The Surgical Treatment and Outcome of Nonmetastatic Extremity Osteosarcoma with Pathological Fractures

Zhi-Ping Deng¹, Yi Ding¹, Ajay Puri², Edward H M Wang³, Ashish Gulia², Claire Durban³, Xiao-Hui Niu¹

¹Department of Orthopaedic Oncology Surgery, Beijing Ji Shui Tan Hospital, Peking University, Beijing 100035, China
²Department of Orthopaedic Oncology, Tata Memorial Hospital, Mumbai, Maharashtra 400012, India
³Department of Orthopaedics, Philippine General Hospital, University of the Philippines, Manila 1000, Philippines

Abstract

Background: Recent studies have suggested that the presence of a pathological fracture does not impact on oncologic outcomes and the feasibility of limb salvage surgery (LSS) in appropriately selected patients when combined with neoadjuvant chemotherapy. These have largely been single institutional studies with limited numbers. The Eastern Asian Musculoskeletal Oncology Group reviewed the data from three large volume Asian orthopedic oncology centers to determine whether the presence of a pathologic fracture affected outcomes in osteosarcoma patients.

Methods: A retrospective review of the data was conducted. Ninety-five cases of nonmetastatic extremity osteosarcoma with a pathological fracture and 887 cases without fracture treated during the same period were compared.

Results: In the fracture group, the LSS rate was 62.1%, and the rate of amputation was 37.9%. In the nonfracture group, the LSS rate was 74.7%, and the amputation was 25.3%. In patients with a pathologic fracture, the rate of local recurrence for LSS and amputation groups was 8.5% and 2.8%, respectively. In this group, the 5-year survival in the LSS group was 66% as against. 46.8% in the amputation group.

Conclusions: Our study suggests that surgically treated patients with pathologic fractures in osteosarcoma have adequate local control and do not have a poorer outcome compared to patients without a fracture. Though osteosarcoma with a pathologic fracture is not a contraindication for limb salvage, appropriate case selection is important when deciding local control options to ensure adequate oncologic clearance.

Key words: Fracture; Local Recurrence; Osteosarcoma; Survival

INTRODUCTION

Historically, the presence of a pathologic fracture in osteosarcoma has been associated with a poor outcome and has also been considered a contraindication for limb salvage. Recent studies have however refuted these claims and suggested that the presence of a pathologic fracture does not impact on outcomes and the possibility of safe limb salvage surgery (LSS) for appropriately selected pathologic fractures when combined with neoadjuvant chemotherapy. These have largely been single institutional studies with limited numbers. The Eastern Asian Musculoskeletal Oncology Group reviewed the data from three large volume Asian orthopedic oncology centers to determine whether the presence of a pathologic fracture affected outcomes in osteosarcoma patients. We analyzed local control rates and overall survival as outcome measures in these cases and compared them with a group of patients without a pathologic fracture treated during the same period.

METHODS

A retrospective review of the data of three Asian orthopedic oncology centers was carried out. Inclusion criteria included treatment-naïve solitary nonmetastatic osteosarcoma of the extremity with pathological fracture. The Surgical Treatment and Outcome of Nonmetastatic Extremity Osteosarcoma with Pathological Fractures. Chin Med J 2015;128:2605-8.

Address for correspondence: Prof. Xiaohui Niu,
Department of Orthopaedic Oncology Surgery, Beijing Ji Shui Tan Hospital, No 31, Xinjiekou East Street, Xicheng District, Beijing 100035, China
E-Mail: niuxiaohui@263.net

Access this article online

Quick Response Code: 
Website: www.cmj.org
DOI: 10.4103/0366-6999.166025

© 2015 Chinese Medical Journal | Produced by Wolters Kluwer - Medknow

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com
similar osteosarcoma patients without a pathologic fracture treated during the same time period at each institute was also analyzed for comparison. Ninety-five cases of nonmetastatic extremity osteosarcoma with pathologic fracture were enrolled, and 887 cases without fracture were compared as the control group. The ethnic distribution included Chinese, Indians, and Filipinos; the baseline demographic criteria of the two groups were similar, the age and gender in two groups had no difference significantly but the LSS rate was higher in non-fracture group [Table 1]. Histopathological diagnosis was obtained or reviewed in all the cases. Prior to surgery, all patients underwent a thorough oncological assessment to determine the extent of local disease and exclude the presence of distant metastases. Staging studies included plain radiographs and magnetic resonance imaging of the limb, computed tomography scans of the chest, and total body scintigraphy. All patients with pathological fracture were immobilized immediately after fracture by skeletal traction or cast. No internal fixation was employed. Neoadjuvant chemotherapy was given according to the respective hospital protocol, and immobilization was continued during this period. Surgical local control was with either an amputation or LSS. Limb-sparing resection was planned only if oncologically free margins could be achieved while yet retaining useful limb function. After resection, various methods of reconstruction were adopted. These were based on the type of resection, amount of residual bone, individual surgeon preference, and the functional desires of the patient as assessed during preoperative counseling.

