

Pathologic Fractures in Osteosarcoma

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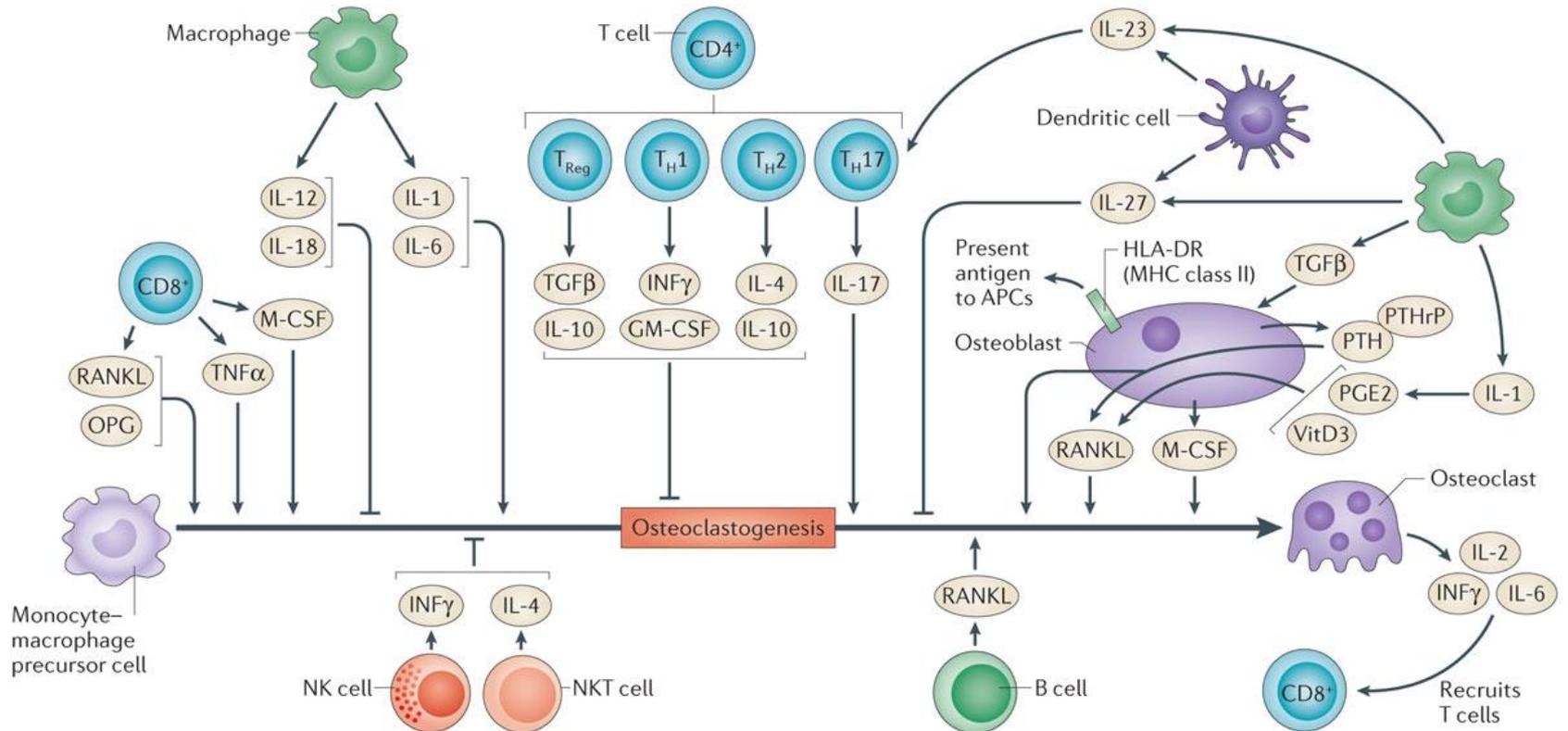
Is Limb Salvage safe?

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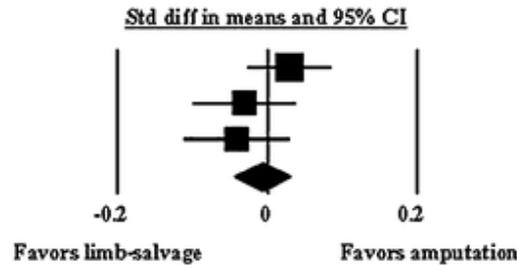
Osteosarcoma



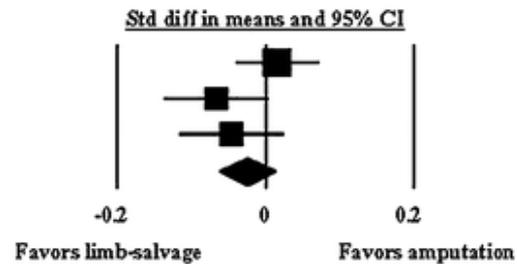
Nature Reviews | Cancer

Quality-of-life outcome measures – limb salvage vs amputation in osteosarcoma patients

