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A Comparative Study on the Clinical and Functional Outcome of Limb Salvage Surgery and Amputation in Tibial Osteosarcoma

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Conflicts of Interest
There are no conflicts to declare.

ABSTRACT

The aim of this study was to analyze the survival, recurrence, complications as well as the quality of life (QOL) in tibial osteosarcoma (OSA) patients managed by limb salvage surgery (LSS), either by a prosthesis, resection or graft or by amputation.

106 tibial osteosarcoma patients were enrolled where 39 had custom-designed endoprosthetic arthroplasty (LSS1), 36 underwent resection and bone graft (LSS2) while only 31 underwent amputation. A Comparison was done based on post-operative survival rates, postoperative recurrence, and complications. The impact of the patient's QOL was also evaluated.

The results of our study showed that the incidence of tibial OSA was higher in <20 years (63%) where M: F was 1.52:1. The mean survival of patients with LSS1 was 2.51 years(Confidence interval-95%;0.3-7.58 years), LSS2 was 4.15 (CI-95%;0.35-8.65 years) and amputation was found to be 4.79 years(CI-95%;0.6-8.39 years) with overall mean survival time was 3.72 years (CI-95%;p=0.0002). The Complication rate was lower in LSS1 and LSS2 (46.67%, CI-95%; p = 0.048). The mean MSTS score was 68.8% (range, 43.56%-89.16%) with significantly lower results than in amputations (p = 0.007). The QOL assessment done by SF-36 revealed a better state of LSS1 and LSS2 patients. The sarcoma led to emotional and functional disturbances in amputated patients (CI-95%, p =0.004). The complication-free patients were found to be higher in LSS groups (53.33%) (CI-95%, p =0.048).

Limb Salvage Surgery for tibial osteosarcoma is superior to amputation due to its better functional outcome and fewer complications.

Abbreviations:
OSA, Osteosarcoma;
LSS, limb salvage surgery ;
QOL, Quality of Life;
MSTS, Musculoskeletal Tumor society System;
MRI, Magnetic Resonance Imaging;

Keywords: TIBIAL OSTEOSARCOMA, LIMB SALVAGE, AMPUTATION, PROSTHESIS, RESECTION, SARCOMA

Introduction

This century is a highly innovative era in surgery due to surgical techniques advancements, but for patients diagnosed with tibial Osteosarcoma (OSA), Amputation is still considered a dominant surgical treatment[1] With the rise in adjuvant therapies and neoadjuvant chemotherapies, Limb sparing surgery is becoming a more acceptable option for tibial OSA. It is a scarcely occurring malignant bone tumor (20% of primary bone cancers) and is the second most common primary malignant tumor of bone.[2] It has a higher incidence in the distal femur, proximal tibia (around the knee joint) followed by proximal Humerus, and then the distal tibia. OSA's incidence in the distal Tibia is 19%, while 80% is in the Proximal Tibia.5 It appears that the incidence in younger aged group of individuals (10-25years) is higher than in other groups. [2,3]

Various Limb sparing techniques are available for tibial OSA, such as megaprosthesis, allograft, and autograft bone reconstruction techniques.[4] Megaprosthesis have survival rates of 40-100%, a function of 50-93%, and complications of 17-60%, while for bone reconstruction, survival is 40-100%, the function is 53-100%, and complications are 12-92%. Moreover, for Amputation, survival is 84-100%, and the complication rate ranges from 12-70%.[5] Due to advancements in Limb sparing techniques, surgeries have been possible without influencing the tibial OSA patients' survival rate.[6] Although various studies have different findings for survival and function, the survival rates after limb-sparing surgeries range from 0.5-24 years, while for Amputation, it ranges from 3-5 years.

Regarding various studies on OSA, controversies are still prevalent to decide which the better treatment option is.[4] Therefore, our study's main aim was to analyze the survival rate, recurrence, and complication in patients who underwent limb-sparing surgeries (endoprosthesis, resection, and graft) and amputations. Moreover, to check the health status, quality of life, and functional scores of the operated patients of Tibial Osteosarcoma. Moreover, to assess the operative measure's outcome, we chose for the patient whether it was fruitful or not. Our objective is to determine which treatment option is better by comparing limb salvage techniques and Amputation for tibial osteosarcoma patients.

