



Quality of Life and Limb Functionality in Adolescents and Young Adults Surviving Bone Tumors in the Lower Extremity in a Developing Country: A Cross-Sectional Study

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Abstract

Introduction Due to higher survival rates among patients with bone tumors, there is a growing interest in determining these individuals' limb functionality and psychosocial prognosis.

Objectives This study aimed to analyze the differences in functionality and quality of life (QoL) related to health in patients diagnosed with a malignant bone tumor during childhood, according to the type of surgery performed.

Materials and Methods A cross-sectional study was performed for patients older than 14 years who treated for osteosarcoma or Ewing's sarcoma of the lower limb by who receiving surgery. To assess lower limb functionality and QoL among patients surviving malignant bone tumors, 19 patients surviving osteosarcoma or Ewing's sarcoma of the lower extremity were studied. An evaluation of functionality and QoL was done using the "Enneking and Medical Outcomes Study Short-Form 36 scales." We compared the functional results according to the surgical technique used. Categorical variables were compared according to the Mann-Whitney and Kruskal-Wallis tests, with an established 95% level of significance.

Results QoL among patients who had conservative surgery was not significantly better than amputee patients in the physical or mental aspects, nor in any of their components. Limb functionality, according to Enneking's staging, was significantly higher in non-amputee patients ($p = 0.035$).

Conclusion According to the data analysis done in this study, the QoL was found to be not significantly different, based on the type of surgery performed; however, there were differences in limb functionality.

Keywords

- ▶ survivorship
- ▶ quality of life
- ▶ osteosarcoma
- ▶ Ewing's sarcoma

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Introduction

In the last few decades, advances in the oncologic treatment of patients with malignant pediatric bone tumors have observed an improvement in cure rates, leading to higher numbers of cancer surviving patients.¹ In Peru, osteosarcoma and Ewing's sarcoma are the most common malignant bone tumors, reporting aggressive and metastatic behavior in around 40% of cases. The most common location for tumor development is the lower extremity of the human body.² Due to the high intensity of the oncologic treatment that includes chemotherapy, surgery, and radiotherapy, survivors could be stricken by a series of future sequelae affecting their quality of life (QoL), both physically and mentally.³

Definitive surgery of malignant bone tumors with the aim of complete removal of the tumoral lesion (amputation or member disarticulation) can be radical. However, the conservative surgery approach has been most commonly used by Peruvian institutions throughout the years.² Even though differences have been noted in limb functionality between nonamputee and amputee patients, studies on the QoL show contradictory results.^{4,5} Ignorance of long-term sequelae, both medical and psychological, is a growing public health issue, since conducting such research studies on those topics would allow for formulation of preventive measures or early intervention approaches which are important among surviving patients who reach adulthood.⁶

This study compares lower extremity functionality and the QoL of young patients surviving malignant bone tumors who have undergone a specific type of surgery performed in a developing country. The study also examines statistically significant differences between the two gender populations, since vast literature and extensive research support the fact that the incidence of bone tumors (of lower extremity) occurs considerably more in male populations than in their female counterparts; the gender differences are shown to differ statistically in their postsurgical prognosis. This study included key postsurgery metrics of QoL and overall functionality. They were further explicitly evaluated in the nonamputee surviving patients with lower extremity malignant bone tumors and compared, as well as contrasted the gender-based differences.

Methods

Study Population

Peru is a South American country with a total population of 32.2 million inhabitants. At least 1,790 children and adolescents (0–19 years old) are affected with cancer each year.⁷ Principal hospitals attending children with cancer in Peru are either a part of the Ministry of Health (MINSA), Social Security (EsSalud), or private sector. Rebagliati Hospital works as a public general hospital of EsSalud, attending nearly 120 children and adolescents with cancer every year.

Inclusion Criteria

Patients older than 14 years old at the time of the study and diagnosed with osteosarcoma or Ewing's sarcoma of the lower extremity as a child or adolescent (younger than

18 years old) were included for treatment from January 2002 to December 2014 in the Adolescent and Pediatric Oncology Unit at Rebagliati Hospital in Lima, Peru. Patients who had received surgical treatment and follow-up for at least 2 years after the end of treatment were included as well.

