a parent or guardian proxy-report. If an adolescent chooses not to report or is unable to report, a proxy-report given by persons selected for their emotional and geographic closeness to the ill adolescent will contribute a family perspective that likely reflects concerns or impressions that influence family interactions with the ill adolescent. When both adolescents and proxy-ratings are reported, clinicians gain an expanded understanding of the family perspectives during treatment (Parsons et al., 1999). The two sets of ratings do not replace but rather supplement each other. An additional approach to understanding HRQoL reports from adolescents is to compare their reports with those of a different age group with same diagnosis.

Our purpose was to evaluate the ability of adolescents at the time of their diagnosis with osteosarcoma (OS) or acute myeloid leukemia (AML) – two of the most common cancers during adolescence (Bleyer, 2007) - to self-report their HRQoL and the ability of their parents to similarly participate as proxy raters. The feasibility of soliciting adolescents' HRQoL reports at the time of diagnosis of OS or AML has not previously been established. In addition, we compared the adolescent reports with those of younger children (ages 8 to 12 years) who were also newly diagnosed with OS or AML and enrolled on the same protocols as were the adolescents. The specific aims of our study were to:

1. assess the feasibility of measuring patient- and proxy-reported HRQoL at the time of diagnosis of OS or AML in terms of participation rates and missing item responses by patient age, gender and diagnosis.
2. assess the agreement between adolescent and parent ratings of the adolescent's HRQoL.
3. compare HRQoL ratings of adolescents diagnosed with OS with those of adolescents diagnosed with AML, and with the reports of children 8-to 12-years of age with same diagnoses.

Background

Health-Related Quality of Life in Adolescents with Cancer

Health-related quality of life (HRQoL) in adolescents with cancer is defined in only a minority of research reports but a definition based on interviews with children and adolescents with cancer was recently reported: “an overall sense of well-being based on

being able to participate in usual activities, to interact with others and feel cared about; to cope with uncomfortable physical, emotional and cognitive reactions; and to find meaning in the illness experience” (Hinds, et al., 2004). Clinical investigators offer a similar though expanded definition that also includes the importance of the family perspectives (Nathan, et.al., 2004).

Diverse methods (guided or open-ended interviews, a variety of single-item or multidimensional questionnaires, and symptom reports) and different data collection schedules have been used to measure HRQoL in adolescents with cancer (Gerharz, et al., 2003; Hinds, et al., 2005), suggesting that no single standard for measuring HRQoL in pediatric oncology yet exists. HRQoL of adolescents with cancer has been measured using the instruments used in this study, but none of these reports included measuring HRQoL at the time of cancer diagnosis. In addition, previous studies did not include patients with OS or AML (Meeske, et al., 2004) or their inclusion could not be determined as all reports from pediatric oncology patients (children and adolescents) were presented only in total group scores (Hutchings, et al., 2007; Razzouk, et al., 2006; Varni, 2004; Varni, 2007a).

Of the available studies, more have addressed HRQoL in adolescents with OS than AML. Study designs most commonly involved survivors *or* their parents reporting on the adolescent's HRQoL from 3 to 6 months after diagnosis to 31 years after completion of all therapy for OS patients (Christ, 1995; Earle et al., 2005; Frances et al., 2007; Greenberg, et al., 1994; Koopman et al., 2005; Marchese, et al., 2004; Nagarajan, et al., 2004) and from 2 or more years after transplantation for AML patients (Bhatia, et al., 2005; Perkins, et al., 2007). Only three reports included both the adolescent and parent reports of the adolescents' quality of life (Perkins, et al., 2007; Koopman, et al., 2005; Tabone, et al., 2005). When compared to their ill child's HRQoL ratings, parent-proxy ratings tend to be an underestimate (Eiser & Eiser, 2000; Koopman, et al., 2005) with parent ratings more discordant with the ratings of adolescents than with younger age children (Chang & Yeh, 2005; Eiser & Eiser, 2000). In summary, adolescents' HRQoL at the time of a cancer diagnosis or the perceptions of their parents' regarding the adolescents' HRQoL at that critical time have not been previously documented.