Materials and methods

106 patients diagnosed with tibial OSA in 1st affiliated hospital of Zhengzhou University from January 2011 to July 2020 was included in the study. The patients who have all the necessary electronic data were only enrolled. The tibial OSA patient who is still on chemotherapy and has not been operated or died of disease, as well as OSA patients other than tibial OSA were not enrolled in the study. Among 106 patients, 64 were males and 42 females with a mean age of 44 years (range, 5-62 years). The decision regarding the surgical procedure was based on biopsy and staging. On the basis of surgical procedure, patients were divided into three groups, 1) LSS1 (endoprosthesis), 2) LSS2 (resection and bone graft), and 3) Amputation. 39 had custom-designed endoprosthetic arthroplasty (LSS1), 36 underwent resection and bone graft (LSS2) while only 31 underwent amputation.

No patients were recalled for the study. Patients were contacted by telephone and all patients' data was obtained from the medical records. Complications, local recurrences, metastasis were also recorded from patients' files. The median follow-up was 3.16 years (range 4.2-103.8 months). Verbal informed consent was taken from each and every patient. To every osteosarcoma patient, after the positive biopsy (pathological) reports, neoadjuvant chemotherapies were administered. Ifosfamide and doxorubicin were given in every cycle. Additionally, Methotrexate and Cisplatin were given, depending on the patient's physical condition and efficiency. Pre-operatively three cycles and post-operatively six cycles of chemotherapies were given.

Limb sparing surgery, using endoprosthetic joint replacements or megaprosthesis, are available, custom-made. They can replace the entire bone as well as both adjacent joints. Its merit allows immediate joint stability and weight-bearing to provide higher joint functions leading to a higher functional status. There is a chance of prosthesis implant failure, loosening, and infection, but we did not have any rejection cases. It wears out with time, and eventually, it might require it to be replaced at some time.

In proximal tibial OSA, Limb sparing surgery was done by wide en-bloc resection and custom- designed endoprosthetic arthroplasty, which has been the best choice.[7] (Figure 1) While in patients who did not require arthroplasty, only resection with graft (allograft, autograft) implantation was done. (Figure 2) The graft could be a fibula graft or a commercially available graft.

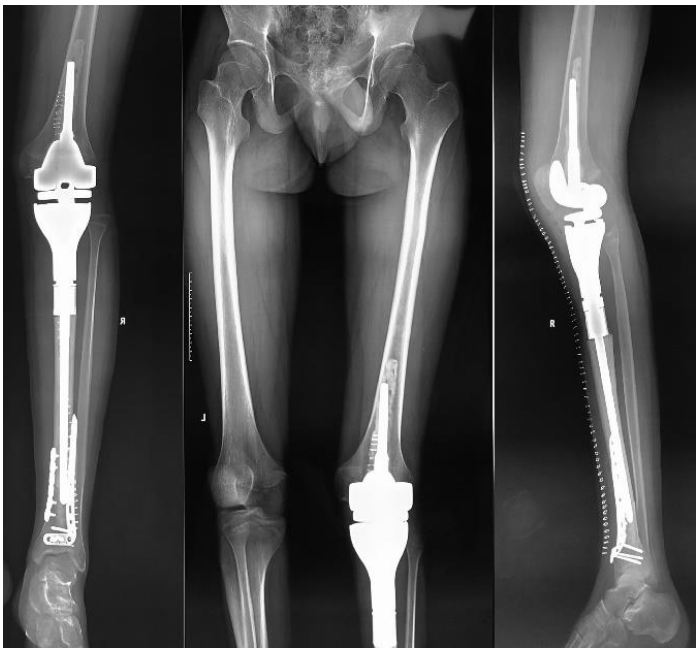

Figure 1 X-ray (PA view and Lateral view along with the normal side) of a post-operative case on follow up showing the custom- designed endoprosthetic implant with ankle arthrodesis.

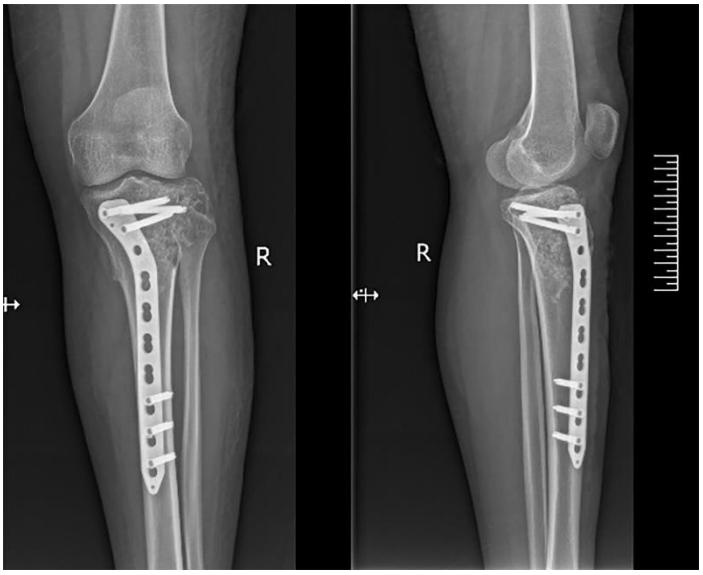

Figure 2 A follow up X-ray (PA and Lateral view) of a post-operative case after resection and fixation with a plating

