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Patient-Reported Functional and Quality of Life Outcomes in a Large Cohort of Long-Term Survivors of Ewing Sarcoma

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Abstract

Background—Little data exist regarding long-term functional and quality of life (QOL) outcomes for survivors of Ewing sarcoma (ES). Specifically, there are few reports assessing the impact of patient characteristics and local therapy modalities on patient-reported outcomes (PRO).

Procedure—Long-term survivors of ES treated between 1977 and 2009 completed self-assessed functional and QOL surveys, using the Toronto Extremity Salvage Score (TESS) and PEDSQL 4.0 generic core instruments, respectively. Statistical analyses were performed to correlate these outcomes to clinical presentations and treatment regimens.

Results—Subjects (n = 74) with a mean duration from diagnosis of 17.8 years completed the survey. Mean TESS and PEDSQL total scores for the entire cohort were 93.0 ± 10.3 and 81.6 ± 18.0 , respectively. No significant differences were appreciated between adult and pediatric patients, although increasing age was associated with lower functional scores ($P=0.04$). Mean PEDSQL total scores were significantly lower for female patients (74.6 ± 19.7) compared to males (85.7 ± 15.7) ($P=0.01$). Mild to moderate disability was reported by 32% of respondents and was associated with lower TESS and PEDSQL scores. Local control modality did not significantly affect functional and QOL scores. Patients with pelvic tumors had significantly lower TESS scores compared to those with nonpelvic tumors ($P=0.04$), especially amongst patients treated with both surgery and radiation.

Conclusions—Although many survivors of ES report excellent functional and QOL outcomes, a significant number report long-term disability and impairments. Older patients, females, and those with pelvic primary tumors appear at the greatest risk for long-term decrements and may benefit from early therapeutic interventions.

Keywords

adult; Ewing sarcoma; patient outcome assessment; pediatrics; quality of life; radiotherapy; surgery; survivors

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Introduction

Ewing sarcoma (ES) is the second most common bone tumor in pediatric and young adult patients, with approximately 200 cases diagnosed in the United States each year.[1] Patients with newly diagnosed ES are treated with an intense regimen of multiple chemotherapeutic agents, in addition to local therapy directed at the primary tumor. Local therapy can consist of surgery, radiation, or a combination of both modalities and is determined by the location of the tumor, as well as the opinions of the treating physicians. Historically, the best rates of local control (92–95%) have been observed when surgery is utilized for local therapy.[2] However, in locations where wide resection is more challenging, such as the spine or the pelvis, the benefit of surgery is less clear.[3,4]

Cureratesfor non-metastaticEShave improved significantly with the use of aggressive systemic and local therapies, evidenced by a recently published trial demonstrating 5-year overall survival of 83%.[5] As treatment strategies continue to improve disease-specific outcomes, additional focus has shifted to assessing treatment related late effects in the growing population of long-term survivors.

Improved understanding of patient-reported outcomes (PRO) could be useful to help guide clinicians caring for patients with ES. If patients at higher risk of long-term functional or quality of life (QOL) decrements can be prospectively identified at diagnosis, the early use prophylactic interventions may be able to improve these outcomes. Similarly, PRO can provide additional data and guidance for treating clinicians when deciding the optimal local control strategy for patients with ES. This study was undertaken to assess patient-reported functional and QOL outcomes in a large, single institutional cohort consisting exclusively of ES survivors.

Methods

Patients and Treatment

All surviving patients treated for pathologically verified ES at Mayo Clinic between 1977 and 2009 were eligible for enrollment. Patient records were reviewed to determine clinical characteristics including sex, age at diagnosis, date of diagnosis, location of primary tumor, size of the primary tumor, presence of metastatic disease, local tumor therapy, and any subsequent relapse. The chemotherapeutic agents used, duration of chemotherapy, and modality of local control were determined at the discretion of the treating oncologists. Relapse was defined as either pathologic or radiographic confirmation of ES that had previously completely responded to initial treatments. Patients were listed as having metastatic disease if they had confirmed distant disease at the time of their initial diagnosis.

Functional and QOL Assessment

Functional outcomes were measured using the Toronto Extremity Salvage Score (TESS).[6] A scaled score, ranging from 0 to 100 (higher score indicates better function), was calculated based on the patient's responses to questions about their ability to perform a variety of activities. Unique TESS surveys were used for patient with tumors located in the

upper (31 questions) or lower (32 questions) extremity. Patients with primary tumors located in the head and neck, chest wall, cervical spine, or thoracic spine completed the upper extremity survey. Patients with pelvic, abdominal, or lumbar spine tumors completed the lower extremity form. Pelvic tumors were defined as any tumor involving the pelvic girdle, sacrum, coccyx, or soft tissues contained within these boundaries.

