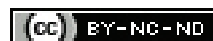


Outcome Analysis of En-bloc Excision and Endoprosthetic Replacement among the Cases Operated for Distal Femoral and Proximal Tibial Giant Cell Tumour around the Knee: A Retrospective Study

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ABSTRACT

Introduction: Giant Cell Tumour (GCT) around the knee joint is the most common site for this locally malignant bone tumour and, in advanced stages, requires excision of the tumour mass. Current recommendations promote joint salvage procedures in allograft or mega prosthetic replacement. Patients undergoing this surgery need massive changes in their lifestyle to cope with their activities of daily living. The psychological and social impact following these procedures has not been extensively studied.

Aim: To observe the long term functional results as well as the impact on quality of life in patients undergoing endoprosthetic replacements in GCT around the knee with emphasis on any difference in results among the cases operated for distal femoral and proximal tibial GCT.

Materials and Methods: This retrospective study was conducted in the Department of Orthopaedic Surgery at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow from June 2015 to June 2019 with a total sample size of 21 cases. The two groups formed were; one having GCT of distal end femur and the other group with GCT of proximal end tibia. The evaluation was done for outcome measures by Oxford Knee Score (OKS) and Musculoskeletal Tumour Society score (MSTS) for their functional outcome and Short Form Health Survey (SF-12) for their quality of life effect at two years postoperatively. Students unpaired t-test

was performed for intergroup analysis and Analysis of Variance (ANOVA) was done for within the group analysis for subsequent follow-up visits. Data was analysed using Statistical Package for Social Sciences (SPSS) version 21.

Results: The mean age of study population was 33.67±8.674 years. The male-female distribution was insignificant ($p=0.673$), providing with a homogenous study group. Recurrent GCT was found significantly more commonly in the proximal tibia group than in the distal femur group ($p=0.031$). Comparison of OKS and MSTS preoperatively, at six months, at one year, and two years showed statistically significant improvement in successive follow-ups in both the distal femur and proximal tibia groups ($p<0.001$ in both groups). Intergroup analysis also showed significantly better scores in the distal femur group compared to the proximal tibia group in the preoperative period and all successive follow-ups. On intergroup analysis at 2 years, both the OKS ($p=0.0206$) and MSTS score ($p<0.0001$) were found to be statistically significant. SF-12 mental and physical scores preoperatively also showed statistically significant improvement in all cases ($p<0.001$) for mental and physical components.

Conclusion: Early functional outcomes of en-bloc excision and reconstruction with modular endoprosthesis are good in terms of joint function and the patient's overall mental and physical well-being.

Keywords: Bone tumour, Malignant, Musculoskeletal tumour society score, Oxford knee score

INTRODUCTION

The Giant cell tumour is a benign aggressive tumour of the bone. It has the capability to metastasise and has a very high recurrence rate after surgery [1-3]. The peak incidence of this tumour is in the third and fourth decade and it comprises 5% of all primary tumours of the bone [1-3]. GCT mostly involves the distal femur, followed by the proximal tibia [4]. Several cases have been reported in other parts of the skeletal system like calcaneum, pelvis, fibula, and other bones [5]. Early stages of this tumour have been traditionally treated with curettage and bone grafting. This procedure has a local recurrence rate of more than 25% [2]. Extended chemical curettage with hydrogen peroxide, liquid nitrogen, phenol, and absolute alcohol can decrease the recurrence rate to 6-25% [2,6]. In the advanced stages, wide en-bloc excision is the preferred method of management. Many techniques of reconstruction have been advocated after en-bloc excision of these tumours [2,3,6].

