Self-reported global function among adult survivors of childhood lower-extremity bone tumors:

a report from the Childhood Cancer Survivor Study (CCSS)

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Abstract

Introduction—Adult survivors of childhood lower-extremity bone tumors may experience physical and psychosocial late effects that impact physical performance, global function and quality of life. The identification of survivors at greatest risk for poor outcomes will inform potential intervention targets.

Methods—Study participants were selected from the Childhood Cancer Survivor Study (CCSS), a multi-institutional study of childhood cancer survivors. Adult survivors (n=629) of either childhood onset osteosarcoma or Ewing's sarcoma, with a primary tumor location in the lower-extremity were identified and contacted via mail to complete an additional questionnaire. Participants completed the Reintegration into Normal Living Index (RNL) to evaluate global function (maximum score of 22), daily function (maximum score of 16) and self perception (maximum score of 6).

Results—Survivors reported high levels of global function with an adjusted mean overall RNL index score of 20.6 (SE 0.14), mean daily function score of 15.0 (SD 0.10) and mean self perception score of 5.6 (SE 0.05). While female gender and increasing age were associated with lower RNL scores, the magnitude of difference is of questionable clinical significance. Global function was only moderately correlated with physical performance (r=0.56) and QOL (r=0.59).

Discussion—Based upon the RNL index, the vast majority of long-term survivors of childhood lower extremity bone tumors adapt well to their environment.

Implications for cancer survivors—While some long-term survivor of lower-extremity bone tumors may report measurable limitations in physical performance and quality of life, the majority do not report moderate or severe difficulties with social integration.

Keywords

Bone sarcoma; Global function; Physical performance; Quality of life; Childhood cancer survivor

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INTRODUCTION

Significant improvements in surgical interventions and chemotherapeutic regimens for children and young adults with malignant bone tumors have improved 5-year survival rates from 49% in 1984 to 65% in 2005 [1]. However, long-term survivors may have disease and therapy associated late-effects that affect physical and psycho-social well-being. Among children with bone tumors, medical late effects include structural and functional impairments of the affected limb and associated musculoskeletal deficits that limit physical performance. These types of restrictions can interfere with participation in normal daily activities, participation in life roles, and may influence overall quality of life [2,3].

Physical performance limitations, restricted participation in life-roles, and reports of reduced scores on QOL instruments are prevalent in some bone tumor survivors, but not in others. In a report from the Childhood Cancer Survivor Study (CCSS), 37% of bone tumor survivors reported physical limitations, while only 11% reported that health prevented them from attending work or school [4]. In the same cohort, bone tumor survivors scored lower than an age and gender referenced population comparison group on the physical component summary (PCS) of the Medical Outcomes Survey Short Form-36 (SF-36), but higher than an age and gender referenced population comparison group when asked about their current life satisfaction [5].

Wood-Dauphinee defines a construct of global function as reintegration into normal living (RNL), which is defined as "the individual reorganization of physical, psychological, and social characteristics into a harmonious whole so that one can resume well-adjusted living after an incapacitating illness" [6,7]. RNL encompasses global functioning and provides a common end-point for evaluating the association between musculoskeletal impairments and motor performance, and for evaluating the impact of physical performance limitations on participation and perception of quality in expected family and societal roles [8]. Evaluation of the RNL construct among adult survivors of childhood onset lower-extremity bone tumors may help identify those long-term survivors at the greatest risk for physical performance limitations and for reduced capacity to participate in their desired family and societal roles.

PURPOSE

The aims of this report were to describe global function in a cohort of CCSS lower-extremity bone tumor survivors, to evaluate demographic and treatment variables that may predict lower global function, and to explore associations between physical performance, global function, and self-reported QOL. This ancillary analysis supports information presented in an earlier manuscript that documented function and QOL in this cohort of survivors of lower extremity bone tumors [2}.

METHODS

Participants and data collection

Study participants included members of the Childhood Cancer Survivor Study (CCSS). The CCSS, described in detail elsewhere [9], includes over 14,000 five year survivors of childhood cancer diagnosed between 1970-86. The criteria for eligibility for these analyses included a diagnosis of a lower extremity bone tumor, completion of the CCSS baseline questionnaire (available at www.stjude.org/ccss), and willingness to release their cancer and treatment related medical records. All documents for CCSS and for this study were approved by the Human Subject Committees at each of the collaborating institutions.