Exclusion Criteria

Patients were excluded if they were critically ill or unable to consent.

The sample size used in this study was determined based on a sufficient statistical power (80%) to detect at least 10% differences in outcome measures at a 5% significant level. According to the study protocol, the lowest age to answer questionnaires was decided to be 14 years of age.

Data Collection

Data on demographics, clinical characteristics, and treatment outcomes were collected by revision of medical records. Based on the type of surgery, patients were separated into amputees and those who received conservative surgery. This study further analyzed the gender differences with similar diagnoses and surgical approaches (in nonamputee survivors). Patients were contacted by phone or interviewed in person to answer the questionnaire on Medical Outcomes Short (MOS) Form-36 Health Survey (SF-36; **Supplementary Material S1**; available in the online version); a tool widely used internationally to rate the QoL. Additionally, the Enneking score (Musculoskeletal Tumor Society [MSTS]; **Supplementary Material S2**; available in the online version) was used to estimate the functionality of the previously affected extremity. Based on the questionnaire responses, the analysis was done to understand differences in life quality and extremity functionality since disparities in those areas had been reported in the past based on the gender of the patient. Primary outcomes measured were limb functionality and QoL, whereas secondary outcomes measured were social functioning and overall health perception.

Statistical Analysis

Categorical variables were compared according to Mann-Whitney (bivariable) and Kruskal-Wallis (multivariable) tests to the scores obtained in the questionnaire on MOS SF-36 and the Enneking score, with an established 95% level of significance.

Ethics

The study was performed following the principles set out in the Helsinki Declaration and was approved by the Rebagliati Institutional Ethics Committee in July 2018. Informed patient consent was obtained prior to enrolment to all participants (**Supplementary Material S3**; available in the online version). In the case of patients younger than 18 years, parental consent was also needed.

Results

From 2002 to 2014, 27 cases of patients surviving bone sarcomas of the lower extremity were registered. Out of those, five could not be located, and three patients died in

another institution due to the progression of the disease. Nineteen patients (11 males and 8 females) with an average current age of 20 years were studied. Seven patients were from Lima while 12 were from several regions of Peru (Arequipa, Callao, Cajamarca, Trujillo, and Tacna). Seventeen patients received a diagnosis of osteosarcoma and two were diagnosed with Ewing's sarcoma. The most common surgical approach used was conservative surgery (15 cases, 78.9%), amputation being the least frequent among survivors (4 cases, 21.1%). At the time of diagnosis, the average age of patients was 15 years, that is, most were adolescents. Most survivors of bone sarcomas of the lower extremity presented localized disease (16 cases, 84.2%). The group of patients who underwent conservative or salvage surgeries presented a higher incidence of postsurgical complications (neurovascular injuries and deep wound infections) compared with the group of amputee patients (33.3 vs. 0%; ►Table 1).

QoL among patients who had conservative surgery was not significantly better than amputee patients in either the physical or mental aspects, nor in any of their components (►Fig. 1). Among nonamputees, social functioning ($p = 0.014$) and overall health perception ($p = 0.026$) were better among men

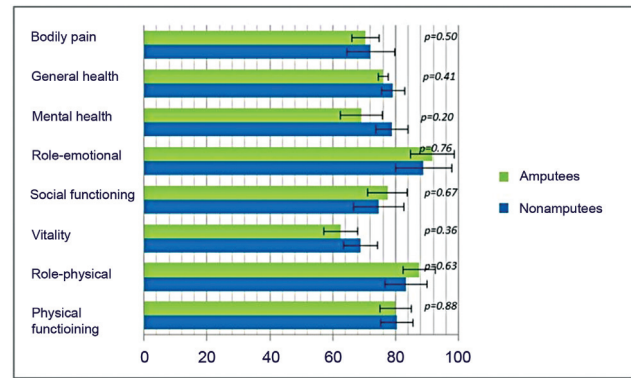


Fig. 1 Quality of life among patients who had conservative surgery.