Post en-bloc resection reconstruction option depends on patient factors and the expertise of the surgical team. Limb salvage surgery in GCT around the knee may be broadly divided into two categories, one in which joint mobility is maintained and the other in which this mobility is hampered. Biological reconstruction with osteoarticular allograft and use of modular endoprosthesis are reconstruction options with preservation of knee joint motion [7,8]. Among the reconstruction methods, use of endoprosthesis has been widely accepted, as it offers the advantages of near-complete resection, low recurrence rate, good short-term postoperative limb function [9-12]. Endo-prosthetic reconstruction in musculoskeletal tumours has evolved over the past four decades with newer implants and techniques developed constantly. Limb-salvage surgery has been made possible by the use of endoprosthesis in many cases, leading to a steady decrease in the rate of amputations [13,14]. Long-term results of tumour endoprostheses in terms of quality of life function and possible complications are important to evaluate [15]. Only one

publication in the literature which has compared the outcomes of GCT of distal end femur and proximal end tibia, managed by endoprosthesis replacement [16]. This study was done with the aim of observing the long-term functional results as well as the impact on quality of life in patients undergoing endo-prosthetic replacements in GCT around the knee with emphasis on any difference in results among the cases operated for distal femoral and proximal tibial GCT.

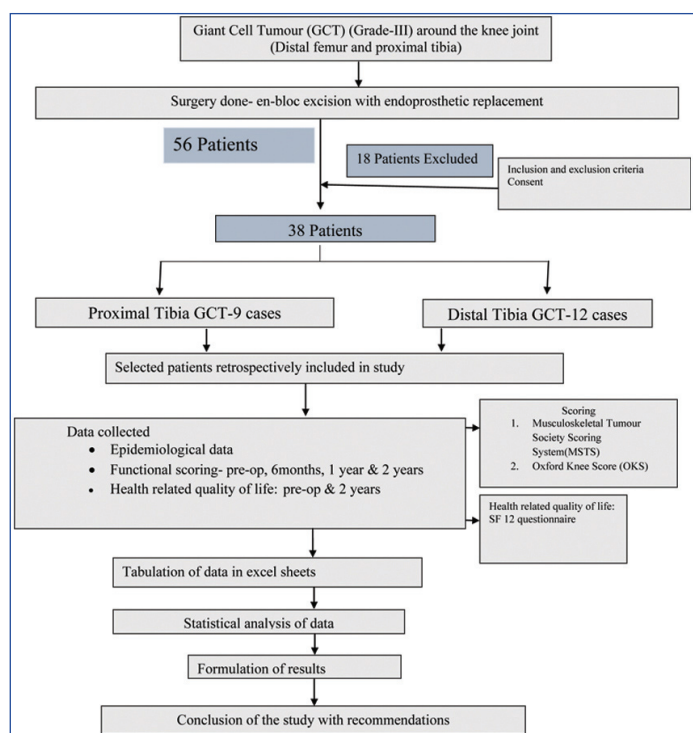
MATERIALS AND METHODS

This retrospective study was conducted in the Department of Orthopaedic Surgery at Dr. Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India, from June 2015 to June 2019 after due permission from the Institutional Ethics Committee (IEC no. 06/21). Patients with GCT around the knee who had been operated on in the department from June 2015 to June 2019 were identified as per the records. The data was collected and analysed on December 2021. All the cases were fulfilling the inclusion criteria formed in the study sample.

Inclusion criteria: All cases with GCT around the knee with Campanacci grade III [17, 18] who had undergone en-bloc excision of the tumour and endoprosthetic replacement were included in the study.

Exclusion criteria: Pregnant patients, patients with significant life-threatening co-morbidities, previous surgery in the same lower limb for reasons other than GCT, those associated with pathological fractures, and patients with neurovascular compromise in the affected lower limb were excluded from the study.

The flow chart of methodology is shown in [Table/Fig-1].



[Table/Fig-1]: Methodology flowchart.

Study Procedure

The cases were categorised into two groups based on the site involved: GCT of the distal femur (N=12) and GCT (N=9) of the proximal tibia. The cases included in the study were assessed for the predetermined outcome measures in terms of functional outcome and health-related quality of life. MSTS [19] and OKS [20] were used for assessing functional outcomes and for assessing the health-related quality of life SF-12 [21] questionnaire was used. Apart from the epidemiological data, clinical examination and relevant scores were collected preoperatively at six months, one year and two years postoperatively. The SF-12 score for the health related quality of life was assessed preoperatively and at two years.