Global Functioning

Global function, the outcome of interest for these studies, was evaluated by the Reintegration into Normal Living Index (RNL), a tool developed by Wood-Dauphinee and colleagues [7] to determine adjustment to normal living following illness. For this study, we utilized a modified version of the original RNL index developed by Nissen and Newman for evaluation of individuals who had experienced a lower extremity amputation [10]. The eleven items included in the assessment were: (1) I move around my living quarters as I feel is necessary; (2) I move around my community as I feel is necessary; (3) I am able to take trips out of town as I feel is necessary; (4) I am comfortable with how my self-care needs are met; (5) I spend most of my days occupied in a work activity that is necessary or important to me; (6) I am able to participate in recreation hobbies as I want to; (7) I participate in social activities with family, friends, and / or business acquaintances as is necessary or desirable to me; (8) I assume a role in my family which meets my needs and those of other family member; (9) in general, I am comfortable with my personal relationships; (10) in general, I am comfortable with myself when I am in the company of others; and (11) I feel that I can deal with life events as they happen. For each of the eleven items, participants were asked to indicate if they (1) disagreed with the statement, (2) neither agreed nor disagreed with the statement, or (3) agreed with the statement. Maximum scores of 22 overall, 12 on the daily function subscale (first 8 questions), and 6 on the self-perception subscale (last 3 questions) were possible. Persons who indicated disagreement with the statement on the RNL index, who scored in the lowest 10th percentile on the two subscales, and who scored in the lowest 10th percentile on the overall index were classified as being dissatisfied with function in that domain.

Demographic and treatment variables

The demographic and treatment variables of interest were gender, age at the time of survey completion, age at diagnosis, tumor type, tumor location and surgery. The four age groups included younger than 30, 30-34, 35-39, and 40 years or older. The treatment variables considered for comparative analysis were age at diagnosis, tumor type, tumor location, and treatment. Age at diagnosis was determined by subtracting of the date of birth from the date of diagnosis, and then grouped into two categories (12 years or younger and 13 years or older). A cut-off age of 12 years old was selected because it is an approximate marker of emotional maturity [11] and is the age at which significant bone growth is initiated [12]. Tumor types were determined by examining medical records, and included osteosarcoma and Ewing sarcoma. Tumor location was also determined by examining the medical record, and was classified as either above (pelvis or femur) or below (tibia, fibula or other) the knee. Surgical treatment was dichotomized as either amputation or limb sparing based on a review of the surgical record.

Correlations between physical performance, global function, and quality of life

Physical function was measured by having participants complete the Toronto Extremity Salvage Scale (TESS) [13,14], which has been tested in childhood cancer survivors [15]. Quality of life was evaluated with the 41-item Quality-of-Life-Cancer Survivors (QOL-CS), an instrument designed specifically for cancer survivors to evaluate overall quality of life across physical, psychological, social, and spiritual domains [16,17].

Data Analysis

Descriptive statistics for demographic and treatment variables included calculations for frequencies, percents, means, medians, standard errors, and ranges and were compared among participants and non-participants with Chi-squared tests and two sample t-tests. Means and standard errors were calculated for the RNL index, TESS and QOL-CS responses. For each RNL outcome, means and proportions were compared for demographic and treatment variables

in general linear regression models, and then in multiple variable logistic regression models. Pearson correlation coefficients were calculated to evaluate the association between the TESS score, RNL index, and QOL-CS score. SAS version 9.1 (Cary, NC) was used for all analyses.

RESULTS

Participation

We contacted 629 CCSS participants who had a previous diagnosis of a lower extremity bone tumor when younger than 21 years of age. Among those contacted, 528 (84%) returned their mailed questionnaires. Non-participants included 75 (12%) individuals who were lost to follow-up, and 26 (4%) who declined participation. Compared to participants, non-participants were similar with regard to gender, age at contact, tumor type or treatment. Non-participants were somewhat younger at cancer diagnosis (12.8 years vs. 13.5 years) and less likely to have a tumor location in the pelvis (3% vs. 9%).

Characteristics of the study participants

The characteristics of the study participants are shown in Table I. Osteosarcoma accounted for 79.9% of cases, the most common tumor location was the distal femur (42.8%) and 60% of cases had undergone amputation without radiation. On average, participants were 13.5 years old (SD 3.8) at cancer diagnosis, had survived 20.8 years (SD 4.3) since diagnosis and were 34.8 years old (SD 5.8) when assessed for global function with the RNL index. TESS and QOL-CS have been reported previously, but are shown in Table I for reference [18].

Global function

The overall score on the RNL index and both the daily living and self-perception subscales are shown in Table II. Adjusted mean values were generally high and fall within the range of population values that are associated with mild impairment for overall RNL index (mean=20.6, 93.6% of maximum score), daily living subscale (mean=15.0, 88.2% of maximum score), and self-perception subscale (mean=5.6, 93.3% of maximum score). No significant predictors of a lower mean score among demographic and treatment variables (including surgery amputation vs. limb-sparing surgery) were revealed by multiple variable analysis.