(►Table 2). Limb functionality, according to Enneking's staging, was significantly higher in nonamputee patients ($p = 0.035$).

Discussion

Our study focuses on evaluating the QoL and lower extremity functionality among patients surviving malignant bone

Table 1 Clinical features of patients surviving malignant bone tumors of the lower extremity according to type of surgery

	Patients who had conservative surgery of lower limb (n = 15) Median (range)/n (%) / mean ± SD (range)	Patients who had amputation surgery (n = 4) Median (range)/n (%) / mean ± SD (range)	p-Value
Age at diagnosis (y)	15 (11–17)	15 (13–15)	
Current age (y)	20 (14–25)	21.5 (16–27)	
Gender			
Male	7 (46.7)	1 (25)	
Female	8 (53.3)	3 (75)	
Diagnosis			
Osteosarcoma	13 (86.7)	4 (100)	
Ewing's sarcoma	2 (13.3)	0 (0)	
Stage			
Localized	14 (93.3)	2 (50)	
Metastatic	1 (6.7)	2 (50)	
Tumor location			
Distal femur	8 (53.3)	3 (75)	
Proximal femur	2 (13.3)	1 (25)	
Proximal tibia	4 (26.7)	0 (0)	
Fibula	1 (6.7)	0 (0)	
Postsurgical complications			
Yes	5 (33.3)	0 (0)	
No	10 (66.7)	4 (100)	
Quality of life			
Physical functioning SF-36	79.1 ± 7.4 (64.8–93.2)	78.04 ± 5.1 (71.6–83.7)	0.76
Mental health SF-36	76.2 ± 9.6 (60–97.3)	71.6 ± 7.1 (62.2–68.6)	0.45
Enneking's test			
Total score (%)	78 ± 14.6 (53.3–100)	59.1 ± 18.3 (50–86.6)	0.035

Abbreviations: SD, standard deviation; SF-36, Short Form-36 Health Survey.

Table 2 Comparison by gender of different scales of quality of life and functionality in nonamputee patients surviving malignant bone tumors of the lower extremity

Category	Male (n = 7) Mean ± SD (range)	Female (n = 8) Mean ± SD (range)	p-Value
Enneking's test			
Score (%)	76.2 ± 12.7 (53.3–86.7)	79.6 ± 16.9 (53.3–100)	0.75
Quality of life			
Physical functioning SF-36	79.5 ± 7.7 (64.9–90.5)	78.7 ± 7.7 (68.9–93.2)	0.82
Mental health SF-36	79.8 ± 9.9 (65.3–97.3)	73.2 ± 8.8 (60–88)	0.18
Components			
Bodily pain	70.1 ± 12.5 (45.5–81.8)	73.9 ± 18.5 (45.5–90.9)	0.31
General health	83.4 ± 6.3 (72–92)	75.5 ± 6.6 (68–88)	0.026
Mental health	81.4 ± 11 (66.7–100)	76.7 ± 10.4 (66.7–96.7)	0.38
Role emotional	90.5 ± 13.1 (66.7–100)	87.5 ± 23.1 (50–100)	0.78
Social functioning	82.9 ± 17 (50–100)	67.5 ± 12.8 (50–80)	0.014
Vitality	72 ± 13.8 (58.3–100)	66.1 ± 7.9 (54.2–75)	0.45
Role: physical	80.4 ± 15.9 (62.5–100)	85.9 ± 12.4 (62.5–100)	0.47
Physical functioning	79.5 ± 9.7 (66.7–90)	81.3 ± 11.8 (66.7–96.7)	0.86

Abbreviations: SD, standard deviation; SF-36, Short Form-36 Health Survey.