STATISTICAL ANALYSIS

The statistical analysis of the data was done using SPSS version 21. The analysis between the two groups (distal femur GCT and proximal tibia GCT) i.e., the intergroup analysis at different follow-up visits for the OKS and the MSTS score was done by student t-test (unpaired). The intragroup analysis of either groups at subsequent follow-up visits was done by ANOVA (one-way) test. Paired t-test was used to analyse the results of SF-12 score in preoperative period and the final follow-up visit (at 2 years).

RESULTS

A total of 21 cases were retrieved for analysis from the database, fulfilling the inclusion and exclusion criteria- 13 males (61.9%) and eight females (38.1%). The mean age of study population for distal femur and proximal tibia was 33.67±8.674 years [Table/Fig-2]. Recurrent GCT was found significantly more commonly in the proximal tibia group than in the distal femur group (p=0.031).

Variables		Distal femur (N=12)	Proximal tibia (N=9)	p-value
Age	Mean	33.5±8.629	33.89±8.781	t=0.1014 p=0.9203
	20-30 years (N)	7	5	
	31-40 years (N)	5	4	
Sex	Male	8	5	*p=0.6731
	Female	4	4	
Location		12	9	*p=0.0318*
Duration of symptoms (in months)		6±2.663	6.889±2.315	t=0.7992 p=0.4341

[Table/Fig-2]: Demographic parameters of patients.

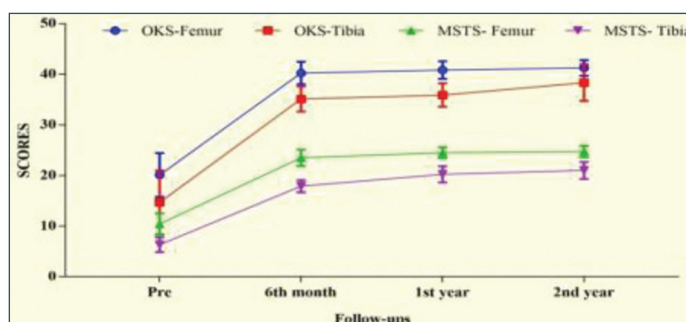
*Significant, *Fisher's-exact test, Student t-test (unpaired)

Comparison of OKS preoperatively, at six months, at one year, and at two years showed statistically significant improvement in successive follow-ups in both the distal femur and proximal tibia groups (p<0.001 in both groups). Intergroup analysis also showed significantly better OKS in the distal femur group compared to the proximal tibia group in the preoperative period and all successive follow-ups [Table/Fig-3,4].

Oxford Knee Score (OKS)	Distal femur (N=12)	Proximal tibia (N=9)	p-value
Pre	20.08±4.337	14.67±6.305	t=2.337 p=0.0305*
6 th month	40.25±2.221	35.11±2.472	t=5.002 p<0.0001*
1 st year	40.83±1.749	35.89±2.315	t=5.586 p<0.0001*
2 nd year	41.25±1.545	38.33±3.606	t=2.526 p=0.0206*
ANOVA	F=176.3 p<0.0001*	F=67.52 p<0.0001*	

[Table/Fig-3]: Pre and Postoperative Oxford Knee Score (OKS) (Distal femur and proximal tibia).

*Significant, Student t-test (unpaired), ANOVA test (one-way)



[Table/Fig-4]: Graph showing serial follow-up OKS and MSTS in distal femur and proximal tibia GCT.

Comparison of MSTs preoperatively, at six months, at one year, and at two years showed statistically significant improvement in successive follow-ups in the distal femur and proximal tibia groups ($p < 0.001$ in both groups). Intergroup analysis also showed a significantly better MSTs in the distal femur group compared to the proximal tibia group in the preoperative period and all successive follow-ups [Table/Fig-5].