Characteristics of participants with moderate impairment

The cut-off points for the lowest 10th percentile were high for each of the three scales: 17/22 on the overall RNL index, 12/16 on the daily functioning subscale, and 4/6 on the self-perception subscale fall within the defined range of moderate impairment. There were no significant demographic or treatment variables associated with global functioning as reported on the RNL index. However, the proportion of females reporting difficulty on any item on these scales was slightly, but not significantly, higher than the proportion of males with difficulty. The proportion of those in the lowest 10th percentile on the overall RNL index increased by age group (p-value <0.05 for trend).

Physical function and quality of life correlates

The correlations between the RNL index and subscale scores with the TESS and QOL-CS scores ranged from 0.13 to 0.62 (Table III). Moderate correlations were present between the overall RNL index and TESS scores (0.56), total QOL-CS scores (0.59), and QOL-CS psychological scores (0.50). Overall, the QOL-CS social score had the strongest correlation with the RNL index and its subcategories and accounted for 38% of the total variance in the RNL responses. Greater than 60% of the variance in QOL scores remains unexplained by the RNL functioning index.

DISCUSSION

This large multi-institution evaluation of young adult survivors of childhood lower extremity bone tumors indicates that, on average, children who survive bone tumors adapt well to their environment and report high levels of global function. Study participants reported higher scores on the RNL index than other studies that have used the same measure.

In a matched case-control study of lower extremity sarcoma survivors by Davis and colleagues, those who had amputation (n=12) and a limb sparing surgery (n=24) were compared using the RNL measure with those with a limb-sparing surgery scoring higher than those undergoing an amputation[19]. In the present study, survivors with amputation and those with limb sparing procedures did not report RNL mean values that corresponded with the higher scores reported by the limb-sparing surgery group in the Davis' study. Participants in our study were further from diagnosis (249 months vs. 30 months) and did not include patients diagnosed as adults, both factors that may explain the difference in results between the two studies. Nissen and colleagues examined another group of 42 persons following amputation [10]. On average, their participants were 68 years old and 8 years post-amputation, who reported the most difficulty with recreational activities. In both studies, the authors concluded that amputations in the evaluated populations and timeframes resulted in impaired participation and reintegration into normal living. Tunn et al described another group of 87 bone tumor survivors 12 to 73 years of age at diagnosis. This study included survivors who had limb-sparing procedures to treat upper or lower bone lesions, a median of 5.8 years from surgery [20]. These survivors reported RNL scores similar to the scores reported by participants in our study, lending further support to the positive news that successful integration into life roles is likely after invasive treatment for extremity tumors. Finally, Schreiber et al. evaluated the association between scores on the Musculoskeletal Tumor Society Rating Scale, an impairment measure, scores on the TESS, an activity measure, scores on the RNL, a participation measure, and Health Related Quality of Life (HRQOL) [21] among 100 extremity sarcoma survivors, 16-55 years of age. In their study, participation restrictions (RNL) had the largest impact on HRQOL. Our investigation also reports a high degree of correlation between scores on the RNL and QOL.

When compared with a group of individuals with chronic illnesses such as spinal cord injury or stroke (illness not involving amputation or the diagnosis of lower extremity sarcoma), our study survivors also appear to score higher on the RNL index. Scores from three studies ranged from 85.8 to 86.5 (vs. 103) [22-24]. Predictors of poor RNL in these populations included pain, older age, depression, lack of independence, and markers of poor interpersonal relationships. The younger age at both onset of disability and at interview, longer time since treatment and lack of medical co-morbidities of participants in our cohort may account for the higher daily living satisfaction scores.

The results of our analyses should be considered in the context of some study limitations. First, this is an observational evaluation of global function among a group of cancer survivors. We did not collect information from a group of young adults without a history of cancer for comparison; however, the RNL index is designed for application in an impaired population. Healthy young adults are theoretically without impairment and should achieve the maximum, or best score, on this questionnaire. We were able to compare our results to previous studies that used the same assessment tool. Second, most participants scored relatively high on the RNL index which led us to conclude that survivors do relatively well; however, it is also possible that the questionnaire was not sensitive enough to distinguish between those with and without extremely poor outcomes. Finally, the cross-sectional design of this investigation precluded characterization of changes in global function over time among this cohort of adult survivors of childhood cancer. Reintegration issues relevant at the time of diagnosis may have been resolved in our survivor group, all of who were temporally removed from their original

diagnosis by a minimum 13 years. Therefore, we were unable to evaluate early impairments relating to integration.

CONCLUSIONS

This large study of global function revealed positive outcomes for most adult survivors of childhood onset lower-extremity bone tumors. These survivors reported few physical limitations and only mild impairment of global functioning. However, from our study and others, it appears that global function and re-integration into normal living does play a role in QOL. These outcomes are quite remarkable given that over 60% of the survivors in this study had an amputation as part of treatment for their childhood onset lower-extremity tumor. It is unclear, however, if the reports of reintegration among this cohort reflect fairly normal global function or adapted expectations of function, that is, a "response shift." [25]. Only prolonged, prospective studies among more recently diagnosed patients will help determine if there are impairments in reintegration that occur early following a lower extremity bone tumor.