QOL was evaluated with the age-appropriate PEDSQL 4.0 generic core survey. This 23-item questionnaire assesses QOL in four domains (physical, emotional, social, school/work functioning) and has been validated in both healthy and oncology patient populations.[7–9] PEDSQL total scores were tabulated as a weighted average of the four individual domains. Scores were scaled based on patient responses with a possible range of 0–100, with higher scores once again indicating better QOL.

Quantitative and qualitative inquiries derived from the Childhood Cancer Survivor Study public domain forms that related to disability, symptoms, QOL, and educational/occupational outcomes were included in the self-assessments.[10]

All study documents, consent forms, and survey materials were reviewed and approved by the Mayo Clinic Institutional Review Board. Informed consent was provided for all individual participants included in the study. For patients under the age of 18 years, a parent/guardian provided assent for participation, and the child completed the survey forms themselves, with assistance from an adult (if required). Age and tumor location specific surveys were mailed to eligible patients by the Mayo Clinic Survey Research Center. After two mailings, non-responders were contacted by phone on two separate occasions.

Statistics

Patient demographic and tumor characteristic data are reported as number (percent) or as mean (standard deviation or range), as appropriate. Logistic regression analysis was performed to compare the characteristics of respondents and non-respondents in order to assess any potential biases in completion of the survey. The correlation of TESS and PEDSQL scores was examined using a Pearson correlation coefficient. Comparisons of TESS and PEDSQL scores according to patient, tumor, and treatment characteristics were performed using a two-sample *t*-test for binary variables and analysis of variance (ANOVA) for variables with more than two levels. QOL outcomes according to patient-reported disability, symptoms, and treatment complications were assessed with a two-sample *t*-test or ANOVA, as appropriate. TESS and PEDSQL total scores were categorized as the lowest 25th percentile versus the upper 75th percent of the scores. For TESS this represented a score of <90 versus ≥90 and for PEDSQL total this meant a score of <72 versus ≥72. The association of patient and tumor data with the odds for a QOL score in the lowest 25th percentile was assessed using logistic regression, reporting the results as an odds ratio (OR) and 95% confidence interval (CI). The alpha level was set at 0.05 for statistical significance.

Results

Patient Characteristics

Of 131 living patients that were contacted to participate in the survey, 74 completed all required materials yielding a response rate of 56%. The characteristics of the patients included for this study are listed in Table I. Comparative analyses showed that those responding to the survey were statistically older at the time of diagnosis and had shorter interval from diagnosis to the date of survey than those who did not participate, otherwise the two groups were similar. Nearly all respondents (96%) were > 18 years of age at the time of assessment; however, approximately half were <18 years at the time of initial diagnosis. Mean interval from time of diagnosis to survey completion was 17.8 years, with 24 (32%) patients exceeding 20 years duration. Limb-sparing procedures were common; only two (6%) patients with extremity tumors required an amputation for primary tumor control. Although seven patients experienced relapse following their initial treatment, only one participant indicated ongoing treatment for ES at the time of survey completion.

Function and Quality of Life

TESS and PEDSQL scores for all survey respondents are listed in Table II. Mean TESS score for the entire surveyed population was 93.0 ± 10.3 . Those treated as pediatric patients had a higher mean TESS score than those treated as adults (94.9 vs. 91.0, $P = 0.1$). Female respondents had a lower mean TESS score compared to males (91.2 vs. 94.1); however, this did not reach statistical significance ($P = 0.24$).

The mean PEDSQL total score for the entire patient population was 81.6 ± 18 . Among the PEDSQL domains, mean scores were highest for social functioning (89.9) and lowest for physical functioning (74.7). Similar to the TESS scores, those treated as pediatric patients had higher PEDSQL total scores compared to those treated as adults (83.8 vs. 79.3, $P = 0.29$). Male respondents had significantly higher PEDSQL total scores compared to females with mean values of 85.7 vs. 74.6 ($P = 0.01$), respectively. This difference was consistent in all PEDSQL domains, with significant differences between male and female patients in the physical (79.8 vs. 66.0, $P = 0.02$) and social (93.6 vs. 83.7, $P = 0.01$) domains.

TESS and PEDSQL total scores were strongly correlated with a Pearson correlation coefficient of 0.82 (Fig. 1). Among the PEDSQL individual domains, TESS most strongly correlated with the physical score (Pearson = 0.81) and demonstrated the least correlation with the emotional score (Pearson = 0.67).