For distal tibial Limb sparing surgery, fibula graft followed by arthrodesis was done using plates and calcaneal nails or tibiotalar screws. We did not implant any prosthesis for the distal tibial OSA. Among the various methods available for reconstruction of the Distal Tibia, we tried few ways such as using a pasteurized autograft, allograft, autogenous fibular graft along with megaprosthesis, tumor wide en-bloc resection, and bone recycling using liquid nitrogen or just hypertonic saline or gentamicin at high temperature for half an hour or the portion was either ablated with microwave-induced hyperthermia generating heat ablating very high volumes of tumor sections. The distal tibial artery and arteria dorsalis pedis were checked for their salvage ability, and reconstructive surgery was done with adequate fixation.

For both proximal and distal regions, above-knee amputation was done with proper planning in patients who were not suited for LSS. Tentative markings were done over the amputation planned area. While amputating, resection was done at least 2 cm or 3 cm proximal to the affected region determined by radiological examination and obtaining enough soft tissue coverage with the adequate remaining portion of the limb. Stump was created with standard surgical procedures.

Quality assessment

There is a high demand for analyzing the QOL and functional outcomes in OSA patients. QOL is an independent survival and response predictor, which plays a vital role in evaluating cancer patients. In some studies, results were significantly better in Limb sparing surgery (via TESS and MSTS scoring system). In contrast, other studies did not report to have a remarkable one, so the controversy is still prevalent in deciding which has better outcomes. In our research, we chose MSTS and SF-36 forms to assess the health conditions of operated patients.SF-36 structure and MSTS scoring system were done in three groups. Patients who had to undergo secondary Amputation due to recurrence were included in the amputation group and likewise for secondary prosthetic knee arthroplasty in group LSS1.

Each patient was contacted by telephone and was asked relevant questions, which is a standard questionnaire designed to assess the quality of life. The SF-36 form consisted of 36 questions that set nine parameters, which were 1) physical functioning (PF), 2) role limitations due to physical health (PH), 3) role limitations due to emotional problems (EP), 4) energy or fatigue (EF), 5) emotional wellbeing (EW), 6) social functioning (SF),7) Pain (P),8) General Health (GH) and 9)Health change (HC). Moreover, range from 100 optimal to zero being the poorest.

The MSTS scoring system, which was given to every patient, comprised of 6 parameters: 1) pain, 2) function, 3) emotional acceptance, 4) use of external support, 5) walking ability 6) gait alterations. Each parameter was scored from 0-5 with a total score of 0-30, higher the score was, higher the function. The functional scoring system was categorized into three score groups: 1) <49% Fair; 2) 50-75% good; and 3) >75% excellent. MSTS scores range from 50-100% for Limb sparing surgery and 53-90% for amputation patients of OSA.[9]

Statistical analysis

The statistical program SPSS 25 for windows 8.1 and Microsoft Excel 2013 was used for analysis. Tests such as the Chi-squared test, student's t-test were used to calculate the p values while for the survival, the Kaplan-Meier analysis was done. (Figure 5) Values were compared, differences between variables were analyzed and p-value <0.05 was considered to be significant.