Conceptual Model

The conceptual model guiding this study was the model of environmental (internal, immediate, and institutional environments) influences on HRQoL of adolescents with cancer (Hinds, 1990). The assumptions underlying this model are that adolescents with cancer are a) sensitive to the moods, attitudes, values and knowledge of others, b) affected by daily events and ongoing problems related to health and illness, and c) mindful of their own desires, values, expectations and preferences. The three levels of environment directly influence the adolescents' HRQoL at the time of diagnosis and during cancer treatment. The definitions of these levels include: the internal environment (representing factors within the adolescent such as gender, age, the adolescent's feelings about self including competence to handle the illness demands, and as well as the adolescent's genetic makeup), the immediate environment (factors of significant others such as family members and care providers and their ability to respond to the demands of the adolescent's illness), and the institutional

environment (factors of the health care system as a whole as well as of the treatment setting such as financial support for the costs of care or for research). Patient and parent perceptions of the patient's HRQoL as factors influencing the domains of the patient's HRQoL are represented in two of the environmental levels. The components of this model that were addressed in this study are highlighted in Figure 1.

Methods

Patients included in this study participated in HRQoL studies that were part of two pediatric therapeutic trials: one for the treatment of newly-diagnosed osteosarcoma (OS99) and the other for treatment of newly-diagnosed acute myeloid leukemia or myelodysplasia (AML02). These two multi-institutional trials were approved by the institutional review boards of all participating institutions, and the analysis specific to comparing the HRQoL of the OS and AML patients was approved by the institutional review board at St. Jude Children's Research Hospital.

Sample and Setting

A total of 142 patients (42 adolescents and 23 children with OS and 43 adolescents and 34 children diagnosed with AML) and their parents were eligible for inclusion in this study. Thirty-nine of the 42 adolescents with OS (93%) completed the HRQoL instruments at diagnosis as did 40 of the 43 adolescents with AML (93%). Of the 39 adolescents with OS, all had localized resectable tumors and a slight majority were male (54%) the primary site of disease for a majority of the adolescents was the femur (Table 1). Of the 40 adolescents with AML, a similar majority were male (53%) and the largest risk group was Standard (40%). The two groups of adolescents were similar in age and gender distribution but not in race as the OS group was primarily White (46%) or Hispanic (38%) and the AML adolescent group was primarily White (70%) or Black (23%) (Table 1). Two sites (the largest free-standing pediatric cancer center in the United States (St. Jude) and a children's medical center in Chile) participated in the OS99 trial and six sites in diverse geographic areas in the United States including St. Jude participated in the AML02 trial.

At the time of diagnosis, the aims of the HRQoL studies were explained to the parents and with parent permission, to the ill adolescent or child. Patients completed both the PedsQL v. 4.0 and the SDS while parents completed only the PedsQL v.4.0. We defined participation rates as the number of adolescents who completed the HRQoL instruments (PedsQL v.4.0 and/or the SDS) divided by the total number of eligible adolescents. The same definition was applied to parents and to 8-to-12- year old patients.

Instruments

The PedsQL v.4.0 (Pediatric Quality of Life Inventory, Version 4.0): This 23-item, generic quality of life instrument solicits respondents' ratings of problems during the past 30 days in four domains: 1) physical functioning -8 items that reflect problems the respondent may have with completing usual daily activities as well as sports-related activities or with pain or low energy, 2) emotional functioning -5 items that reflect problems with fear, sadness, anger, sleeping or worry, 3) social functioning -5 items that reflect problems with getting

along with others, being teased, or not being able to keep pace with peers, and 4) school functioning -5 items that reflect problems with paying attention in class, forgetfulness, and missing school. Two summary scores are also calculated; the Physical Health Summary Score (equivalent to the physical functioning domain score) and the Psychosocial Summary Score (computed as the sum of the item scores divided by the number of items answered in the emotional, social, and school functioning domains). If a patient or parent did not report on one of the three domains comprising the Psychosocial Summary Score, then that latter score was not computed. The PedsQL v.4.0 has age-specific versions and matched parent versions (Varni, et al., 2002; 2007b). In this study, we used the PedsQL v.4.0 Teen Report (13 years and older), Child Report (8-to 12-years), the Parent Report for Teens, and the Parent Report for Children. A likert-type response format is used and scores are then transformed to a 0, 25, 50, 75 and 100 point scale for each item and domain with higher scores representing better HRQoL. Completing each instrument generally requires 4 to 6 minutes.