Univariate logistic regression analysis was performed to identify risk factors associated with TESS and PEDSQL total scores in the lowest quartile (Table III). Age of greater than 18 at diagnosis was significantly associated with a TESS score below the 25th percentile (OR 3.39, $P = 0.03$). When analyzed as continuous variables (per 10 year increments) both increasing age at diagnosis (OR 1.56, $P = 0.04$) and increasing age at survey completion (1.52, $P = 0.02$) were associated with functional scores in the lowest quartile. Among all variables analyzed, only female gender (OR 3.27, $P = 0.03$) was correlated with PEDSQL total scores below the 25th percentile.

Impact of Disability, Symptoms, and Treatment Complications

Qualitative patient self-assessments of outcomes/symptoms are detailed in Table IV. The majority of survey patients (66.7%) rated themselves as “Not at All disabled”, whereas 22.2% and 11.1% indicated they were “mildly” or “moderately” disabled, respectively. Both TESS and PEDSQL scores were significantly lower among study participants with self-reported disability ($P < 0.001$). More than 20% of patients reported symptoms of pain, stiffness, fatigue, and weakness. Functional and QOL scores were significantly lower ($P < 0.001$) among those reporting these symptoms. Although 50% of respondents reported that their current health limited strenuous activity, 34 (46%) patients indicated participation in exercise at least three times in the most recent week. However, 23 (31%) patients stated that they did not exercise at least once in the past 7 days. Use of prescription pain medications or prescription muscle relaxants was reported by 13 (18.1%) and six (8.3%) of survey respondents, respectively. Patients taking prescription pain medications, but not muscle relaxants, had statistically lower TESS and PEDSQL scores ($P = 0.001$). Additional surgeries related to complications or relapsed ES were necessary in 13 (17.6%) patients and these included four amputations. Mean TESS scores were significantly lower amongst those requiring the additional surgeries compared to the remainder of the responding cohort (87.7 vs. 94.1, $P = 0.01$).

Education and Employment Outcomes

College or post-graduate degrees were obtained by 32 (50.8%) of the 63 patients who were at least 25 years of age at the time of survey and reported an educational status. All respondents had received at least a high school diploma and the three surveyed patients under 18 were enrolled full time in school. Current full time or part time employment were listed for 43 (58%) and five (7%) patients, respectively. Of the remaining respondents, 11 (15%) indicated they were currently students and six (8%) were reported as retired. Four (5%) patients indicated that they were currently not working due to disability.

Impact of Tumor Location and Local Therapy

Table II shows mean TESS and PEDSQL scores for survey respondents according to the location of their primary tumor. There was no significant difference in TESS scores when comparing upper extremity, lower extremity, pelvis, and other primary tumor locations ($P = 0.12$). However, Figure 2A demonstrates that mean TESS scores were significantly lower ($P = 0.04$) for patients with pelvic primaries (mean 87.8 ± 13.9) compared to those with nonpelvic tumors (mean 94.2 ± 8.9). Locations of the primary tumor did affect PEDSQL scores. PEDSQL total score were moderately decreased for pelvic tumors compared to those with nonpelvic tumors, with mean values of 82.9 and 75.8 ($P = 0.19$), respectively.

Functional and QOL scores according to local therapy modality are shown in Figure 2B. Mean TESS scores were not significantly different for patients treated with surgery (Sx), radiation (RT), or surgery + radiation (Sx+RT) with values of 92.1, 95.8, and 92.2 ($P = 0.42$), respectively. Mean PEDSQL total and subset scores were also not affected by primary tumor control modality, with statistically similar scores for each local therapy. Patients with pelvic tumors who received both Sx and RT ($n = 3$) had lower mean TESS (77.0 ± 18.0) and PEDSQL total (54.1 ± 15.2) scores compared to patients receiving Sx ($n = 5$, TESS 87.4

± 16.5 PEDSQL 76.7 ± 25.6) or RT alone ($n = 6$, TESS 93.6 ± 7.0 PEDSQL 85.9 ± 11.6). Those with nonpelvic tumors had no significant difference in function or QOL measures based upon local control modality.

Discussion

This study represents an important evaluation of long-term functional and QOL outcomes in a large cohort consisting exclusively of ES patients. With a mean follow-up of more than 17 years from diagnosis, these data provide insight into the lives ES survivors lead following the completion of treatment. With dedicated cooperative group research, 5-year survival for patients with ES has increased from 60% in the 1970s (IESS-1) to 83% on the most recent study of interval-compressed chemotherapy.[5,11] With these gains in treatment outcomes, additional research has focused on the late effects of treatments.[12]