Musculoskeletal Tumour Society Score (MSTS)	Distal femur (N=12)	Proximal tibia (N=9)	p-value
Pre	10.42±2.109	6.333±1.581	t=4.862 p<0.0001*
6 th month	23.5±1.624	17.89±1.269	t=8.57 p<0.0001*
1 st year	24.5±1.087	20.22±1.641	t=7.193 p<0.0001*
2 nd year	24.75±1.138	21±1.732	t=5.994 p<0.0001*
ANOVA	F=241.7 p<0.0001*	F=170.5 p<0.0001*	

[Table/Fig-5]: Pre and Postoperative MSTs (Distal Femur and Proximal Tibia).

*Significant, Student t-test (unpaired), ANOVA test (one-way)

Comparing the SF-12 mental and physical score preoperatively and at two years showed statistically significant improvement in both the distal femur and proximal tibia groups ($p < 0.001$ for mental and physical components). Intergroup analysis also showed significantly better SF-12 mental and physical score in the distal femur group compared to the proximal tibia group during the preoperative and two-year follow-up [Table/Fig-6].

Score		Distal femur (N=12)	Proximal tibia (N=9)	p-value
SF-12 Physical score	Preop	26.13±2.132	22.99±1.974	t=3.453 p=0.0027*
	2 years	57.47±1.22	53.39±1.162	t=7.732 p<0.0001*
Student t-test (paired)		t=38.21 p<0.0001*	t=25.86 p<0.0001*	
SF-12 Mental score	Preop	27.78±2.056	25.72±1.743	t=2.413 p=0.0261*
	2 years	60.46±1.189	55.08±0.918	t=11.26 p<0.0001*
Student t-test (paired)		t=25.87 p<0.0001*	t=40.96 p<0.0001*	

[Table/Fig-6]: SF-12 mental and physical score.

*Significant, Student t-test (unpaired and paired), ANOVA test (one-way)

Delayed incision site healing was noticed in nineteen patients. These cases were kept on an extended regime of oral antibiotics, and most of them responded to this conservative management. One patient in the proximal tibia group had wound dehiscence for which a flap coverage was done which resulted in good healing.

DISCUSSION

In present study of GCT around the knee, distal femur GCT is found more commonly, as per the data available in the literature [22]. The presentation time in index cases was predominantly in the fourth decade of their life, and the number of male patients was more. This was in contrast to the existing literature where the most common age group affected was the third decade with a female preponderance [23,24]. The late presentation is probably due to avoidance and ignorance of the symptoms by the patients.

It was observed that patients with GCT of the proximal tibia have a poor functional score regarding OKS and MSTs in the preoperative and postoperative follow-up period. The authors believe that pain in the GCT of the proximal tibia is earlier and more severe than in the GCT of the distal femur. This is due to less muscular coverage leading to increased stretch on the surrounding soft tissue structures

making pain more evident and severe earlier in the course of the disease. These impacts a patient's mental status at a much earlier stage compared to the distal femoral tumour. Poor score in the postoperative period can be explained by the involvement of the knee extensor mechanism due to the tumour and poor soft tissue coverage of the implant leading to compromised knee function and increased soft tissue and implant-related complications. However, Sharil A et al., in their article on endoprosthetic replacements in primary bone tumours around the knee, found no difference in functional outcome between the two anatomical sites [16]. The reason for this discrepancy in finding as compared to this study can be clarified by more prospective studies with larger sample size. On analysing the OKS values, the OKS was found to be improved even after the first year of reconstruction in the proximal tibia group. The improvement of OKS was found to be higher than MSTs. This observation could be attributed to the fact that OKS purely considers function, whereas MSTs considers emotional factors. Further, it is also proposed that the ligament reconstruction was done in the proximal tibia tumour group and the extensor mechanism continues to gain strength even after one year.