Symptom Distress Scale (SDS): This 10-item, Likert-type (ratings from 1 to 5 with 5 representing higher intensity; total scale scores ranging from 10 to 50) self-report instrument has been previously used for self-reported symptom presence, intensity and distress in pediatric oncology patients who were 8 years of age and older. The ten items include feelings about appearance, ability to get around, tiredness, sleep, mood, pain, appetite, nausea, bowel pattern, and ability to concentrate 'today'. The SDS has been assessed for clinical feasibility and content and construct validity in pediatric oncology patients (Hinds, et al., 2000; Hinds, 2002). Completing the instrument generally requires 3 to 4 minutes.

Statistical Methods

We applied the score calculation methods used by Varni et al., (2007a) to the adolescent, parent and child reports of the PedsQL v.4.0 i.e., if 50% or more of the items of a domain was missing (not answered), that domain was eliminated from the analysis. The total score for the SDS was calculated for patients who completed at least 8 of the 10 SDS items as the sum of the item scores answered divided by the number of items answered and this score was then multiplied by 10 so that the score range of 10 to 50 was maintained. Descriptive univariate analyses were used for the first study aim, and the intraclass correlation coefficient (ICC) was used to assess agreement between patient and parent HRQoL reports. Agreement was designated as poor to fair for ICC values 0.40, moderate for ICC 0.41-0.60, good for ICC 0.61-0.80, and excellent for ICC 0.81-1.00. Spearman correlation coefficients were used to explore associations between symptom distress and HRQoL, and the Wilcoxon rank sum test was used to compare HRQoL and symptom distress scores by age group (adolescents vs. children aged 8-12-years). Linear regression was used to explore the effect of diagnosis on each domain of the PedsQL v.4.0; models (based on the underlying conceptual framework) also included patient age group, gender, and SDS total score. Model assumptions were assessed using diagnostic plots.

Results

Feasibility of measuring patient-reported and parent-reported HRQoL at the time of diagnosis of AML or OS in terms of participation rates and missing values by patient age and gender

Thirty-nine (93%) of the 42 OS adolescents and 40 (93%) of the 43 AML adolescents completed the PedsQL v. 4.0 and/or the SDS at the time of diagnosis. Thirty-nine (93%) of the 42 OS adolescents and 39 (91%) of 43 AML patients completed the SDS. All but one adolescent with OS and all but two with AML answered all 10 SDS items. One OS adolescent left the bowels item blank, one AML patient left both the appearance and getting around items blank, and one AML patient left only the getting around item blank. In contrast, 19 (83%) of 23 OS patients and 28 (82%) of 34 AML patients who were 8- to 12-years of age completed the SDS at the time of diagnosis. All but one of the 19 children with OS answered all of the items; one child left the 'tired' item blank. All but one child with AML answered all of the SDS items; one child left the appearance item blank and the getting around item blank. Overall for both diagnoses, females had a higher rate of participation (Table 2). Females also had a higher rate of participation for both age groups within each diagnosis (data not shown).

Fifty-six percent of adolescents with OS completed the HRQoL instruments on or just prior to the day that they received their first chemotherapy, while most (85%) completed the HRQoL instruments within 4 days of beginning chemotherapy. Less than a majority (33%) of adolescents diagnosed with AML completed the HRQoL instruments on the day they began chemotherapy but most (85% for the SDS and 89% for the PedsQL v.4.0) completed the instruments within 4 days of beginning chemotherapy.

Participation rates for OS adolescents by domain and summary score of the PedsQL v.4.0 ranged from 79% to 93% with the lowest rates occurring in the Psychosocial Summary Score and in the school functioning domain; in contrast, participation rates for the 8- to 12-year-old children was 83% for all domains and both summary scores (Table 3). Participation rates for the AML adolescents ranged from 81% to 88% with lower rates occurring in the Psychosocial Summary Score and school functioning domain. Participation rates for the 8-to-12 year olds were lower ranging from 71% to 76%. Rate of domain completion tended to be higher for female patients than for males in both age groups within each diagnosis (data not shown). Reasons for non-completion among adolescents included patient missed by the study staff at the time of the scheduled clinic visit (n=2 AML and n=3 OS) and patient too ill to complete instruments (n=2 AML). The amount of missing item responses was low and no pattern in missing item responses was apparent.

Thirty-nine (93%) of 42 parents completed the PedsQL v.4.0 at the time of their adolescent's diagnosis of OS. Completion rates for parents by domain and summary scores of the PedsQL v.4.0 ranged from 79% to 93% with the lowest completion rates in the Psychosocial Summary Score and in the school functioning domain (Table 4). Of the 43 parents of AML adolescent patients, 39 (91%) completed the PedsQL v.4.0 at the time of their child's diagnosis. Completion rates by domains ranged from 79% to 91% with lowest completion rates being for the Psychosocial Summary Score and the school functioning domain.