The TESS is a widely utilized and well-validated tool for analyzing patient-assessed, long-term functional outcomes among those treated for bone and soft tissue sarcomas.[13,14] We elected to utilize the PEDSQL 4.0 generic core form in this study, as it provided comparable, age-specific forms that could be administered to heterogeneous patient population spanning from age 12 to 83 years. A previous study looking at survivors of pediatric pelvic and lower extremity sarcomas showed that decreased functional and QOL metrics are strongly correlated with self-rated disability, educational attainment, and overall health.[15] Our data revealed that functional and QOL measures were strongly correlated with one another and lower scores in each domain were associated with self-appraised disability. Respondents who reported use of prescription pain medications, decreased frequency of exercise, the presence of symptoms, and receipt of additional surgery for treatment complications had significantly lower functional and QOL scores. These findings highlight some of the significant long-term implications associated with self-reported deficits on functionality and QOL for not only these patients, but also their families and society.

In our series, TESS scores in the bottom quartile were seen with both increasing age at diagnosis and current age at survey completion. It is difficult to discern whether patients who are diagnosed and treated at an older age are truly at risk for poorer functional outcomes, as age at diagnosis and age at time of survey are strongly correlated. Loss of physical function is common with the normal process of aging, as demonstrated in a study of healthy, unoperated adults that revealed increasing age was correlated with lower TESS scores.[16] However, it must also be considered that patients undergoing treatment for ES at a younger age are better able to accommodate psychologically and physically to their treatment-related changes and thus report an elevated self-perception of function. Obtaining baseline surveys prior to treatment would certainly help provide answers to this question.

Female gender has been shown in previous studies of childhood cancer survivors, including those with bone and soft tissue sarcomas, to be associated with lower QOL scores.[15,17,18] Our data demonstrated that female respondents had a mean PEDSQL total score that was more than 11 points lower than males. This difference was not only statistically significant, but also exceeds the 4.4 point threshold that has been established for clinical significance with this instrument.[19] Given that female patients scored lower in all domains of the

PEDSQL assessment, it is likely that this gender difference is multi-factorial. Some have hypothesized that these differences are simply related to females being more willing to report symptoms.[20] It also may be that factors not assessed in our study, such as fertility, income, and marriage, may contribute to QOL difference. Nevertheless, these data demonstrate that female ES patients are at the increased risk for lower QOL scores and may benefit from additional interventions.

When specifically analyzing long-term survivors of bone and soft tissue sarcomas, numerous studies have demonstrated the long-term functional and QOL outcomes.[15,21] In these primarily pediatric populations, the majority of subjects were those treated for osteosarcoma (OS), with relatively few ES patients.[22] As opposed to OS, where surgical resection predominates, curative treatment for patients with ES can involve either surgery, primary radiation, or a combination of both treatment techniques. To date, there is no definitive data suggesting superiority in oncologic outcomes among these local therapy modalities and this question is not likely to be directly addressed in a randomized, controlled manner. Additionally, there are little published PRO data relating to various treatment strategies in ES. One study published PRO outcomes for 528 patients with pelvic and lower extremities from the CCSS, including 106 with ES. This study did not specifically address the impact of local therapy, but did show that patients with pelvic tumors and those receiving pelvic irradiation had decreased QOL, but not TESS, scores. In our study, mean functional scores were significantly lower in the pelvic tumor population, whereas QOL scores were not different. Local therapy modality did not have any influence on TESS or PEDSQL score in this patient population. Further research is certainly warranted with regard to ES patients with pelvic tumors to identify strategies for improving functional/ QOL outcomes, without compromising our ability to cure.

The strength of this study is the ability to analyze a patient population consisting solely of ES survivors treated at a single institution. The ability to correlate outcomes with accurate treatment records helps us understand the impact of various treatment strategies on these patients' daily lives. These data also benefit from robust long-term follow-up, providing insight into the impacts of treatment well after its completion. Despite the impressive number of participants on this study relative to others in the literature, the sample size does limit advanced statistical analyses and discernment of subtle differences that may exist. In addition, it is difficult to assess the impact of advances in chemotherapy regimens, radiation delivery, imaging capabilities, and surgical technique over the course of 30 years on these findings. A final limitation to this research is that TESS and PEDSQL results are only recorded as a single occurrence. It would be useful to have each survey completed at varying time points, including prior to treatment, to understand the temporal dynamics of PRO.

This study reveals that the majority of patients undergoing definitive treatment for ES report excellent long-term functional and QOL outcomes. When looking at the impact of local therapy, all accepted modalities (S, RT, and S+RT) yield similar PRO. Incorporation of functional and QOL outcomes into current or future cooperative group trials would provide additional data from patients treated across the country to verify and enhance the findings of this study. Older patients, females, and those pelvic primary tumors were identified as being at risk for decrements in PRO. Additional study investigating strategies such as early,

sustained interaction with physical therapy and comprehensive cancer survivorship counseling for these patients are warranted to determine if they can improve long-term outcomes.