Results

Of 106 patients initially, 39 (37%) patients had custom-designed endoprosthetic arthroplasty, 36 (34%) patients underwent resection and bone graft, while only 31 (29%) patients underwent amputation. The Male to female ratio for LSS1 was 2:1, LSS2 was 7:5 and amputation was 8:7, overall M: F ratio in our study was found to be 1.52:1 (p = 0.57). LSS1 patients in the age group < 20 years were 27, 20-40 years were 10 and >40 years were 2, in LSS2 patients in the age group < 20 years were 22, 20-40 years were 9 and >40 years were 5 while amputated patients in the age group < 20 years were 14, 20-40 years were 9 and >40 years were 8 (p = 0.133). In total, 75 patients had Limb sparing surgery in the initial phase, among which 3 had to undergo secondary endoprosthetic arthroplasty after wide en-bloc resection. In comparison, 7 patients had to undergo a secondary amputation, and 31 had primary amputation. Proximal tibial OSA patients were found to be 85(39 LSS1, 26 LSS2, 20 Amputation) while distal tibial OSA was found to be 21 (10 LSS2, 11 Amputation) (p = 0.0003). The mean and median survival of patients with LSS1 was 2.51 years, 2.00 years, LSS2 was 4.15, 4.46 and amputation was 4.79 years, 5.33 years with overall mean survival time of 3.72 years {Confidence interval (CI)-95%; p= 0.0002}. The number of deaths in proximal tibial OSA patients was 12 while in distal were 6. Among all, 56 patients had various post-operative complications, which were pain and swelling (15), joint stiffness (4), joint effusion (4), wound and skin infection (4), soft tissue edema (2), numbness (3), lung inflammation (1), and lung metastasis (15). Only pain complaints without swellings were seen higher in amputation patients. (Table 1)

Variables	LSS1	LSS2	Amputation	Total	
No. of Patients	39	36	31	106	
Gender					
Male	26	21	17	64	P = 0.57
Female	13	15	14	42	
Age					
<20 years	27	22	14	63	P = 0.133
20-40 years	10	9	9	28	
>40 years	2	5	8	15	
Location of Tumor					
Proximal Tibia	39	26	20	85	P = 0.0003
Distal Tibia	0	10	11	21	
Complications					
Pain + Swelling	5	5	5	15	
Joint Stiffness	2	2	0	4	
Joint Effusion	2	2	0	4	
Wound and Skin Infection	0	3	1	4	P=0.0049
Soft Tissue edema	0	0	2	2	
Numbness	0	0	3	3	
Recurrence	3	14	3	20	
Lung inflammation	0	1	0	1	
Lung Metastasis	2	8	5	15	

Table 1 Age, gender, site, complications distribution of the tibial Osteosarcoma patients in the three operative groups LSS1, LSS2, and Amputations

The recurrence was seen higher in the LSS2 group (14) while in LSS1 and amputation were found to be the same (3 in each) (CI-95%; p = 0.004). A higher complication rate was seen in amputated patients (67.7%) compared to patients who had endoprosthesis (28.2%) but had similar complications with those who had resection (66.7%). Complete complication-free patients were 50 (28, 70.8% LSS1, 12, 33.3% LSS2, 10, 32.3% amputees) showing higher numbers in limb salvaged patients. Before surgeries 48 patients were students, 18 were farmers, 5 were jobless, 4 were on technical fields and 31 were on other odd jobs (p=0.47). After the surgery, patients who are still alive and those who had LSS had continuity in their previous state of lifestyle.

We evaluated the SF-36 form questionnaire of a total of 88 patients (40 LSS1, 19 LSS2 and 29 amputation) (remaining 18 patients died due to recurrences and lung metastases). The health survey done on all revealed that the status of limb-sparing surgeries was in better state than in those who went through amputation. And all parameters of QOL were found to be significant for Limb sparing surgery ($p < 0.05$) except for the general health (GH) and health change (HC) parameter which were not that significant. (Table 2) (Figure 3) Comparing to other cancer survivors, sarcoma survivors have relative physical limitations with lesser SF-36 scores. The sarcoma led to higher emotional disturbance in amputated patients than in Limb sparing surgery patients.

The mean MSTS score was 68.8% (43.56%-89.16%). The amputees had a significantly lower score in comparison to Limb sparing surgery. Patients had complaints of pain either due to altered gait or due to operative measures, or either due to prosthetic problems. Amputated patients had difficulty in maintaining normal gait, required more external support, and were emotionally weaker, pain problems were seen higher and emotionally and functionally dependent on others. Therefore the mean functional results were excellent in LSS1 (89.17%), good in LSS2 (73.69%) while fair in amputees (43.57%) (Table 3) (Figure 4)

SF-36	PF	PH	EP	EF	EW	SF	PAIN	GH	HC
LSS1	76.55	83.88	70.35	86.13	89.1	87.5	88.19	89.25	81.75
LSS2	73.42	81.05	72.13	80	80.08	88.15	88.02	83.94	83.94
Amputation	60.68	53.44	58.62	63.62	63.37	60.77	71.98	66.37	55.68
p-value	0.012	0.05	0.008	0.036	0.048	0.071	0.04	0.05	0.139

Table2 QOL SF-36 form Questionnaire mean values obtained from patients. physical functioning (PF), physical health (PH), emotional problems (EP), energy or fatigue (EF), emotional wellbeing (EW), social functioning (SF), Pain (P), General Health (GH) and 9)Health change (HC).