Agreement between adolescent and parent ratings of the adolescent's HRQoL

Summary statistics by domain of the PedsQL v.4.0 for the OS adolescent and parent reports were similar (Table 5). Agreement coefficients for the domains ranged from 0.29 (emotional functioning) to 0.60 (physical functioning) with a total score agreement of 0.71. Agreement was good (ICC=0.62) for the Psychosocial Health Summary score. Agreement coefficients ranged from 0.44 (social functioning) to 0.52 (emotional functioning) at the domain level between adolescents with AML and their parent raters (Table 5).

Comparison of symptom distress and HRQoL scores for adolescents diagnosed with OS vs. AML and with Younger Children with Same Diagnosis

The mean number of symptoms reported by adolescents with OS was 6.62 (SD = 2.28) with the mean number of symptom scores reaching the distress level of 3 or higher being 4.26 (SD=2.46). Thirty-eight of 39 OS adolescents (97%) had at least one symptom that achieved the distress criterion meriting a clinical intervention. Symptoms with the higher mean scores included getting around (3.3, SD=1.3), tired (3.0, SD=1.3), appetite (2.7, SD=1.3), sleep (2.7, SD=1.2) and feeling sad (2.6, SD=1.0). The mean number of symptoms reported by adolescents with AML was 7.15 (SD=2.44) with the mean number of symptoms reaching the distress level of 3 or higher being 5.09 (SD=2.52). Thirty-three of 39 (85%) adolescents with AML had at least one symptom meriting intervention. Symptoms with the higher mean scores included getting around (2.6, SD=1.3), tired (3.0, SD=1.3), appetite (3.0, SD=1.2), sleep (3.0, SD=1.3), and feeling sad (2.7, SD = 1.0). Additionally, the median and mean total scale scores of the SDS were similar between the two groups of adolescents (means: 24 (SD, 7) for OS vs. 25 (SD, 9) for AML adolescents). In contrast, the mean and median domain and summary scores on the PedsQL v.4.0 differ between the two groups by 10 to 24 points with adolescents diagnosed with AML reporting better HRQoL scores than adolescents with OS (Table 6). The largest difference reported was for the Physical Health Summary score. We also examined the PedsQL v.4.0 items for differences between adolescents with OS and those with AML and used a 25-point difference in mean scores as our criterion for clinical significance. Four of the physical functioning items achieved this difference with the OS adolescents reporting lower scores for a) able to walk more than a block, b) able to run, c) participate in sports or exercise, and d) take a shower or bath by self. Three other physical functioning items nearly met that criterion including a) difficulty lifting heavy objects, b) able to do household chores, and c) hurting or aching. One school functioning item, missing school to go to the doctor or hospital, also achieved the criterion of a 25-point difference with the OS adolescents reporting this to be a lower scoring item (missing more school in the past 30 days) than did the AML adolescents.

Total scale scores of the SDS and the PedsQL v.4.0 as well as domain scores of the PedsQL v.4.0 were similar between the adolescent and the younger children groups who were newly diagnosed with OS or with AML (Table 6) with only one statistically significant difference. Adolescents with OS reported better social functioning scores and a trend towards better psychosocial summary scores than children 8 to 12 years of age with OS.

In separate regression models, we explored the effect of disease (OS or AML) on each domain of the PedsQL v.4.0 while adjusting for patient gender, age group, and SDS total

scale score. In all domains, OS patients had significantly lower PedsQL v.4.0 scores (Table 7). Gender was a significant predictor only of school functioning with male patients having lower scores. Age was a significant predictor only of social functioning with adolescents having the higher school-related quality of life scores. The SDS was a significant predictor of physical, emotional, and school functioning after adjusting for the other factors (Table 7).

Discussion

The high participation rates in both groups of adolescents and their parents and the low rates of missing item responses in all participants attest to the feasibility of soliciting self- and parent- reports of HRQoL at the time of adolescents' diagnosis with OS or AML. Most adolescents, children, and their parents are able and willing to offer their impressions of HRQoL at this critically important time, and thus future HRQoL study designs could and ought to include this early point as the baseline measurement. The impressive rates of participation and low rates of missing values may be related to the low burden of the two-instrument packet (in terms of time required to complete) for the adolescents and the single instrument for parents. The high participation rates combined with the limited number of reasons for non-participation by adolescents and parents, and the adequate sample size of participants also support the potential generalization of our HRQoL feasibility findings to children and adolescents with other types of cancer. The high rates of participation also indicate that at least two levels of environment as specified in the study conceptual model (internal and immediate levels) can be measured.