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References

1. Esiashvili N, Goodman M, Marcus RB Jr. Changes in incidence and survival of Ewing sarcoma patients over the past 3 decades: Surveillance epidemiology and end results data. *J Pediatr Hematol Oncol.* 2008; 30:425–430. [PubMed: 18525458]
2. Schuck A, Ahrens S, Paulussen M, Kuhlen M, Konemann S, Rube C, Winkelmann W, Kotz R, Dunst J, Willich N, Jurgens H. Local therapy in localized Ewing tumors: Results of 1058 patients treated in the CESS 81, CESS 86, and EICESS 92 trials. *Int J Radiat Oncol Biol Phys.* 2003; 55:168–177. [PubMed: 12504050]
3. Yock TI, Krailo M, Fryer CJ, Donaldson SS, Miser JS, Chen Z, Bernstein M, Laurie F, Gebhardt MC, Grier HE, Tarbell NJ. Local control in pelvic Ewing sarcoma: Analysis from INT-0091—a report from the Children’s Oncology Group. *J Clin Oncol.* 2006; 24:3838–3843. [PubMed: 16921035]
4. Vogin G, Helfre S, Glorion C, Mosseri V, Mascard E, Oberlin O, Gaspar N. Local control and sequelae in localised Ewing tumours of the spine: A French retrospective study. *Eur J Cancer.* 2013; 49:1314–1323. [PubMed: 23402991]
5. Womer RB, West DC, Krailo MD, Dickman PS, Pawel BR, Grier HE, Marcus K, Sailer S, Healey JH, Dormans JP, Weiss AR. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: A report from the Children’s Oncology Group. *J Clin Oncol.* 2012; 30:4148–4154. [PubMed: 23091096]
6. Davis AM, Wright JG, Williams JI, Bombardier C, Griffin A, Bell RS. Development of a measure of physical function for patients with bone and soft tissue sarcoma. *Qual Life Res.* 1996; 5:508–516. [PubMed: 8973131]
7. Varni JW, Burwinkle TM, Katz ER, Meeske K, Dickinson P. The PedsQL in pediatric cancer: Reliability and validity of the pediatric quality of life inventory generic core scales, multidimensional fatigue scale, and cancer module. *Cancer.* 2002; 94:2090–2106. [PubMed: 11932914]
8. Varni JW, Limbers CA. The PedsQL 4.0 generic core scales young adult version: Feasibility, reliability and validity in a university student population *J Health Psychol.* 2009; 14:611–622. [PubMed: 19383661]
9. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: Reliability and validity of the pediatric quality of life inventory version 4.0 generic core scales in healthy and patient populations *Med Care.* 2001; 39:800–812. [PubMed: 11468499]
10. [September 23, 2014] The Childhood Cancer Survivor Study. 09/23 <https://ccss.stjude.org/documents/original-cohort-questionnaires>
11. Nesbit ME Jr, Gehan EA, Burgert EO Jr, Vietti TJ, Cangir A, Tefft M, Evans R, Thomas P, Askin FB, Kissane JM, Pritchard DJ, Herrmann J, Neff J, Makley JT, Gilula L. Multimodal therapy for the management of primary, nonmetastatic Ewing’s sarcoma of bone: A long-term follow-up of the First Intergroup study. *J Clin Oncol.* 1990; 8:1664–1674. [PubMed: 2213103]
12. Ginsberg JP, Goodman P, Leisenring W, Ness KK, Meyers PA, Wolden SL, Smith SM, Stovall M, Hammond S, Robison LL, Oeffinger KC. Long-term survivors of childhood Ewing sarcoma:

Report from the childhood cancer survivor study. *J Natl Cancer Inst.* 2010; 102:1272–1283. [PubMed: 20656964]