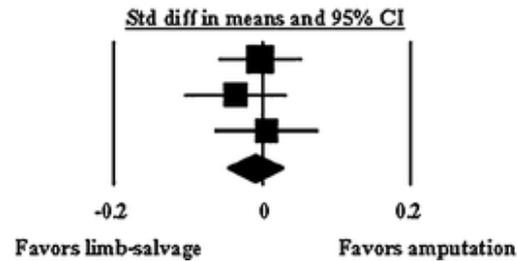
Mental component summary



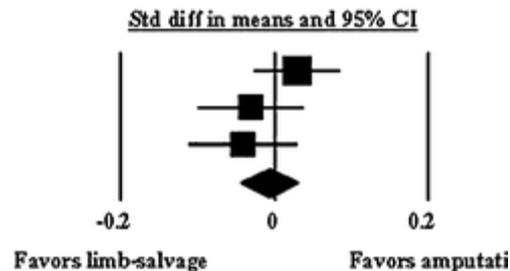
Social functioning



Emotional role



Mental health



Prognostic factors

- Location of the tumour (proximal vs distal)
- Margins
- Chemotherapy response
- Tumour size
- Age of patient
- Serum alkaline phosphatase levels
- Pathological fracture?

Pathological fractures

- Prevalence: 5-10% (in literature)
- Prognostic and treatment implications are widely debated

Carefully selected patients with a pathological fracture undergoing limb salvage may have similar outcomes to those who undergo amputation in terms of

- local recurrence and
- survival compared

when

- adequately treated with neoadjuvant and adjuvant chemotherapy
- adequate surgical resection (margin control)

Factors to consider when advising treatment options

- Response to neoadjuvant chemotherapy
- Evidence of bony union after chemotherapy
- Involvement of soft-tissue
- Joint structures
- Neurovascular structures
- Evidence of metastases at presence



■ ONCOLOGY

Does a pathological fracture affect the prognosis in patients with osteosarcoma of the extremities?