Patient and parent agreement ratings at the time of diagnosis of cancer were similar to those reported in other studies that compared ratings obtained later in treatment. Differences in strength of agreement varies by type of HRQoL domain but most typically the highest agreement is in the physical functioning domain (Chang & Yeh, 2005; Eiser & Eiser, 2000). In previous reports, the proxy-report by both mothers and fathers was significantly lower than that of their ill child, particularly in the emotion functioning domain and the Psychosocial Health Scale (Reinfjell et al., 2007). It is interesting that adolescents with AML and their parents have somewhat higher agreement by domain than do the adolescents with OS. The diagnosis of AML tends to have a more acute onset than OS and perhaps the parents and adolescents with AML are more focused on this emergent experience and the ill adolescents' suffering as supported by the higher mean distress symptoms reported by this patient group.

Patient and parent PedsQL v.4.0 scores for the OS adolescents were notably lower than other previously reported scores for healthy children and adolescents and their parents (Varni, 2006a), for similarly aged patients with ALL who were 4.2 to 12.5 years after their diagnosis (Reinfjell et al., 2007), and for children and adolescents treated for a brain tumor, ALL, non-Hodgkin's lymphoma, Wilm's tumor, neuroblastoma or Hodgkin's lymphoma, diabetes, cardiac conditions, asthma, obesity or rheumatology conditions (Varni, 2007b). The scores for the OS adolescents were also lower for the total score (which includes physical functioning, psychosocial functioning and emotional functioning) than those reported for children and adolescents with a brain tumor who were either on treatment, off-treatment less than 12 months, or off-treatment more than 12 months but were similar to

their social and school functioning scores (Palmer, et al., 2007). The scores from the OS adolescents and their parents were also lower than scores reported by children with psychiatric disorders or cerebral palsy (Varni, et al., 2007b). Scores from the parents of the OS adolescents were lower in the Total Scale scores, physical functioning and emotional functioning domains than those reported by parents of children and adolescents with brain tumors who were a median of 3.2 years from diagnosis but were similar to the parent proxy reports for the social and school functioning domains (Bhat, et al., 2005). The scores reported by the adolescents with AML and their parents are similar to those of well children and adolescents except for a 20-point lower mean score in the Physical Health Scale (Varni, et al., 2006). The differences in scores for patients in our study compared to those reported in these other studies by domain ranged from 3 to more than 40 points lower for patients and from 5 to 24 points lower for parents. The lower scores in our study may be related to the much earlier point in treatment (at diagnosis) when compared to other studies or to the more obvious differences in health status when compared to the healthy children and adolescents, and to the intensity of the diagnostic phase and disease symptoms of OS and AML. The score differences support the sensitivity of the instrument to document differences between groups of children and adolescents and the ability of these different groups to accurately report their HRQoL.

That adolescents with OS consistently reported lower domain scores on the PedsQL v.4.0 as compared to the AML adolescents is interesting. Perhaps the measurement period (the last 30 days) may contribute to this as adolescents with OS typically have a period of symptoms most commonly pain and swelling at the site followed by a diagnostic work-up that can span two weeks whereas adolescents with AML present with a more acute illness with shorter duration of symptoms. In addition, the physical functioning items appear to particularly distinguish between the two groups of adolescents and the content of these items would be difficult for patients with tumors located in the femur (most common site of OS) to complete.

Our strategy of comparing the HRQoL reports from 8 to 12 year old children with same diagnosis as the adolescent patients did not yield striking differences between the two age groups other than in the social functioning domain. It may be that the disease and treatment are a more shared experience for adolescents and children than their age difference with respect to HRQoL during cancer.

The influence of symptom distress as measured by the SDS on the physical, emotional and school domains of the PedsQL v.4.0 is an important point of clinical concern. This direct and significant influence indicates the clinical need for health care providers to intervene to prevent and to diminish symptoms of the disease and toxicities of treatment as strategies to improve the HRQoL of adolescents from the very beginning of treatment.