tumors in the transition period between adolescence and adulthood facing challenges linked to the oncologic treatment they received. We found no significant difference in the QoL, neither in the physical or mental aspects, nor in any of their components among patients who had conservative surgery versus amputation. In past decades, amputation was the treatment of choice for localized disease control of malignant bone tumors. Now, both national and international organizations support the idea that conservative surgery is the standard treatment and a priority in the multidisciplinary team against osteosarcoma and Ewing's sarcoma.^{2,8,9} This subject is acquiring relevance in public health due to the potential need to employ additional resources or support services in physiotherapy and psychosocial therapy.^{7,10}

Most studies involving patients surviving pediatric bone tumors have been conducted in high-income countries and do not specifically examine patients whose lower limbs have been compromised.^{11,12} In our study, the QoL among amputee patients compared with that of the group who underwent conservation surgery did not change significantly, a finding similar to that of most studies,^{8,9,13–17} but different from others.^{18–20} Nevertheless, the functionality of the extremity was significantly higher in the group of patients who had conservative surgery, as reported in other studies.^{21,22}

Although patients surviving bone sarcomas could suffer a series of subsequent events (recurrences, new surgeries on the affected limb, metastasis, or retarded effects of medication), their adaptation level to the social environment relating to educational, or employment level is not much different from that of the general population.^{4,5} It is important to note that postsurgical complications are generally more common

in patients who had conservative surgery, as shown in our study.^{16,19}

Related to gender, this study showcases that social functioning and overall health perception were better among men in the group of patients who had conservative surgery. This is consistent with several literature reviews produced which predominantly stated, although lower extremity bone tumors are more common in males, their QoL and functional scores are statistically more than that of females (based on variations of the Mann–Whitney test).^{23,24} In contrast, a study showed that men had diminished performance in the work environment and were less likely to be married.⁷

Limitations and Strengths

Within the limitations of our study, there is a potential selection bias. This is because some patients were excluded from this study, since they could not be located or contacted, probably leaving aside survivors with more significant performance difficulties or greater negative impact on their QoL. Another drawback involves the retrospective nature of the study with the limited number of cases per group since bone sarcomas are infrequent pathologies with high mortality rates, especially in lower- and middle-income countries. Among the strengths of this study, it is essential to note that evidence has been produced of a relatively homogeneous group of patients who have mostly undergone conservative surgeries, a treatment approach demonstrating an upward trend in terms of its utility, further providing evidence in a country of limited resources. Future research should focus on a better understanding of these patients' functional status and QoL.

Conclusion

In conclusion, this study indicates that the QoL of patients who have suffered bone neoplasia of the lower extremity during their pediatric years in a developing country is not significantly different due to the nature of the surgery performed, even though there were differences in limb functionality. The latter increased among patients who underwent conservative surgery. A subsequent analysis with a larger number of patients is needed to verify such results.

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Conflict of Interest
None declared.