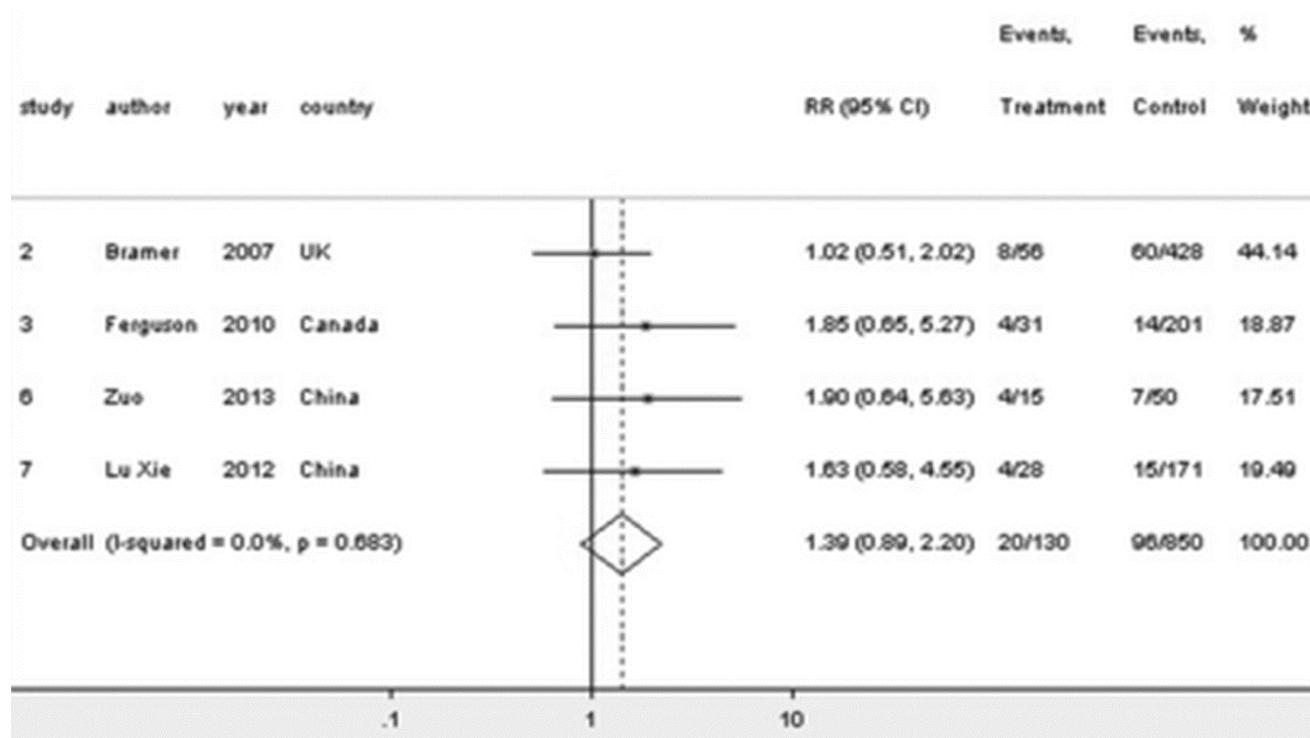
A SYSTEMATIC REVIEW AND META-ANALYSIS

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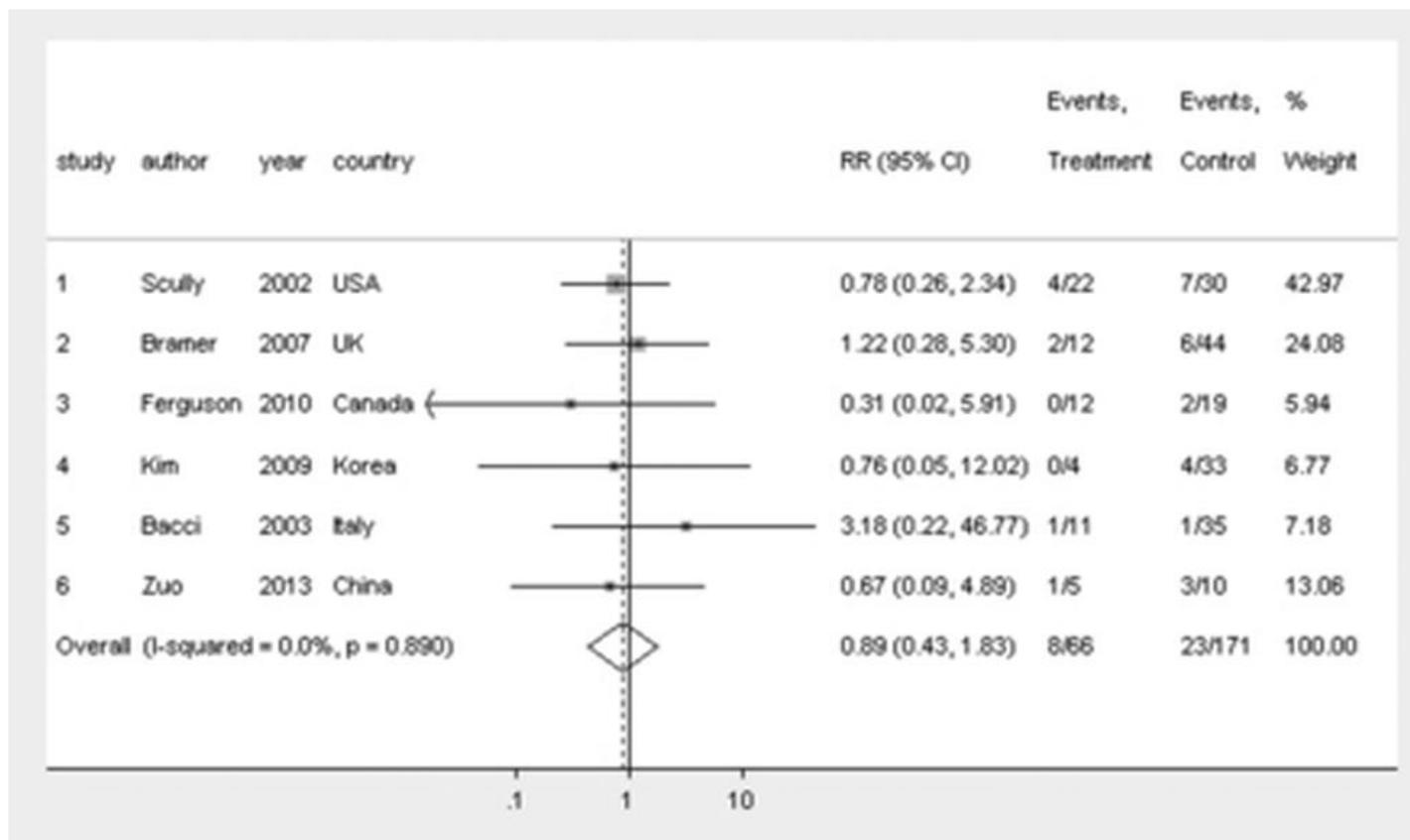
'Limb salvage surgery in the presence of a pathological fracture confers equivalent outcomes to amputation, provided margin control is adequately respected'

Relative risk with 95% confidence intervals for local recurrence between the pathological fracture and non-fracture groups