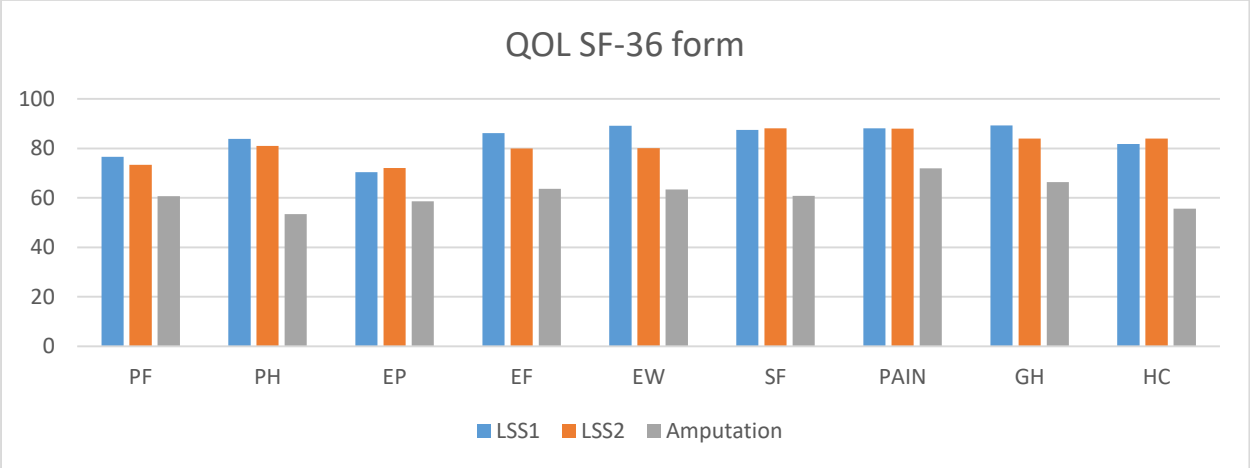

Figure 1 QOL SF-36 form questionnaire mean values obtained in the form of a graph.

Mean MSTS	Pain	Function	Emotional	External Support	Functional Independence	Gait	MSTS %
LSS 1	4.16	4.04	3.38	5	5	5	89.17
LSS 2	4.10	4.26	3.39	2.53	4.37	4.32	73.69
Amputation	2.89	3.07	2.48	1.17	2	1.48	43.57
P-value	0.04	0.04	0.01	0.1	0.15	0.16	Mean (68.8)

Table 3 MSTS score mean results obtained from the three groups LSS1, LSS2 and Amputations patients.

Our study's outcomes favored Limb salvage surgeries (LSS1 and LSS2 groups) for tibial Osteosarcoma regardless of its location on the basis of functional assessments, complication rates, QOL SF-36 scores, and MSTS scores. But the survival parameter in our study was found to be in favor of amputations group.