Conclusion

Adolescents diagnosed with OS or AML and their parents are willing and able to participate in HRQoL study aims at the time of their diagnosis. This finding supports the feasibility of measuring adolescents' HRQoL at this early point in the cancer experience and its use as a

baseline for longitudinal measurement of adolescents' HRQoL during cancer care. Obtaining HRQoL measurements at the time of diagnosis may potentially help establish effective communication and a trust relationship between the patient/family and the clinicians, improve patient and family satisfaction with cancer care, and facilitate treatment decision-making. Adolescents with OS have significantly lower HRQoL than do adolescents with AML at the time of diagnosis, indicating that HRQoL reports can differ between patient groups and that score differences can help to identify adolescents in particular need for interventions designed to improve their HRQoL. Addressing symptom distress secondary to disease is one way of promoting a more positive HRQoL for these ill adolescents. Although adolescent and parent-proxy HRQoL reports are somewhat to moderately associated, the strength of the statistical association is not such that we could recommend that the parent proxy report replace the adolescent self-report at diagnosis. Instead, we recommend the complementary approach of including both reports.

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Figure 1.
Study Conceptual Model of Environmental Influences on Quality of Life During Cancer.

Table 1
Patient and Disease Characteristics for Adolescent Patients who Completed Either the SDS or the PedsQL v.4.0 Instruments at Diagnosis

	OS99	AML02
No. of adolescents	39	40
Age at Study Enrollment (in years)		
Median	15.4	16.3
Range	13.0 – 23.0	13.0 – 21.2
Mean (SD)	15.9 (2.4)	16.0 (2.0)
Gender		
Male	21 (54%)	21 (53%)
Female	18 (46%)	19 (48%)
Race		
White	18 (46%)	28 (70%)
Black	6 (15%)	9 (23%)
Hispanic	15 (38%)	0 (0%)
Other	0 (0%)	3 (8%)
Primary Site of Disease		
Femur	23 (59%)	n/a
Tibia	10 (26%)	
Fibula	2 (5%)	
Humerus	2 (5%)	
Ulna	1 (3%)	
Rib	1 (3%)	
Risk Group		
Low	n/a	11 (28%)
Standard		16 (40%)
High		13 (33%)

Table 2
Patient Participation Rates for SDS Items for All Patients by Disease, Age Group, and Gender

OS						
	All eligible OS patients	By Age Group		By Gender		
		8-12	13-25	Male	Female	
N	65	23	42	38	27	
SD Total Scale Score	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How much you are able to get around	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How tired you are feeling	57 (88%)	18 (78%)	39 (93%)	31 (82%)	26 (96%)	
How good your appetite is	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How much pain you are having	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How much nausea you have	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How well you slept last night	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How you feel about your appearance	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How you are feeling	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
How regular your bowels are working	57 (88%)	19 (83%)	38 (90%)	31 (82%)	26 (96%)	
How well you are able to concentrate	58 (89%)	19 (83%)	39 (93%)	32 (84%)	26 (96%)	
AML						
	All eligible AML patients	By Age Group		By Gender		
		8-12	13-25	Male	Female	
N	77	34	43	46	31	
SD Total Scale Score	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	
How much you are able to get around	64 (83%)	27 (79%)	37 (86%)	38 (83%)	26 (84%)	
How tired you are feeling	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	
How good your appetite is	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	
How much pain you are having	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	
How much nausea you have	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	
How well you slept last night	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	
How you feel about your appearance	65 (84%)	27 (79%)	38 (88%)	38 (83%)	27 (87%)	
How you are feeling	67 (87%)	28 (82%)	39 (91%)	39 (85%)	28 (90%)	

OS				
	All eligible OS patients	By Age Group		By Gender
		8-12	13-25	Male
				Female
N	65	23	42	38
				27
How regular your bowels are working	67 (87%)	28 (82%)	39 (91%)	39 (85%)
How well you are able to concentrate	67 (87%)	28 (82%)	39 (91%)	28 (90%)
				28 (90%)

Table 3
Patient Participation Rates by Domain of PedsQL v.4.0 for All Patients by Age Group, Gender, and Disease