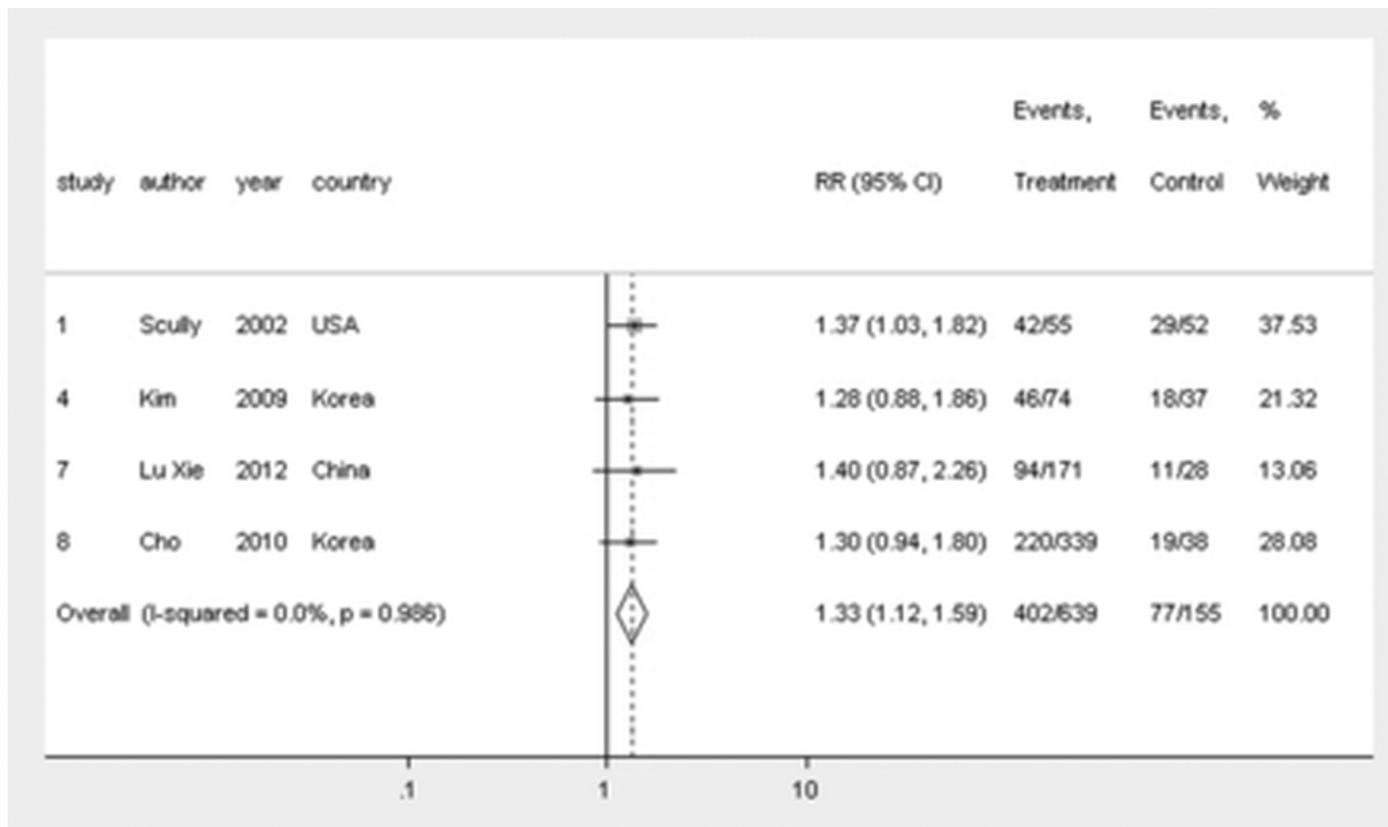
Salunke AA, Chen Y, Tan JH, Chen X, Khin LW Puhaindran ME. Does a pathological fracture affect the prognosis in patients with osteosarcoma of the extremities? : a systematic review and meta-analysis. Bone Joint J. 2014 Oct;96-B(10):1396-403

Relative risk with 95% CI for local recurrence between the amputation and salvage groups in patients with pathological fracture



Salunke AA, Chen Y, Tan JH, Chen X, Khin LW, Puhaindran ME. Does a pathological fracture affect the prognosis in patients with osteosarcoma of the extremities? : a systematic review and meta-analysis. Bone Joint J. 2014 Oct;96-B(10):1396-403

Relative risk with 95% CI for 5-year event-free survival between the non-fracture and pathological fracture groups



Salunke AA, Chen Y, Tan JH, Chen X, Khin LW Puhaindran ME. Does a pathological fracture affect the prognosis in patients with osteosarcoma of the extremities? : a systematic review and meta-analysis. Bone Joint J. 2014 Oct;96-B(10):1396-403