On comparing the distal femur and the proximal tibia score at each follow-up period postoperatively, the p-value was found to be statistically significant. The scores of distal femur tumours were better than proximal tibia tumours. The present study concludes that the distal tumours have a poor prognosis compared to proximal tumours. This is because the proximal tibia tumour resection requires extensor mechanism reconstruction and a poor soft tissue cover. Study proposes that, owing to the biomechanics of the lower extremity, in weight-bearing joints, the farther the disease area is from the axial skeleton, the more debilitating it is. The maximal improvement in the functional status of cases in both groups is seen in the initial six months after surgery. After that, the improvement in functional status is there but insignificant. Both the scoring systems have more or less a similar trend. Thus, study conclude that, for evaluating the cases of GCT around the knee joint, either of the scoring systems can be used.

Significant improvement was found in SF-12 scores at the final follow-up as compared to the preoperative scores. Intergroup analysis at two years also showed a statistically significant difference between the groups ($p < 0.0001$). This finding is in synchrony with the observations of both the functional scoring systems. Thus, evaluating the cases of GCT around the knee joint, MSTs can be used as a sole scoring system as it also includes the emotional factor variable, which covers the mental well-being part of the evaluation. There is very scarce literature available where there has been a comparison of functional outcomes between the cases undergoing endo-prosthetic replacement for GCT of distal end femur and proximal end tibia. Moreover, none of the studies have evaluated the need of using an additional scoring system to improve the efficacy of assessment of functional status and quality of life in the postoperative period. In the present study have tried to address the above lacunae.

Limitation(s)

The first is the small sample size. Increasing the sample size will add to the generalisability of results and will provide better strength to the study by increasing its power. This can be done by conducting a multicentre study which will help improve the study sample. A prospective study with an extended follow-up can provide data regarding implant tolerability, duration of lifestyle maintenance and tumour biology in terms of recurrence, if any. The counselling was not done by a trained psychologist, which could have probably helped us, to have better patient outcomes in terms of mental health.

CONCLUSION(S)

Early functional outcomes of en-bloc excision and reconstruction with modular endoprosthesis are very good in terms of joint function

and the overall mental and physical well-being of the patient. MSTs scoring system has been found to be an appropriate scoring system evaluating both the functional and quality of life outcomes. There is a significant difference in functional outcome between the distal femur and proximal tibia with better results seen in distal femur patients.