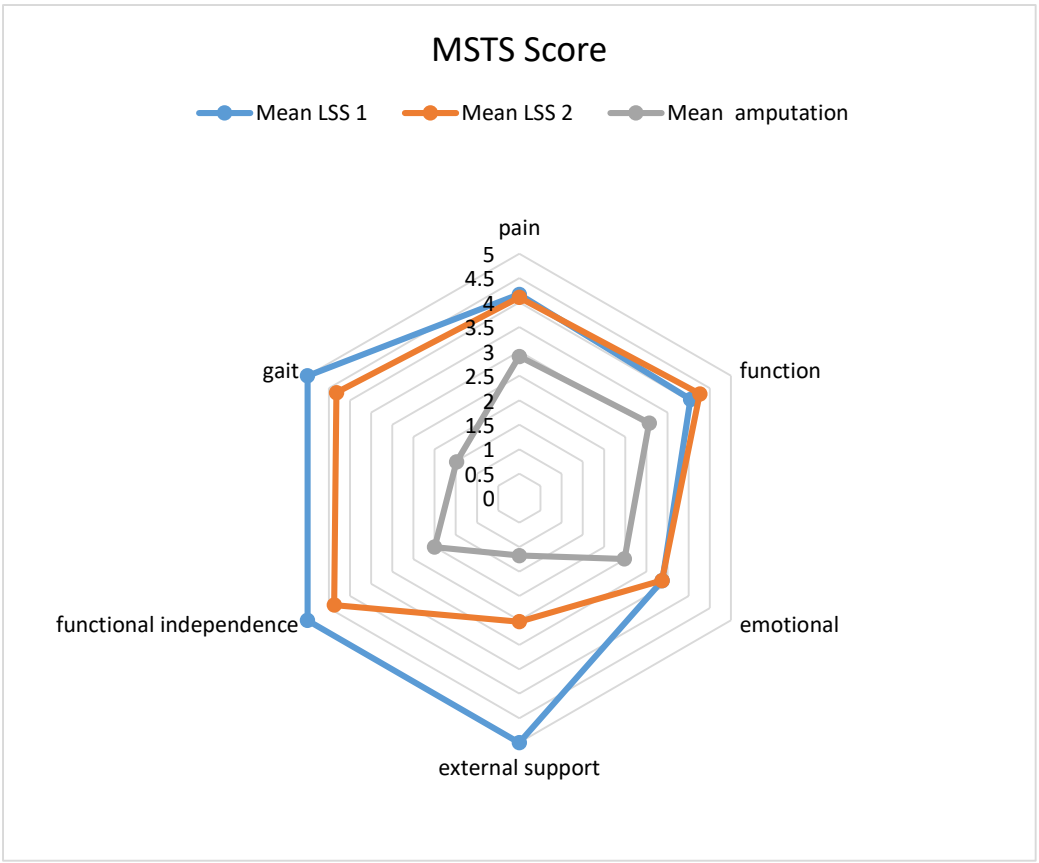

Figure 4 MSTS score mean results obtained from patients under LSS1, LSS2, and Amputation groups.

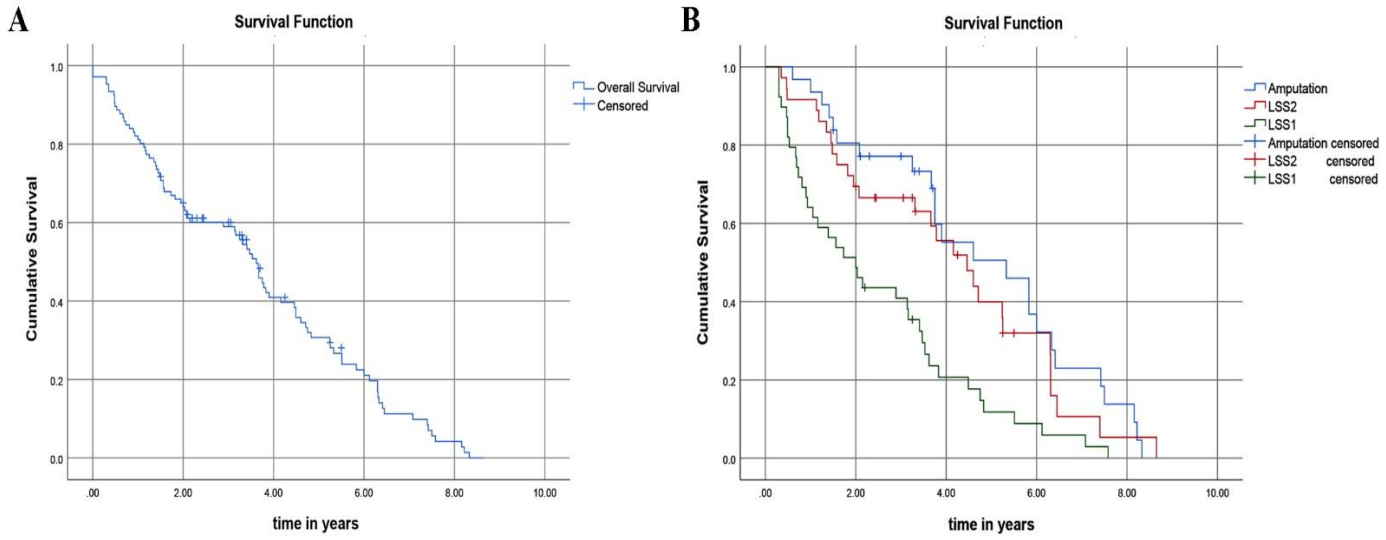

Figure 5 Kaplan Meier Survival plots in a Graph showing censored and non-censored patients. A) Total patients plot showing the cumulative survival graph over the time in years and B) the comparative survival graphs plotting their survivability of the patients of the three groups over the time in years.