Fracture and tumour characteristics in patients with pathological fractures

| Study | Number of pathological fractures | Number of fracture at presentation | Number of fracture during treatment | Displaced pathological fracture | Undisplaced pathological fracture | Margins (inadequate) | Margins (adequate) | Enneking staging ³² |
|------------------------------|----------------------------------|------------------------------------|-------------------------------------|---------------------------------|-----------------------------------|----------------------|--------------------|--------------------------------|
| Scully et al ⁸ | 52 | 29 | 23 | 16 | 36 | 2 | 50 | Stage 2b |
| Bramer et al ¹⁷ | 56 | - | - | - | - | 21 | 35 | - |
| Ferguson et al ²⁴ | 31 | 20 | 11 | 22 | 8 | 1 | 30 | - |
| Kim et al ²⁸ | 37 | 25 | 12 | 9 | 28 | 8 | 29 | - |
| Bacci et al ¹¹ | 46 | - | - | 8 | 38 | 40 | 6 | - |
| Zuo et al ²¹ | 15 | 8 | 7 | 6 | 9 | 2 | 13 | Stage 2b |
| Xie et al ²² | 28 | 26 | 2 | 11 | 17 | 1 | 27 | Stage 2b |
| Cho et al ²⁹ | 38 | 24 | 14 | - | - | - | - | AJCC* stage 2 ³³ |

*AJCC, American Joint Committee on Cancer

Comparison of local recurrence rates between amputation and limb salvage groups in patients with pathological fracture

| Study | Number of pathological fractures | Local recurrence in pathological fractures | Number of pathological fractures, amputations (%) | Local recurrence (amputation, %) | Number of pathological fractures, limb salvage (%) | Local recurrence (limb salvage, %) |
|------------------------------|----------------------------------|--|---|----------------------------------|--|------------------------------------|
| Scully et al ⁸ | 52 | 11 (21) | 22 (42.3) | 4 (18) | 30 (57.7) | 7 (23) |
| Bramer et al ¹⁷ | 56 | 8 (14) | 12 (21.4) | 2 (17) | 44 (78.6) | 6 (14) |
| Ferguson et al ²⁴ | 31 | 2 (6.5) | 12 (38.7) | 0 (0) | 19 (61.3) | 2 (10) |
| Kim et al ²⁸ | 37 | 4 (10.8) | 4 (10.8) | 0 (0) | 33 (89.2) | 4 (12) |
| Bacci et al ¹¹ | 46 | 2 (4.3) | 11 (23.9) | 1 (9) | 35 (76.1) | 1 (3) |
| Zuo et al ²¹ | 15 | 4 (26.7) | 5 (33.3) | 1 (20) | 10 (66.7) | 3 (30) |

Prognostic Value of Pathologic Fracture in Patients With High Grade Localized Osteosarcoma: A Systemic Review and Meta-Analysis of Cohort Studies

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ABSTRACT: Consensus has not been reached regarding the ability of pathologic fracture to predict local recurrence and survival in osteosarcoma. We aim to review the available evidence to examine the association between pathologic fracture and osteosarcoma prognosis. A comprehensive literature search for relevant studies published until March 2014 was performed using PubMed, Cochrane and Web of Science. The studies investigating pathologic fracture of osteosarcoma patients were systematically analyzed. The overall relative risk (RR) was estimated using a fixed-effect model or random-effect model according to heterogeneity between the trials. We included nine cohort studies involving 2,187 patients (311 with pathologic fracture and 1,876 without fracture) for the analysis of survival rate and local recurrence. Studies were assessed for quality using the Newcastle–Ottawa Assessment Scale. In the fixed-effects model, the meta-analysis showed that pathologic fracture in osteosarcoma patients predicted poor 3-year overall survival (OS) (RR=1.86, 95% CI: 1.37–2.53, $p < 0.001$) and 5-year OS (RR=1.34, 95% CI: 1.06–1.70, $p = 0.016$). Similarly, pathologic fracture was significantly correlated with worse 3-year event free survival (EFS) (RR=1.52, 95% CI: 1.21–1.92, $p < 0.001$) and 5-year EFS (RR=1.24, 95% CI: 1.03–1.49, $p = 0.021$), whereas no significant association was noted with local recurrence (RR=1.30, 95% CI: 0.84–2.02, $p = 0.233$). The meta-analysis confirmed that pathologic fracture in osteosarcoma was a prognostic marker for both OS and EFS but not for local recurrence. © 2014 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. *J Orthop Res* 33:131–139, 2015.

Keywords: pathologic fracture; osteosarcoma; survival; prognosis; meta-analysis

Pathologic fracture does not influence prognosis in stage IIB osteosarcoma: a case–control study

Dongqing Zuo[†], Longpo Zheng[†], Wei Sun, Yingqi Hua^{*} and Zhengdong Cai^{*}

Objective: This study tested the implication of pathologic fractures on the prognosis in stage IIB osteosarcoma.

Methods: A single center retrospective evaluation of clinical management and oncologic outcome was conducted with 15 pathological fracture patients (M:F = 10:5; age: mean 23.2, range 12–42) and 50 non-fracture patients between April 2002 and December 2010. These stage IIB osteosarcoma patients were matched for age, tumor site (femur, tibia, and humerus), and osteosarcoma subtype (i.e., control patients with osteosarcoma in the same sites as the fracture patients). All osteosarcoma patients with pathological fractures underwent brace or cast immobilization, adjuvant chemotherapy, and limb salvage surgery or amputation. Musculoskeletal Tumor Society (MSTS) functional scores were assessed. The mean follow-up time was 34.7 months (range, 8–47 months).