REFERENCES

- [1] Kamal AF, Simbolon EL, Prabowo Y, Hutagalung EU. Wide resection versus curettage with adjuvant therapy for giant cell tumour of bone. *J Orthop Surg.* 2016;24:228-31.
- [2] Anshul S, Agrawal P, Agarwala S, Agarwal M. Giant cell tumour of bone- an overview. *Arch Bone Jt Surg.* 2016;4:02-09.
- [3] Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA, Matcuk Jr GR. Giant cell tumour of bone: Review, mimics, and new developments in treatment. *Radiographics.* 2013;33:197-211.
- [4] Dahlin DC, Cupps RE, Johnson EW. Giant cell tumour: A study of 195 cases. *Cancer.* 1970;25:1061-70.
- [5] Georgiev GV, Slavchev S, Dimitrova IN, Landzhov BB. Giant cell tumour of bone: Current review of morphological, clinical, radiological, and therapeutic characteristics. *J Clin Exp Invest.* 2014;5:475-85.
- [6] Morii T, Yabe H, Morioka H, Suzuki Y, Anazawa U, Toyama Y. Curettage and allograft reconstruction for giant cell tumours. *J Orthop Surg.* 2018;16:75-79.
- [7] Abed YY, Beltrami G, Campanacci DA, Innocenti M, Scoccianti G, Capanna R. Biological reconstruction after resection of bone tumours around the knee. *J Bone Jt Surg Br.* 2009;91:1366-72.
- [8] Xu XC, Song ZH, Fu XP, Liu. Long-term outcome of giant cell tumours of bone around the knee treated by en bloc resection of tumour and reconstruction with prosthesis. *Orthop Surg.* 2010;2:211-17.
- [9] Meluzio MC, Oliva MS, Minutillo F, Ziranu A, Saccomanno MF, Maccauro G. The use of knee mega-prosthesis for the management of distal femoral fractures: A systematic review. *Injury.* 2020;51(Suppl 3):S17-S22.
- [10] Natarajan MV, Prabhakar R, Mohamed SM, Shashidhar R. Management of juxta articular giant cell tumours around the knee by custom mega prosthetic arthroplasty. *Indian J Orthop.* 2007;41(2):134-38. Doi: 10.4103/0019-5413.32045. PMID: 21139766; PMCID: PMC2989137.
- [11] Yang ZM, Tao HM, Yang DS, Ye ZM, Li WX. The choice strategy of surgical treatment for giant cell tumour close to the knee (Chin). *Zhonghua Wai Ke Za Zhi.* 2006;44:1693-98.
- [12] Myers GJ, Abudu AT, Carter SR, Tillman RM, Grimer RJ. Endoprosthetic replacement of the distal femur for bone tumours: Long-term results. *J Bone Joint Surg Br.* 2007;89:521-26.
- [13] Williard WC, Collin C, Casper ES, Hajdu SI, Brennan MF. The changing role of amputation for soft tissue sarcoma of the extremity in adults. *Surg Gynecol Obstet.* 1992;175:389-96.
- [14] Williard WC, Hajdu SI, Casper ES, Brennan MF. Comparison of amputation with limb-sparing operations for adult soft tissue sarcoma of the extremity. *Ann Surg.* 1992;215:269-75.
- [15] Soares do Brito J, Spranger A, Almeida P, Portela J, Barrientos-Ruiz I. Giant cell tumour of bone around the knee: A systematic review of the functional and oncological outcomes. *EFORT Open Rev.* 2021;6(8):641-50. Doi: 10.1302/2058-5241.6.200154. PMID: 34532071; PMCID: PMC8419793.
- [16] Sharil A, Nawaz A, Nor Azman M, Zulmi W, Faisham W. Early functional outcome of resection and endoprosthesis replacement for primary tumour around the knee. *Malays Orthop J.* 2013;7(1):30-35. Doi: 10.5704/MOJ.1303.01.
- [17] Campanacci M, Baldini N, Boriani S, Sudanese A. Giant-cell tumour of bone. *J Bone Joint Surg Am.* 1987;69(1):106-14. PMID: 3805057.
- [18] Andreas M, Vasilios I, Panayiotis M, Georgios P, Panayiotis P, Panayiotis S. Giant cell tumour of bone revisited. *SICOT-J.* 2017;3:54. Doi: 10.1051/sicotj/2017041.
- [19] Uehara K, Ogura K, Akiyama T, Shinoda Y, Iwata S, Kobayashi E, et al. Reliability and validity of the musculoskeletal tumour society scoring system for the upper extremity in Japanese patients. *Clin Orthop Relat Res.* 2017;475(9):2253-59. Doi: 10.1007/s11999-017-5390-x. Epub 2017 May 30. PMID: 28560530; PMCID: PMC5539034.
- [20] Jenny JY, Diesinger Y. The Oxford knee score: Compared performance before and after knee replacement. *Orthop Traumatol Surg Res.* 2012;98(4):409-12. Doi: 10.1016/j.otsr.2012.03.004. Epub 2012 May 18. PMID: 22609177.
- [21] Huo T, Guo Y, Shenkman E, Muller K. Assessing the reliability of the short form 12 (SF-12) health survey in adults with mental health conditions: A report from the wellness incentive and navigation (WIN) study. *Health Qual Life Outcomes.* 2018;16(1):34. Published 2018 Feb 13. Doi: 10.1186/s12955-018-0858-2.
- [22] Muscolo DL, Ayerza MA, Aponte-Tinao LA. Giant cell tumours of bone. *Curr Orthop.* 2001;15:41-50.
- [23] Pollock R. Management of benign bone tumours. *Orthop Traumatol.* 2009;23:248-57.
- [24] Gitelis S, Mallin BA, Piasecki P, Turner F. Intralesional excision compared with en bloc resection for giant-cell tumours of bone. *J Bone Joint Surg Am.* 1993;75:1648-55.

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