References

- Isakoff MS, Bielack SS, Meltzer P, Gorlick R. Osteosarcoma: current treatment and a collaborative pathway to success. *J Clin Oncol* 2015;33(27):3029–3035
- Vasquez L, Tarrillo F, Oscanoa M, et al. Analysis of prognostic factors in high-grade osteosarcoma of the extremities in children: a 15-year single-institution experience. *Front Oncol* 2016;6:22
- Ottaviani G, Robert RS, Huh WW, Palla S, Jaffe N. Sociooccupational and physical outcomes more than 20 years after the diagnosis of osteosarcoma in children and adolescents: limb salvage versus amputation. *Cancer* 2013;119(20):3727–3736
- Bekkering WP, van Egmond-van Dam JC, Bramer JAM, Beishuizen A, Fiocco M, Dijkstra PDS. Quality of life after bone sarcoma surgery around the knee: a long-term follow-up study. *Eur J Cancer Care (Engl)* 2017;26(04):. Doi: 10.1111/ecc.12603
- Stokke J, Sung L, Gupta A, Lindberg A, Rosenberg AR. Systematic review and meta-analysis of objective and subjective quality of life among pediatric, adolescent, and young adult bone tumor survivors. *Pediatr Blood Cancer* 2015;62(09):1616–1629
- Nagarajan R, Neglia JP, Clohisy DR, et al. Education, employment, insurance, and marital status among 694 survivors of pediatric lower extremity bone tumors: a report from the childhood cancer survivor study. *Cancer* 2003;97(10):2554–2564
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68(06):394–424
- Rödl R, Pohlmann U, Gosheger G, et al. Ablative and extremity salvage tumor surgery of the lower extremity—a 10 year comparison [in German]. *Z Orthop Ihre Grenzgeb* 2001;139(03):183–188
- Ottaviani G, Robert RS, Huh WW, Jaffe N. Functional, psychosocial and professional outcomes in long-term survivors of lower-extremity osteosarcomas: amputation versus limb salvage. *Cancer Treat Res* 2009;152:421–436
- Katsumoto S, Maru M, Yonemoto T, Maeda R, Ae K, Matsumoto S. Uncertainty in young adult survivors of childhood and adolescent cancer with lower-extremity bone tumors in Japan. *J Adolesc Young Adult Oncol* 2019;8(03):291–296
- 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(03):220–225
- Nicholson HS, Mulvihill JJ, Byrne J. Late effects of therapy in adult survivors of osteosarcoma and Ewing's sarcoma. *Med Pediatr Oncol* 1992;20(01):6–12
- Postma A, Kingma A, De Ruiter JH, et al. Quality of life in bone tumor patients comparing limb salvage and amputation of the lower extremity. *J Surg Oncol* 1992;51(01):47–51
- Expósito Tirado JA, Márquez Vega C, Muro Guerra C, et al. Calidad de vida y funcionalidad en pacientes pediátricos intervenidos de tumores óseos en miembros inferiores: Cirugía reconstructiva versus amputación. *Rehabilitacion (Madr)* 2011;45(04):313–319
- Sugarbaker PH, Barofsky I, Rosenberg SA, Gianola FJ. Quality of life assessment of patients in extremity sarcoma clinical trials. *Surgery* 1982;91(01):17–23
- Zahlten-Hinguranage A, Bernd L, Sabo D. Amputation or limb salvage? Assessing quality of life after tumor operations of the lower extremity [in German]. *Orthopade* 2003;32(11):1020–1027
- Silva RS, Guilhem DB, Batista KT, Tabet LP. Quality of life of patients with sarcoma after conservative surgery or amputation of limbs. *Acta Ortop Bras* 2019;27(05):276–280
- Mason GE, Aung L, Gall S, et al. Quality of life following amputation or limb preservation in patients with lower extremity bone sarcoma. *Front Oncol* 2013;3:210
- Barrera M, Teall T, Barr R, Silva M, Greenberg M. Health related quality of life in adolescent and young adult survivors of lower extremity bone tumors. *Pediatr Blood Cancer* 2012;58(02):265–273
- Ginsberg JP, Rai SN, Carlson CA, et al. A comparative analysis of functional outcomes in adolescents and young adults with lower-extremity bone sarcoma. *Pediatr Blood Cancer* 2007;49(07):964–969
- Aksnes LH, Bauer HCF, Jebsen NL, et al. Limb-sparing surgery preserves more function than amputation: a Scandinavian sarcoma group study of 118 patients. *J Bone Joint Surg Br* 2008;90(06):786–794
- Renard AJ, Veth RP, Schreuder HW, van Loon CJ, Koops HS, van Horn JR. Function and complications after ablative and limb-salvage therapy in lower extremity sarcoma of bone. *J Surg Oncol* 2000;73(04):198–205
- Monticelli A, Ciclamini D, Boffano M, et al. Lower Limb Core Scale: a new application to evaluate and compare the outcomes of bone and soft-tissue tumours resection and reconstruction. *BioMed Res Int* 2014;2014:652141
- Janeway KA, Barkauskas DA, Krailo MD, et al. Outcome for adolescent and young adult patients with osteosarcoma: a report from the Children's Oncology Group. *Cancer* 2012;118(18):4597–4605