OS (PATIENT REPORTS)					
	All eligible OS patients	By Age Group		By Gender	
		8-12	13-25	Male	Female
N	65	23	42	38	27
Physical Functioning / Physical Health	58 (89%)	19 (83%)	39 (93%)	33 (87%)	25 (93%)
Psychosocial Health	52 (80%)	19 (83%)	33 (79%)	29 (76%)	23 (85%)
Emotional Functioning	57 (88%)	19 (83%)	38 (90%)	33 (87%)	24 (89%)
Social Functioning	58 (89%)	19 (83%)	39 (93%)	33 (87%)	25 (93%)
School Functioning	53 (82%)	19 (83%)	34 (81%)	29 (76%)	24 (89%)
Total Score	52 (80%)	19 (83%)	33 (79%)	29 (76%)	23 (85%)
AML (PATIENT REPORTS)					
	All eligible AML patients	By Age Group		By Gender	
		8-12	13-25	Male	Female
N	77	34	43	46	31
Physical Functioning / Physical Health	64 (83%)	26 (76%)	38 (88%)	38 (83%)	26 (84%)
Psychosocial Health	59 (77%)	24 (71%)	35 (81%)	34 (74%)	25 (81%)
Emotional Functioning	64 (83%)	26 (76%)	38 (88%)	38 (83%)	26 (84%)
Social Functioning	63 (82%)	26 (76%)	37 (86%)	37 (80%)	26 (84%)
School Functioning	59 (77%)	24 (71%)	35 (81%)	34 (74%)	25 (81%)
Total Score	59 (77%)	24 (71%)	35 (81%)	34 (74%)	25 (81%)

Table 4
Parent Participation Rates by Domain of PedsQL v.4.0 for All Patients by Age Group, Gender and Disease

OS (PARENT-PROXY REPORTS)					
	All eligible OS patients	By Age Group		By Gender	
		8-12	13-25	Male	Female
N	65	23	42	38	27
Physical Functioning / Physical Health	60 (92%)	21 (93%)	39 (93%)	34 (89%)	26 (96%)
Psychosocial Health	54 (83%)	21 (93%)	33 (79%)	29 (76%)	25 (93%)
Emotional Functioning	60 (92%)	21 (93%)	39 (93%)	34 (89%)	26 (96%)
Social Functioning	60 (92%)	21 (93%)	39 (93%)	34 (89%)	26 (96%)
School Functioning	54 (83%)	21 (93%)	33 (79%)	29 (76%)	25 (93%)
Total Score	54 (83%)	21 (93%)	33 (79%)	29 (76%)	25 (93%)
AML (PARENT-PROXY REPORTS)					
	All eligible AML patients	By Age Group		By Gender	
		8-12	13-25	Male	Female
N	77	34	43	46	31
Physical Functioning / Physical Health	70 (91%)	31 (91%)	39 (91%)	40 (87%)	30 (97%)
Psychosocial Health	62 (81%)	28 (82%)	34 (79%)	36 (78%)	26 (84%)
Emotional Functioning	70 (91%)	31 (91%)	39 (91%)	40 (87%)	30 (97%)
Social Functioning	70 (91%)	31 (91%)	39 (91%)	40 (87%)	30 (97%)
School Functioning	62 (81%)	28 (82%)	34 (79%)	36 (78%)	26 (84%)
Total Score	62 (81%)	28 (82%)	34 (79%)	36 (78%)	26 (84%)

Table 5
PedsQL v.4.0 Summary Statistics for Adolescent Patients and Parents by Disease

	Total Score	Physical Health	Psychosocial Health	Emotional Functioning	Social Functioning	School Functioning
OS						
Adolescent patients	n=33 55 (32 – 93) 58.4 (17.1)	n=39 44 (0 – 100) 43.5 (30.3)	n=33 63 (42 – 91) 65.9 (13.1)	n=38 55 (15 – 100) 54.8 (19.9)	n=39 80 (45 – 100) 78.1 (16.0)	n=34 65 (30 – 100) 66.9 (20.7)
Parents of adolescents	n=33 52 (25 – 98) 56.4 (18.5)	n=39 41 (0 – 100) 42.8 (28.2)	n=33 62 (35 – 97) 62.8 (16.1)	n=39 50 (15 – 90) 51.4 (17.3)	n=39 65 (40 – 100) 73.0 (20.7)	n=33 60 (25 – 100) 63.0 (23.9)
ICC[*]	0.7106	0.6004	0.6206	0.2890	0.3766	0.4799
Agreement	Good	Moderate	Good	Poor-Fair	Poor-Fair	Moderate
AML						
Adolescent patients	n=35 74 (36 – 98) 72.7 (15.7)	n=38 68 (9 – 100) 66.2 (23.4)	n=35 77 (32 – 100) 76.6 (15.5)	n=38 65 (25 – 100) 66.5 (22.1)	n=37 95 (40 – 100) 89.2 (14.8)	n=35 80 (25 – 100) 73.8 (19.3)
Parents of adolescents	n=34 76 (31 – 100) 73.3 (18.4)	n=39 75 (12 – 100) 70.6 (24.6)	n=34 75 (27 – 100) 75.3 (17.8)	n=39 60 (30 – 100) 66.1 (20.9)	n=39 100 (25 – 100) 86.3 (19.9)	n=34 80 (15 – 100) 74.8 (22.8)
ICC[*]	0.6242	0.4956	0.6021	0.5221	0.4362	0.5042
Agreement	Good	Moderate	Good	Moderate	Moderate	Moderate