Results: Following limb salvage surgery, no statistical differences were observed in major complications (fracture = 20.0%, control = 12.0%, $P = 0.43$) or local recurrence complications (fracture = 26.7%, control = 14.0%, $P = 0.25$). Overall 3-year survival rates of the fracture and control groups (66.7% and 75.3%, respectively) were not statistically different ($P = 0.5190$). Three-year disease-free survival rates of the fracture and control groups were 53.3% and 66.5%, respectively ($P = 0.25$).

Conclusions: Pathologic fracture was not a prognostic indicator of recurrence or overall survival in localized osteosarcoma patients. Limb salvage can be achieved by and maintaining adequate surgical margins and applying adjuvant chemotherapy.

Keywords: Amputation, Disease-free Survival, Limb Salvage, Osteosarcoma, Pathologic Fracture

Pathological Fracture as the Presenting Feature in Pediatric Osteosarcoma

Ryan K.L. Lee, FRCR,^{1*} Winnie C.W. Chu, MD,¹ Joyce H.Y. Leung, FRCR,¹ Frankie W.T. Cheng, MD,² and C.K. Li, MD²

of the type of operation. **Conclusion.** Osteosarcoma complicated by pathological fracture as first presentation had higher incidence of lung and bone metastases at presentation and worse survival rate when compared with patients without pathological fracture. *Pediatr Blood Cancer* 2013;60:1118–1121. © 2012 Wiley Periodicals, Inc.



Our 18-year experience of high-grade
osteosarcoma with a pathological fracture at
initial presentation

Methods

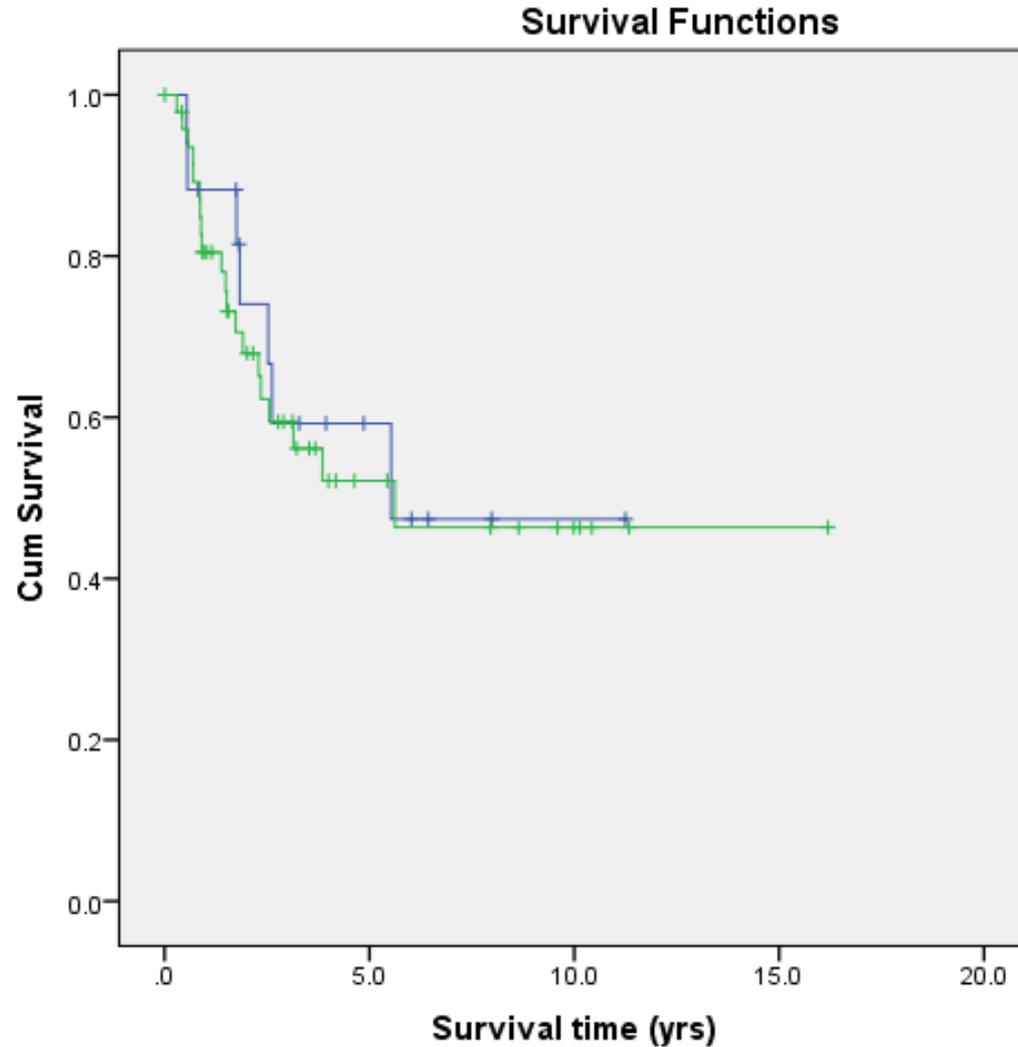
- Prospectively maintained osteosarcoma database
 - 65 patients with primary osteosarcoma
 - 17 patients with pathological fractures at presentation (1994-2012)
- mean follow-up: $3.5 \pm \text{SD}3.4$ years (range 8 months to 18 years)
- Demographic profile, tumour site, metastases, histologic grade, local recurrence rate, overall and event-free survival outcomes