Acknowledgements

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Table I
Characteristics of the study participants

	N	(%)
Gender		
Female	270	(51.1)
Male	258	(48.9)
Tumor type		
Osteosarcoma	422	(79.9)
Ewing's sarcoma	106	(20.1)
Tumor location		
Pelvis	46	(8.7)
Distal femur	226	(42.8)
Other femoral sites	63	(11.9)
Proximal tibia	98	(18.6)
Other tibial sites	46	(8.7)
Fibula	39	(7.4)
Other non-specific, non-pelvic sites	10	(1.9)
Treatment		
Amputation		
Amputation only	317	(60.0)
Amputation & radiation	19	(3.6)
Limb Sparing		
Radiation only	32	(6.1)
Arthrodesis & radiation	1	(0.2)
Endoprosthesis & radiation	7	(1.3)
Unspecified limb surgery & radiation	40	(7.6)
Arthrodesis & radiation	10	(1.9)
Endoprosthesis & radiation	49	(9.3)
Unspecified limb surgery & radiation	53	(10.0)
Age at diagnosis		
Mean (SD)	13.5	(3.8)
Median (Range)	14	(1-20)
Age at questionnaire		
Mean (SD)	34.8	(5.8)
Median (Range)	35.0	(19-49)
Years from diagnosis to questionnaire completion		
Mean (SD)	20.8	(4.3)
Median (Range)	21.0	(13-30)
Physical performance (TESS score)		
Mean (SD)	85.4	(14.3)
Median (Range)		(17.2-100)
Quality of Life - CS overall		
Mean (SD)	6.9	(1.4)
Median (Range)	7.1	(1.4-9.7)

	N	(%)
Quality of Life - psychological		
Mean (SD)	6.4	(1.6)
Median (Range)	6.8	(0.9-9.9)
Quality of Life - physical		
Mean (SD)	7.9	(1.6)
Median (Range)	8.2	(1-10)
Quality of Life - social		
Mean (SD)	7.4	(1.9)
Median (Range)	7.9	(0.9-10)
Quality of Life - spiritual		
Mean (SD)	6.0	(2.0)
Median (Range)	6.1	(0.1-10)

Table II

Multiple variable adjusted means and standard deviations of the RNL Index, Daily Functioning Subscale, and Self Perception Subscale

	Overall Range (2-22)			Daily Function Range (0-16)			Self Perception Range (0-6)		
	Mean	SE	p-value	Mean	SE	p-value	Mean	SE	p-value
Total	20.6	0.14	-	15.0	0.10	-	5.6	0.05	-
Gender									
Male	20.9	0.23	0.08	15.2	0.17	0.07	5.6	0.09	0.41
Female	20.4	0.22		14.8	0.17		5.5	0.08	
Age at diagnosis									
<=12 years	20.7	0.27	0.65	15.1	0.20	0.61	5.6	0.10	0.84
> 12 years	20.5	0.23		15.0	0.18		5.6	0.09	
Age at questionnaire									
<30 years	20.9	0.34		15.3	0.25		5.6	0.13	
30-34 years	20.6	0.30	0.48	14.9	0.22	0.18	5.7	0.12	0.46
35-39 years	20.6	0.28	0.51	14.9	0.21	0.32	5.6	0.11	0.81
40+ years	20.5	0.34	0.44	14.9	0.25	0.36	5.5	0.13	0.82
Tumor type									
Osteosarcoma	20.7	0.19	0.73	15.1	0.15	0.66	5.6	0.08	0.98
Ewing's sarcoma	20.6	0.33		15.0	0.24		5.6	0.13	
Tumor location									
Tibia, fibula, other	20.8	0.25	0.28	15.2	0.19	0.28	5.6	0.10	0.50
Pelvis or femur	20.5	0.20		14.9	0.15		5.5	0.08	
Treatment									
Limb Sparing	20.7	0.24	0.81	15.0	0.18	0.90	5.6	0.09	0.71
Amputation	20.6	0.24		15.0	0.18		5.6	0.09	

Pearson Correlation Coefficients

Table III

	RNL index overall	RNL daily functioning	RNL self perception	TESS Score	QOL-CS Score	QOL-CS psychological score	QOL-CS physical score	QOL-CS social score	QOL-CS spiritual score
RNL index overall	1.00	0.94	0.75	0.56	0.59	0.50	0.45	0.62	0.19
RNL daily functioning		1.00	0.49	0.54	0.48	0.40	0.39	0.53	0.13
RNL self perception			1.00	0.38	0.58	0.53	0.40	0.57	0.23