Discussion

Multidisciplinary treatment (MDT) has been proved to be a better choice in managing bone sarcomas. For proximal tibial OSA, MDT, along with custom-designed endoprosthesis and neoadjuvant chemotherapies, have been sufficient for positive outcomes, prognosis, and survival. LSS is the best way of management for proximal Tibia. For distal tibial OSA, the effectiveness of Limb sparing surgery is still in controversy, while in some studies, megaprosthesis implant has proved to be effective[9] Skill-wise reconstructive surgery for attaining adequate fixation in the distal region is challenging due to its limited surrounding tissue and massive bone loss, leading to a higher rate of complications and inadequate soft tissue coverage. It also has higher chances of recurrences, and even if distal tibial artery and arteria dorsalis pedis is not salvageable, leading finally to Amputation. In Limb sparing surgery, it is a challenge to overcome the soft tissue coverage and joint mechanics. It also has higher chances of muscle and nerve damage leading to higher complications than in amputated patients. But, studies have proven to be in favor of Limb sparing surgery regarding higher functional and emotional results in both proximal and distal osteosarcomas.

Allograft bone can be bought from commercial bone banks and benefit from restoring the wide en-bloc resected portion of bone and delaying joint replacement.[10,11] The implant benefits stability, strength, and modularity with the bone restoring and soft tissue benefits conferred by the bone graft. It allows better soft tissue repair and joint function, especially in the proximal tibia.[10] But, usually does not re-vascularize and is subject to nonunion and infections 15% and fracture 27%, requiring additional surgeries. Complications are challenging and often require further surgery, including at times amputation.[11] Due to the high rate of recurrences after resections and grafts (allograft, autograft), few cases eventually lead to amputation. Gaston et al. reported a high local recurrences rate of 40% in LSS, although long term survival, and concluded that LSS should be attempted whenever possible.[12] JRenard et al. and Mavrogenis et al. both also reported complications in LSS more than in Amputation.[8,13] Schrager et al. reported overall mortality to be 35% more in amputation. [15] Ayerza et al. also reported a better survival rate.[14] Aksnes et al. concluded the bone sarcoma patients who survived managed well with an overall better quality of life adjusting their physical limitations with more impaired function and QOL in amputees.[15]

Some surgeons still choose amputations, while many choose limb-sparing surgeries due to their high emotional value.[11] Post neoadjuvant chemotherapy, most surgeons after an MRI select and opt for Amputation implying that the therapy does not alter much to the tumor instead just decrease the swelling. The metastatic disease typically develops hematogenously, with the most common site of metastasis being the lungs, followed by other bones.[16] Amputation leads to early blockage of further spreading or metastasis of sarcoma to other vital organs leading to death. At the present stage, traditional amputation is still considered to be a choice among surgeons for OSA, although it has a 5-year overall survival rate of only 10-20%. In contrast, advancements in adjuvant chemotherapies and radio imaging techniques limb sparing surgery has been a viable emerging choice providing better results and preventing metastasis of the sarcoma. Amputation is thought to be less expensive than limb sparing surgery procedures; however, some studies have proven to be the opposite. According to a study done by Sluga et al., his team concluded that there were not many differences in the overall survival of a patient who underwent amputation and limb sparing surgeries.[17] Amputation is a suitable oncological procedure and can even maintain an athletic lifestyle as post-amputation patients can have the pleasure to use an external prosthesis thereby attain a higher activity level.[11]

The Quality assessment was done according to the standard SF-36 a form that has been proved to be reliable and validated in the Chinese population.[18] It has been accepted for quality evaluation and assessment. In our study, those who had endoprosthesis arthroplasty (LSS1 group) had better scores of SF-36, MSTS, and also fewer complications but while considering only LSS2 Group the recurrence rates and complications were found to be higher. Johansen et al. reported a significantly higher functional score. Our findings of having a better functional outcome in LSS than in amputation and are also consistent with other studies done.[12,13,15,17,18] Cosmetic and social factors also have a significant influence on LSS over Amputation, due to which Limb sparing surgery is preferred over amputations.

The study is only confined to one institute due to which sample size is small. In comparison to other studies, our study also concludes to have assessed a better QOL and higher MSTS score proving a higher functional and emotional outcome in Limb sparing surgery than in amputation.

Conclusion

As survival is similar in all groups, it would be worth accepting the higher risks for whom Limb sparing surgery is feasible by strict follow-up. While at the same time, reserving amputations only for those having local recurrences and in patients resistant to adjuvant chemotherapies. In conclusion, LSS is the better treatment option for tibial Osteosarcoma for both proximal and distal end based on its better QOL, complication-free survival. Therefore, LSS is superior to Amputation.