13. Davis AM, O'Sullivan B, Turcotte R, Bell R, Catton C, Chabot P, Wunder J, Hammond A, Benk V, Kandel R, Goddard K, Freeman C, Sadura A, Zee B, Day A, Tu D, Pater J. Late radiation morbidity following randomization to preoperative versus postoperative radiotherapy in extremity soft tissue sarcoma. *Radiother Oncol.* 2005; 75:48–53. [PubMed: 15948265]
14. Davis AM, Devlin M, Griffin AM, Wunder JS, Bell RS. Functional outcome in amputation versus limb sparing of patients with lower extremity sarcoma: A matched case-control study. *Arch Phys Med Rehabil.* 1999; 80:615–618. [PubMed: 10378484]
15. Nagarajan R, Clohisy DR, Neglia JP, Yasui Y, Mitby PA, Sklar C, Finklestein JZ, Greenberg M, Reaman GH, Zeltzer L, Robison LL. Function and quality-of-life of survivors of pelvic and lower extremity osteosarcoma and Ewing's sarcoma: The Childhood Cancer Survivor Study. *Br J Cancer.* 2004; 91:1858–1865. [PubMed: 15534610]
16. Clayer M, Doyle S, Sangha N, Grimer R. The toronto extremity salvage score in unoperated controls: An age, gender, and country comparison. *Sarcoma.* 2012; 2012:717213. [PubMed: 23028240]
17. Zeltzer LK, Recklitis C, Buchbinder D, Zebrack B, Casillas J, Tsao JC, Lu Q, Krull K. Psychological status in childhood cancer survivors: A report from the Childhood Cancer Survivor Study. *J Clin Oncol.* 2009; 27:2396–2404. [PubMed: 19255309]
18. Zeltzer LK, Lu Q, Leisenring W, Tsao JC, Recklitis C, Armstrong G, Mertens AC, Robison LL, Ness KK. Psychosocial outcomes and health-related quality of life in adult childhood cancer survivors: A report from the childhood cancer survivor study. *Cancer Epidemiol Biomarkers Prev.* 2008; 17:435–446. [PubMed: 18268128]
19. Varni JW, Limbers C, Burwinkle TM. Literature review: Health-related quality of life measurement in pediatric oncology: Hearing the voices of the children. *J Pediatr Psychol.* 2007; 32:1151–1163. [PubMed: 17347186]
20. Langeveld NE, Grootenhuys MA, Voute PA, de Haan RJ, van den Bos C. Quality of life, self-esteem and worries in young adult survivors of childhood cancer. *Psychooncology.* 2004; 13:867–881. [PubMed: 15386796]
21. Novakovic B, Fears TR, Horowitz ME, Tucker MA, Wexler LH. Late effects of therapy in survivors of Ewing's sarcoma family tumors. *J Pediatr Hematol Oncol.* 1997; 19:220–225. [PubMed: 9201144]
22. Aksnes LH, Bauer HC, Jebsen NL, Folleras G, Allert C, Haugen GS, Hall KS. Limb-sparing surgery preserves more function than amputation: A Scandinavian sarcoma group study of 118 patients. *J Bone Joint Surg Br.* 2008; 90:786–794. [PubMed: 18539673]

Abbreviations

CI	confidence interval
ES	Ewing sarcoma
OR	odds ratio
OS	osteosarcoma
PRO	patient-reported outcomes
QOL	quality of life
RT	radiation
Sx	surgery
TESS	Toronto Extremity Salvage Score

Fig. 1. Dot plot of individual patient TESS and PEDSQL total scores. R-value represents Pearson correlation coefficient.

Fig. 2. Mean TESS and PEDSQL scores according to (A) primary tumor location and (B) local control modality. Bars represent mean scores for each survey with standard deviation bars. *Statistically significant difference between groups ($P < 0.05$).

Table I
Patient Characteristics

Characteristic	Respondents (n=74)	Non-respondents (n=5)
	Value (%)	Value (%)
Age at response, mean (range) (year) ^a	39.3 (12.2–83.8)	37.7 (14.7–61.1)
<18 years	3 (4)	4 (7)
>18 years	71 (96)	53 (93)
Age at diagnosis, mean (range) (year)	21.5 (3.5–54.3)	15.4 (0.6–44.6) *
<18 years	38 (51)	39 (68)
>18 years	36 (49)	18 (32)
Years from diagnosis to response, mean (range) ^a	17.8 (4.3–36.8)	22.3 (5.2–37.8) *
Sex		
Female	28 (38)	24 (42)
Male	46 (62)	33 (58)
Location of primary tumor		
Lower extremity	26 (35)	16 (28)
Upper extremity	10 (14)	7 (12)
Pelvis	14 (19)	9 (16)
Other	24 (32)	25 (44)
Origin of tumor		
Soft tissue	26 (35)	16 (28)
Bone	48 (65)	41 (72)
Local therapy		
Surgery	34 (46)	29 (51)
Radiation therapy	18 (24)	10 (17)
Surgery plus radiation therapy	22 (30)	18 (32)
Metastatic disease at diagnosis		
Yes	10 (14)	10 (18)
No	64 (86)	47 (82)
Any relapse		
Yes	7 (9)	1 (2)
No	67 (91)	56 (98)

^aFor non-respondents, time was calculated using median response date from respondents.

* Statistically significant difference between groups ($P < 0.05$).