Results

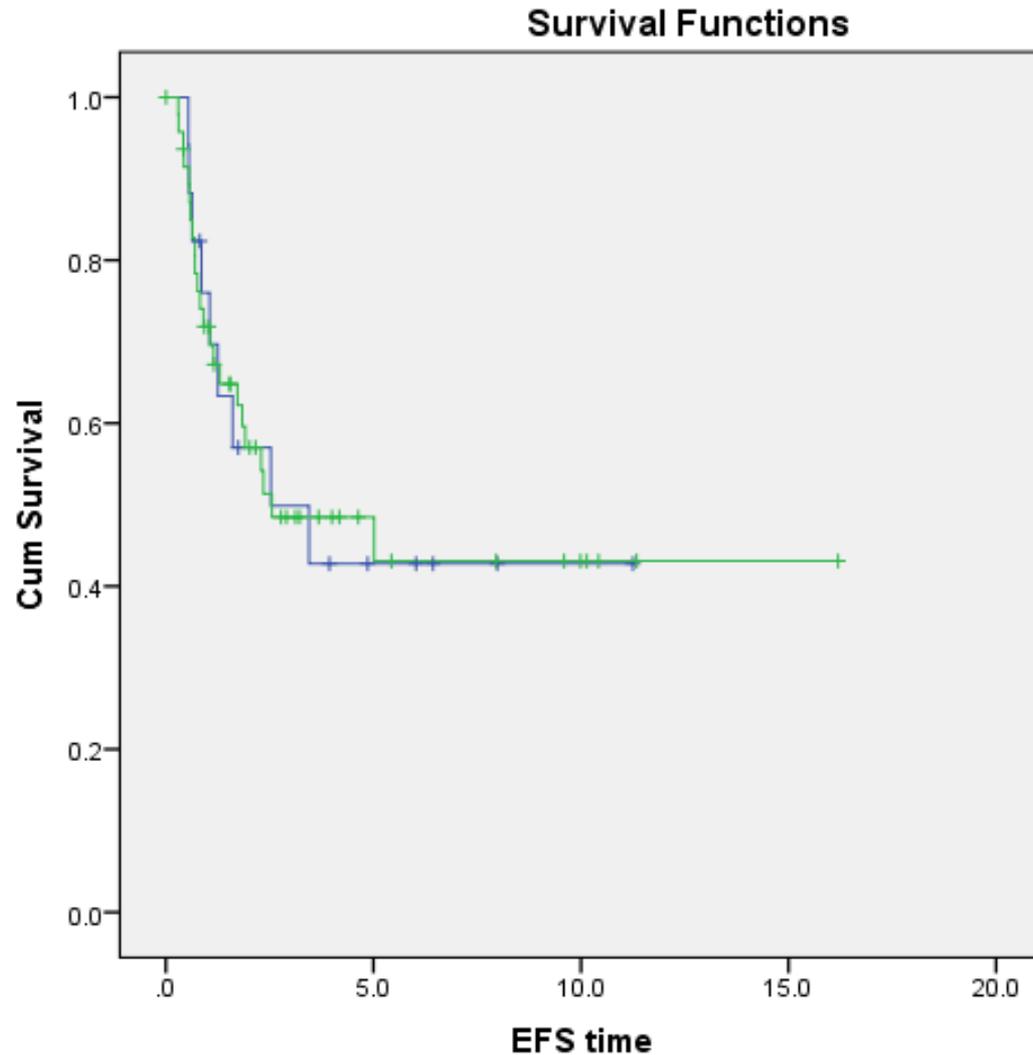
No differences in the survival and recurrence rates of patients with pathological fractures compared to those with no fractures

No difference in survival between amputated and salvaged patients with fractures

Cumulative survival of fractured and non-fractured subgroups



Event-free survival of fractured and non-fractured subgroups



Results II

- The 2 groups were not comparable with respect to extent of local disease
- Resections in pathologically fractured tumours tended to be
 - more extensive
 - dependent less on size of tumour and
 - More on preoperative radiological evaluation of extent of disease using anatomical landmarks

Results III

- 5 local recurrences
 - 1/15 fracture group
 - 4/47 non-fracture group
 - 37 lung metastasis
 - 10/16 fracture group
 - 22/47 non-fracture group
 - Positive margins
 - 1/14 fracture group (marginally resected)
 - 10/38 non-fracture group
- } p = 0.11