References

1. Evans DR, Lazarides A, Visgauss JD, et al. Impact of limb salvage versus amputation on overall survival in patients with osteosarcoma of the extremities: an update in the modern era using the National Cancer Database. 2020.
2. Mirabello L, Troisi RJ, Savage SA. Osteosarcoma incidence and survival rates from 1973 to 2004: data from the Surveillance, Epidemiology, and End Results Program. *Cancer: Interdisciplinary International Journal of the American Cancer Society.* 2009;115(7):1531-1543.
3. Picci P. Osteosarcoma (osteogenic sarcoma). *Orphanet journal of rare diseases.* 2007;2(1):6.
4. Huang J, Bi W, Han G, Jia J, Xu M, Wang W. The multidisciplinary treatment of osteosarcoma of the proximal tibia: a retrospective study. *BMC musculoskeletal disorders.* 2018;19(1):315.
5. Campanacci DA, Scoccianti G, Beltrami G, Mugnaini M, Capanna R. Ankle arthrodesis with bone graft after distal tibia resection for bone tumors. *Foot & ankle international.* 2008;29(10):1031-1037.
6. Stéphane S, Eric M, Philippe W, Félix DJ, Raphael S. Resection arthrodesis of the ankle for aggressive tumors of the distal tibia in children. *Journal of Pediatric Orthopaedics.* 2009;29(7):811-816.
7. Ankalkoti B, Pareekutty NM, Kattepur AK, Kumbakara R, Vazhayil R, Balasubramanian S. Life and limb after limb salvage surgery for osteosarcoma in an Indian tertiary cancer center. *Cancer Research, Statistics, and Treatment.* 2019;2(2):145.
8. Mavrogenis AF, Abati CN, Romagnoli C, Ruggieri P. Similar survival but better function for patients after limb salvage versus amputation for distal tibia osteosarcoma. *Clinical Orthopaedics and Related Research®.* 2012;470(6):1735-1748.
9. Natarajan MV, Annamalai K, Williams S, Selvaraj R, Rajagopal T. Limb salvage in distal tibial osteosarcoma using a custom mega prosthesis. *International orthopaedics.* 2000;24(5):282-284.
10. Shalaby S, Shalaby H, Bassiony A. Limb salvage for osteosarcoma of the distal tibia with resection arthrodesis, autogenous fibular graft and Ilizarov external fixator. *The Journal of bone and joint surgery. British volume.* 2006;88(12):1642-1646.
11. Geller DS, Gorlick R. Osteosarcoma: a review of diagnosis, management, and treatment strategies. *Clin Adv Hematol Oncol.* 2010;8(10):705-718.
12. Gaston C, Nakamura T, Reddy K, et al. Is limb salvage surgery safe for bone sarcomas identified after a previous surgical procedure? *The Bone & Joint Journal.* 2014;96(5):665-672.
13. Mei J, Zhu X-Z, Wang Z-Y, Cai X-S. Functional outcomes and quality of life in patients with osteosarcoma treated with amputation versus limb-salvage surgery: a systematic review and meta-analysis. *Archives of orthopaedic and trauma surgery.* 2014;134(11):1507-1516.
14. Ayerza MA, Farfalli GL, Aponte-Tinao L, Muscolo DL. Does increased rate of limb-sparing surgery affect survival in osteosarcoma? *Clinical Orthopaedics and Related Research®.* 2010;468(11):2854-2859.
15. Aksnes L, Bauer H, Jebsen N, et al. Limb-sparing surgery preserves more function than amputation: a Scandinavian sarcoma group study of 118 patients. *The Journal of Bone and Joint Surgery. British volume.* 2008;90(6):786-794.

16. Hettmer S, Fleischhack G, Hasan C, Kral T, Meyer B, Bode U. Intracranial manifestation of osteosarcoma. *Pediatric hematology and oncology.* 2002;19(5):347-354.
17. Han G, Bi W-Z, Xu M, Jia J-P, Wang Y. Amputation versus limb-salvage surgery in patients with osteosarcoma: a meta-analysis. *World journal of surgery.* 2016;40(8).
18. Li L, Wang H, Shen Y. Chinese SF-36 Health Survey: translation, cultural adaptation, validation, and normalisation. *Journal of Epidemiology & Community Health.* 2003;57(4):259-263.

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