**Statistical analysis**

Statistical analysis was performed using SPSS version 13.0 (SPSS, Chicago, IL, USA), with categorical variables compared using Chi-squared tests with a 95% confidence interval. All survival data were analyzed using the Kaplan–Meier method. Overall survival was taken from the date of diagnosis to the last date when the patient was documented to be alive or the date of death. *P < 0.05* was considered statistically significant.

**Results**

In the fracture group, the LSS rate was 62.1%, and the rate of amputation was 37.9%. In the nonfracture group, the LSS rate was 74.7%, and the amputation was 25.3%. All the patients were followed up according to each center’s methods. The groups were well-matched in terms of follow-up period [Table 2]. The local recurrence (LR) rate and the 5-year survival of the 2 groups are shown in Table 2 and Figure 1, there was no significant difference between two groups in LR and survival. In patients with a pathologic fracture, the rate of LR for LSS and amputation groups was 8.5% and 2.8%, respectively (*P = 0.41*). In this group, the 5-year survival in the LSS group was 66% as against. 46.8% in the amputation group (*P = 0.038*) [Figure 2].

**Discussion**

The incidence of pathologic fractures in our series was 9.7%, which is similar to that reported by other authors. Pathological fracture through an osteosarcoma occurs either spontaneously or as a result of minimal trauma, due to their high cellularity, poor differentiation, and loss of matrix.[8] It was believed that the hematoma of fracture may spread and contaminate the adjacent soft tissue hence leading to failure of local control in case limb-sparing surgery was attempted.[7]

With the advent of effective neoadjuvant chemotherapy, improved imaging and refinement of surgical techniques several studies have reported that LSS can be safely employed even in appropriately selected cases of pathological fracture.[3-8]

Natarajan et al.[3] reported on the outcome of 18 patients with pathologic fractures in osteosarcoma, and concluded that the risk of LR in limb salvage is not higher in the presence of a pathologic fracture, and that adequate margins can still be achieved without compromising survival.

Bacci et al.[4] reported 46 cases of nonmetastatic osteosarcoma of the extremity with pathologic fracture at presentation who had been treated in their institution. There were only 2 LRs, 1 after limb salvage and 1 after amputation. They concluded that these rates were similar to their larger control group of 689 patients without pathologic fracture. Bramer et al.[8] examined 484 patients with localized, high-grade extremity
sarcomas and found no difference in the local control rates between groups with and without pathologic fracture.

Ferguson et al.\(^5\) reported 31 cases of osteosarcoma with a fracture and 201 cases without fracture. In the pathologic fracture group undergoing LSS, there were 2 LRs (10%), while in the group without pathologic fracture undergoing LSS, the LR rate was 8%. There was no difference in LR free survival between these groups.

Our local control rates were marginally better in patients with a pathologic fracture compared to those without (LR = 10.5% vs. 12.1%) but this did not reach statistical significance. Being a retrospective study, there is always an element of selection bias, and it is possible that a greater proportion of patients with a fracture underwent an amputation resulting in more radical margins which translated into better local control.

This small improvement in local control did not however translate into improved survival with overall survival being similar in both the fracture and the nonfracture group.

Similar results have been reported by other authors too. Bacci et al.\(^4\) found that their 5-year disease-free and overall survival rates of 59% and 65%, respectively, were not different from their group of patients without pathologic fracture.