Conclusion I

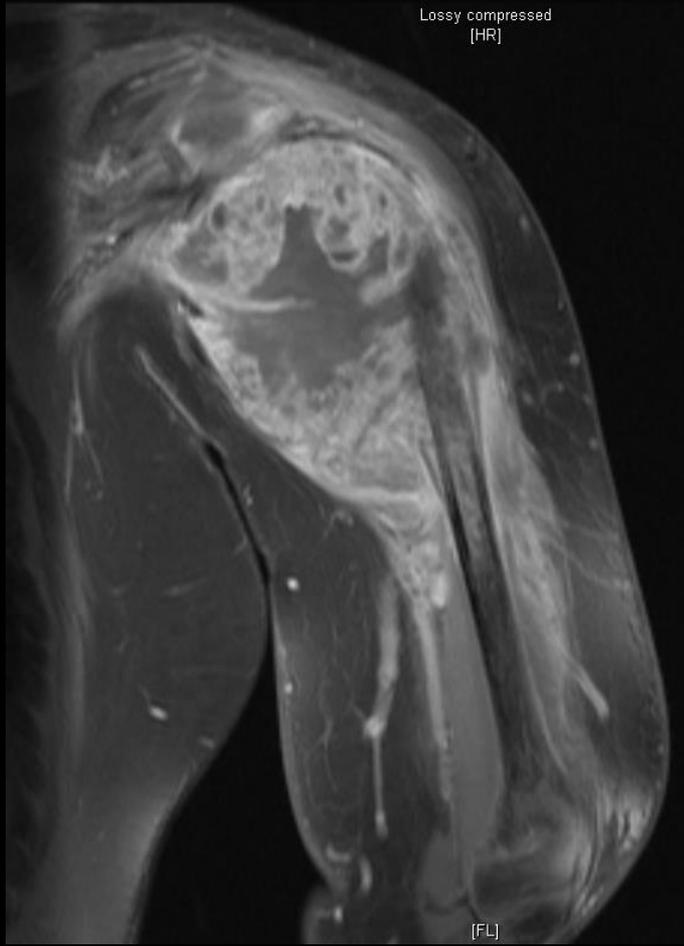
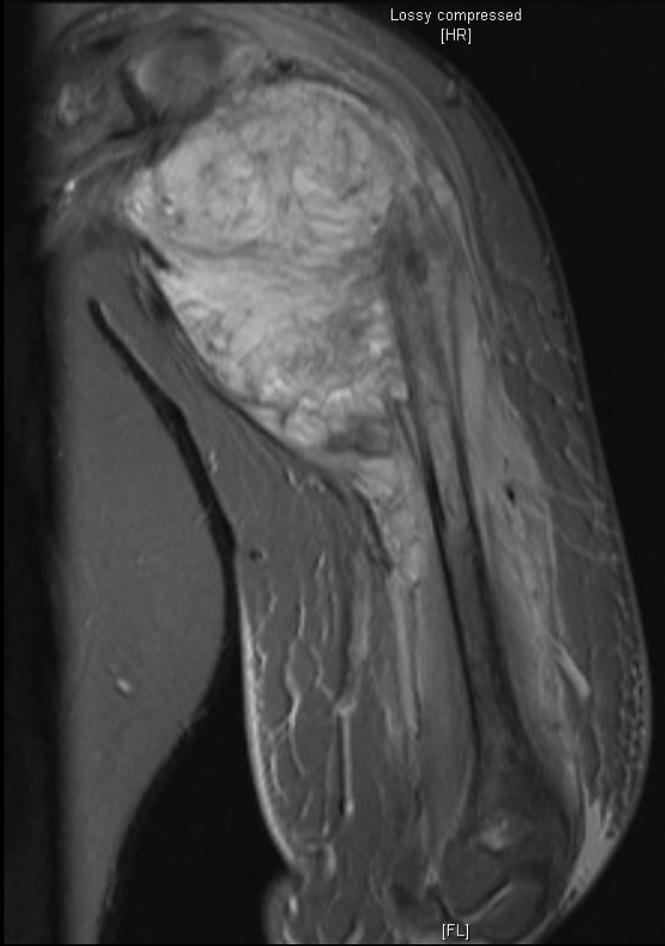
Significant high incidence of pathological fracture in osteosarcoma at initial presentation in our population (17%) as compared to current literature (5-10%)

Conclusion II

Limb salvage surgery does not confer an increased risk of distant or local failure, provided oncological principles are adhered to and margin control attempts are aggressive.

Case example of a 13 year old boy with high grade osteosarcoma of the proximal humerus and pathological fracture at presentation.







Lossy compressed
[H]

L

[F]

L



Intra-Op
Portable



JT

Thank you for your attention

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Faculty of Dentistry
Saw Swee Hock School of Public Health