Functional and Quality of Life Scores for Study Participants According to Patient Characteristics

Table II

	N	TESS ^a		PEDSQL total		PEDSQL-Physical		PEDSQL-Social		PEDSQL-School/Work	
		Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value
Overall	74	93.0 (10.3)	-	81.6 (18.0)	-	81.5 (20.3)	-	89.9 (16.2)	-	84.3 (17.4)	-
Gender			0.24		0.01*		0.21		0.02*		0.20
Male	46	94.1 (9.1)		85.7 (15.7)		86.2 (18.4)		93.6 (12.6)		86.3 (16.8)	
Female	28	91.2 (12.0)		74.6 (19.7)		73.5 (21.3)		83.7 (19.8)		80.8 (18.1)	
Age at diagnosis			0.10		0.29		0.36		0.18		0.88
<18	38	94.9 (9.3)		83.8 (15.8)		83.6 (18.8)		90.9 (14.9)		84.6 (15.2)	
>18	36	91.0 (11.0)		79.3 (20.0)		79.3 (21.8)		88.9 (17.7)		84.0 (19.7)	
Age at survey			0.63		0.27		0.43		0.19		0.63
<30	22	94.6 (9.7)		82.9 (15.6)		81.1 (19.9)		91.4 (14.2)		82.5 (18.9)	
30-9	20	93.4 (11.7)		84.9 (19.5)		85.5 (19.7)		91.5 (19.1)		88.3 (18.7)	
40-49	13	93.6 (8.1)		84.1 (12.9)		84.6 (14.2)		92.7 (9.0)		85.0 (15.5)	
>50	19	90.4 (11.0)		74.4 (21.3)		75.3 (24.8)		84.4 (18.9)		81.5 (15.6)	
Tumor location			0.14		0.28		0.44		0.67		0.22
Bone	48	94.3 (8.9)		83.2 (16.5)		82.9 (20.8)		93.1 (11.0)		86.2 (16.8)	
Soft tissue	26	90.6 (12.3)		78.5 (20.5)		79.0 (19.5)		84.2 (22.0)		81.0 (18.3)	
Primary tumor			0.12		0.51		0.65		0.54		0.46
Upper extremity	10	91.1 (10.7)		79.1 (21.0)		75.0 (29.1)		91.5 (12.9)		81.0 (19.4)	
Lower extremity	26	94.2 (9.4)		84.2 (14.0)		82.9 (18.1)		92.5 (11.5)		87.9 (14.7)	
Pelvis	14	87.8 (14.0)		75.8 (21.1)		79.3 (19.8)		82.5 (22.3)		79.3 (20.2)	
Other	24	95.6 (7.6)		83.1 (19.0)		84.1 (19.2)		90.9 (17.5)		84.8 (17.7)	
Any relapse			0.54		0.57		0.50		0.61		0.57
No	67	92.8 (10.6)		81.2 (18.6)		81.0 (21.1)		89.8 (16.8)		83.9 (18.0)	
Yes	7	95.3 (7.2)		85.2 (10.8)		86.4 (9.4)		91.4 (10.3)		87.9 (10.4)	
Metastases			0.14		0.12		0.08		0.046*		0.60
No	64	92.3 (10.8)		80.2 (18.7)		79.8 (21.0)		89.4 (17.0)		83.9 (18.3)	
Yes	10	97.5 (3.6)		89.9 (9.9)		92.0 (10.6)		93.0 (10.3)		87.0 (10.6)	

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^aToronto Extremity Salvage Score.
^{*}Statistically significant difference between groups ($P < 0.05$).

Table III
Logistic Regression Assessment of the Odds of a TESS^a or PEDSQL Score Less Than the 25th Percentile