Though Kim et al.\(^9\) in a cohort of 384 patients, found that presentation with a pathologic fracture showed a trend toward poorer survival, and it failed to reach significance. In the same paper, there was no difference in overall survival between a case–control study of 37 fractures and 74 matched nonfractured patients. Contrary to these studies, there have been reports that have documented poorer survival in patients with a fracture thus ensuring that the debate regarding outcomes in these patients remains unresolved.\(^5,10\) Further analyzing our group of patients with a pathologic fracture, we found that the rate of LR was higher for the LSS group when compared with the amputation groups (8.5% and 2.8%, respectively) though it failed to reach statistical significance (\(P = 0.41\)). Scully et al. had similar results in a multi institutional retrospective study reviewing 52 patients with a fracture.\(^{10}\) The 5-year survival in the LSS group was significantly better as against the amputation group (66% vs. 46.8%) (\(P = 0.038\)). Though LR may be a harbinger of poorer survival, the significance of LR has not yet been investigated in a suitable multivariable model and LR is not usually quoted as an independent bad prognostic factor for overall survival.\(^{11}\) The improved survival in patients undergoing limb salvage could again be a reflection of selection bias in that patients showing a better response to neoadjuvant chemotherapy (in terms of fracture healing) were chosen for limb salvage while others underwent an amputation.

Our series has its limitations. It is a retrospective review and suffers from the inherent shortcomings of such a study. While comparing the groups with and without a pathologic fracture, we have not analyzed the effect of confounding factors such as tumor volume, margins, and response to chemotherapy while comparing outcomes.

In spite of these shortcomings, we believe that this multi institutional study with large numbers does add to the increasing understanding of the outcome of patients with a pathologic fracture in osteosarcoma, a cohort that is relatively uncommon. Though retrospective, such multi institutional reviews help in generating and supplementing outcome data which eventually may help establish guidelines for the management of these lesions.

In conclusion, our study suggests that surgically treated patients with pathologic fractures in osteosarcoma have adequate local control and do not have a poorer outcome compared to patients without a fracture. Though osteosarcoma with a pathologic fracture is not a contraindication for limb salvage, appropriate case selection is important when deciding local control options (limb salvage vs. amputation) to ensure adequate oncologic clearance.

Acknowledgments

Thanks for the great contribution of my medical statistic colleague Dr. Yan-Wei Lyu. She helped us for the data analysis.
Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Dahlin DC. Osteosarcoma of bone and a consideration of prognostic variables. Cancer Treat Rep 1978;62:189-92.
2. O’Hara JM, Hutter RV, Foote FW Jr, Miller T, Woodard HQ. An analysis of thirty patients surviving longer than ten years after treatment for osteogenic sarcoma. J Bone Joint Surg Am 1968;50:335-54.
3. Natarajan MV, Govardhan RH, Williams S, Raja Gopal TS. Limb salvage surgery for pathological fractures in osteosarcoma. Int Orthop 2000;24:170-2.
4. Bacci G, Ferrari S, Longhi A, Donati D, Manfrini M, Giacomini S, et al. Nonmetastatic osteosarcoma of the extremity with pathologic fracture at presentation: Local and systemic control by amputation or limb salvage after preoperative chemotherapy. Acta Orthop Scand 2003;74:449-54.
5. Ferguson PC, McLaughlin CE, Griffin AM, Bell RS, Deheshi BM, Wunder JS. Clinical and functional outcomes of patients with a pathologic fracture in high-grade osteosarcoma. J Surg Oncol 2010;102:120-4.
6. Jaffe N, Spears R, Eftekhar F, Robertson R, Cangir A, Takaue Y, et al. Pathologic fracture in osteosarcoma. Impact of chemotherapy on primary tumor and survival. Cancer 1987;59:701-9.
7. Abudu A, Sferopoulos NK, Tillman RM, Carter SR, Grimer RJ. The surgical treatment and outcome of pathological fractures in localised osteosarcoma. J Bone Joint Surg Br 1996;78:694-8.
8. Bramer JA, Abudu AA, Grimer RJ, Carter SR, Tillman RM. Do pathological fractures influence survival and local recurrence rate in bony sarcomas? Eur J Cancer 2007;43:1944-51.
9. Kim MS, Lee SY, Lee TR, Cho WH, Song WS, Cho SH, et al. Prognostic effect of pathologic fracture in localized osteosarcoma: A cohort/case controlled study at a single institute. J Surg Oncol 2009;100:233-9.
10. Scully SP, Ghert MA, Zurakowski D, Thompson RC, Gebhardt MC. Pathologic fracture in osteosarcoma: Prognostic importance and treatment implications. J Bone Joint Surg Am 2002;84-A:49-57.
11. Grimer RJ, Sommerville S, Warnock D, Carter S, Tillman R, Abudu A, et al. Management and outcome after local recurrence of osteosarcoma. Eur J Cancer 2005;41:578-83.