Cells contain N / median (range) / mean (SD)

^{*} ICC: intraclass correlation coefficient

Table 6
Descriptive Scores of the PedsQL v.4.0 and the SDS for adolescents and children diagnosed with OS

OS							
Patient Reports	13-25 Years Age Group			8-12 Years Age Group			P
	N	Median (Range)	Mean (SD)	N	Median (Range)	Mean (SD)	
SDS Total Scale Score	39	23 (12-42)	23.6 (6.9)	19	22 (13-41)	23.8 (7.5)	0.89
Total Score	33	55.4 (31.5-93.5)	58.4 (17.1)	19	48.9 (30.4-89.1)	52.6 (15.9)	0.24
Physical Health	39	43.8 (0-100)	43.5 (30.3)	19	31.3 (9.4-90.6)	40.5 (28.2)	0.69
Psychosocial Health	33	63.3 (41.7-91.1)	65.9 (13.1)	19	55.0 (35.0-91.7)	59.1 (17.2)	0.064
Emotional Functioning	38	55 (15-100)	54.8 (19.9)	19	60 (10-100)	55.0 (23.7)	0.77
Social Functioning	39	80 (45-100)	78.1 (16.0)	19	70 (35-100)	67.2 (18.9)	0.026
School Functioning	34	65 (30-100)	66.9 (20.7)	19	60 (20-100)	55.1 (26.0)	0.139
AML							
Patient Reports	13-25 Years Age Group			8-12 Years Age Group			P
	N	Median (Range)	Mean (SD)	N	Median (Range)	Mean (SD)	
SDS Total Scale Score	39	23 (12-50)	24.7 (8.8)	28	23.5 (11-42)	24.4 (8.3)	0.83
Total Score	35	73.9 (35.9-97.8)	72.7 (15.7)	24	73.9 (39.1-100)	71.2 (19.2)	0.94
Physical Health	38	68.3 (9.4-100)	66.2 (23.4)	26	68.8 (6.3-100)	63.5 (28.2)	0.88
Psychosocial Health	35	76.7 (31.7-100)	76.6 (15.5)	24	78.3 (38.3-100)	74.4 (16.9)	0.74
Emotional Functioning	38	65 (25-100)	66.5 (22.1)	26	77.5 (15-100)	65.5 (26.1)	0.94
Social Functioning	37	95 (40-100)	89.2 (14.8)	26	87.5 (55-100)	86.2 (12.9)	0.20
School Functioning	35	80 (25-100)	73.8 (19.3)	24	80 (5-100)	73.3 (21.0)	0.96

Table 7
Results of regression models investigating disease, gender, age group, and SDS score as predictors of PedsQL v.4.0 domain scores

	Physical Functioning		Emotional Functioning		Social Functioning		School Functioning	
	β (95% CI)	p	β (95% CI)	p	β (95% CI)	p	β (95% CI)	p
Disease (=OS)	-23.8 (-33.1, -14.5)	<0.001	-13.6 (-21.6, -5.6)	0.001	-14.9 (-20.6, -9.2)	<0.001	-11.6 (-19.5, -3.8)	<0.001
Gender (=male)	-6.3 (-16.0, 3.3)	0.193	-0.5 (-8.8, 7.8)	0.900	-1.1 (-7.0, 4.7)	0.700	-11.7 (-19.7, -3.6)	0.005
Age Group (=adolescent)	0.7 (-9.1, 10.4)	0.894	1.9 (-6.5, 10.3)	0.656	6.6 (0.6, 12.6)	0.030	4.1 (-4.0, 12.3)	0.320
SDS total scale score	-1.4 (-2.0, -0.7)	<0.001	-0.6 (-1.2, -0.1)	0.021	-0.2 (-0.5, 0.2)	0.428	-0.7 (-1.2, -0.2)	0.010

β : parameter estimate; CI: confidence interval