	TESS				PEDSQL total			
	# (%)	N	OR (95% CI)	P-value	# (%)	N	OR (95% CI)	P-value
Age at diagnosis								
<18	6 (16)	38	1.0 (reference)		8 (22)	37	1.0 (reference)	
>18	14 (39)	36	3.39 (1.13–10.19)	0.03 *	11 (31)	36	1.59 (0.55–8.56)	0.39
Age at survey				0.31				0.56
<30	3 (14)	22	1.0 (reference)		5 (23)	22	1.0 (reference)	
30–39	5 (25)	20	2.11 (0.43–10.28)	0.35	4 (20)	20	0.85 (0.19–3.74)	0.83
40–49	5 (39)	13	3.96 (0.76–20.66)	0.10	3 (23)	13	1.02 (0.20–5.21)	0.98
>50	7 (37)	19	3.69 (0.80–17.12)	0.09	7 (39)	18	2.16 (0.55–8.56)	0.27
Time since diagnosis (years)	20 (27)	74	1.03 (0.97–1.08)	0.37	19 (26)	73	1.03 (0.97–1.09)	0.32
Gender								
Male	12 (26)	46	1.0 (reference)		8 (17)	46	1.0 (reference)	
Female	8 (29)	28	1.13 (0.40–3.24)	0.82	11 (41)	27	3.27 (1.11–9.63)	0.03 *
Tumor location								
Bone	10 (21)	48	1.0 (reference)		11 (23)	47	1.0 (reference)	
Soft tissue	10 (38)	26	2.38 (0.83–6.81)	0.11	8 (31)	26	1.45 (0.50–4.25)	0.49
Site of primary disease				0.29				0.41
Lower extremity	5 (19)	26	1.0 (reference)		5 (19)		1.0 (reference)	
Upper extremity	4 (40)	10	2.80 (0.57–13.83)	0.21	3 (30)		1.80 (0.34–9.54)	0.49
Pelvis	6 (43)	14	3.15 (0.75–13.29)	0.12	6 (43)		3.15 (0.75–13.29)	0.12
Other	5 (21)	24	1.11 (0.28–4.42)	0.89	5 (22)		1.11 (0.28–4.42)	0.83
Local therapy modality				0.52				0.46
RT ^b plus surgery	7 (32)	22	1.0 (reference)		5 (24)	21	1.0 (reference)	
RT alone	3 (17)	18	0.43 (0.09–1.98)	0.28	3 (17)	18	0.64 (0.13–3.16)	0.58
Surgery alone	10 (29)	34	0.89 (0.28–2.85)	0.85	11 (32)	34	1.53 (0.45–5.26)	0.50
Metastatic disease								
No	19 (30)	64	1.0 (reference)		18 (29)	63	1.0 (reference)	

	PEDSQL total					TESS				
	# (%)	N	OR	95% CI	P-value	# (%)	N	OR	95% CI	P-value
Yes	1 (10)	10	0.28	(0.03–2.35)	0.24	1 (10)	10	0.26	(0.03–2.22)	0.22
Any relapse										
No	18 (27)	66	1.0	(reference)		18 (27)	67	1.0	(reference)	
Yes	1 (14)	7	0.44	(0.05–3.95)	0.47	2 (29)	7	1.09	(0.19–6.12)	0.92

^aToronto Extremity Salvage Score.

^bRadiation.

* Statistically significant difference between groups ($P < 0.05$).

Table IVTESS^a and PEDSQL Scores According to Patient Reported Symptoms and Outcomes

Patient-reported symptom/outcome	TESS			PEDSQL total		
	N	Mean (SD)	P-value	Mean (SD)	P-value	
Self-rated disability			<0.001*		<0.001*	
None	48	97.5 (4.4)		88.5 (12.0)		
Mild	16	88.2 (10.7)		76.6 (15.7)		
Moderate	8	74.5 (11.5)		49.1 (15.7)		
Symptom: pain			<0.001*		<0.001*	
Yes	15	79.6 (12.9)		61.0 (16.4)		
No	58	96.4 (5.9)		86.8 (14.4)		
Symptom: stiffness			<0.001*		<0.001*	
Yes	20	81.3 (12.3)		62.5 (17.7)		
No	52	97.4 (4.6)		88.7 (12.1)		
Symptom: fatigue			<0.001*		<0.001*	
Yes	15	79.6 (13.7)		57.8 (16.8)		
No	58	96.4 (5.5)		87.7 (12.5)		
Symptom: weakness			<0.001*		<0.001*	
Yes	15	77.6 (11.9)		55.1 (15.9)		
No	58	96.9 (4.7)		88.4 (10.9)		
Current frequency of exercise			0.026*		0.013*	
<3 days/week	39	90.8 (11.3)		79.6 (18.5)		
3 days/week	34	95.3 (8.6)		86.9 (16.0)		
Use of prescription pain medications			0.001*		<0.001*	
Yes	13	83.0 (14.0)		64.5 (20.4)		
No	59	95.0 (8.0)		85.2 (15.4)		
Use of prescription muscle relaxants			0.16		0.06	
Yes	6	85.2 (15.2)		68.5 (19.6)		
No	66	93.5 (9.7)		82.7 (17.7)		

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Patient-reported symptom/outcome	TESS			PEDSQL total		
	N	Mean (SD)	P-value	Mean (SD)	P-value	
Additional surgery required after ES ^a treatment						0.34 [*]
Yes	13	87.7 (12.9)		78.1 (21.6)		
No	61	94.1 (9.4)	0.01 [*]	82.3 (17.3)		

^aToronto Extremity Salvage Score.

^bEwing sarcoma.

^{*}Statistically significant difference between groups ($P < 0.05$).