

## PAPER 1

**Title:** The prognostic importance of pathologic fracture in limb salvage surgery for primary bone sarcoma of the extremities

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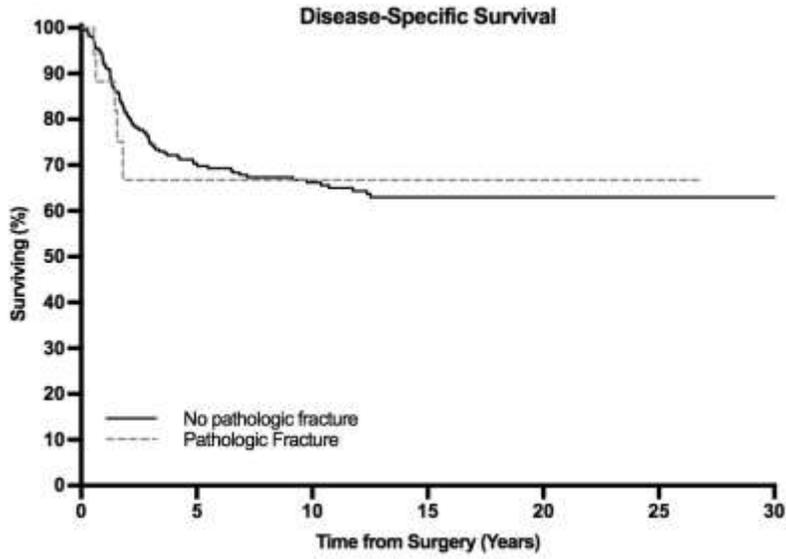
**Background:** Pathologic fracture (PF) has long been regarded as a poor prognostic factor in patients with primary bone sarcoma. The purpose of this study was to determine whether the presence of PF impacts overall survival, the development of distant metastases, local recurrence, or implant survival in patients who undergo limb salvage surgery with endoprosthetic reconstruction for primary bone sarcoma of the extremities, and to determine whether these outcomes differ based upon tumor type.

**Methods:** 373 patients who underwent limb salvage surgery with cemented endoprosthetic reconstruction for extremity primary bone sarcoma between 1980 and 2019 were retrospectively reviewed. 304 patients had osteosarcoma (OS) and 69 patients had chondrosarcoma (CS). The average follow-up of surviving patients was 13.0 years (range: 0.2 – 37.7yrs). Demographic, oncologic, procedural, and outcome data was compared between patients with and without a PF. Implant failure was defined as necessitating revision of the stemmed components or amputation.

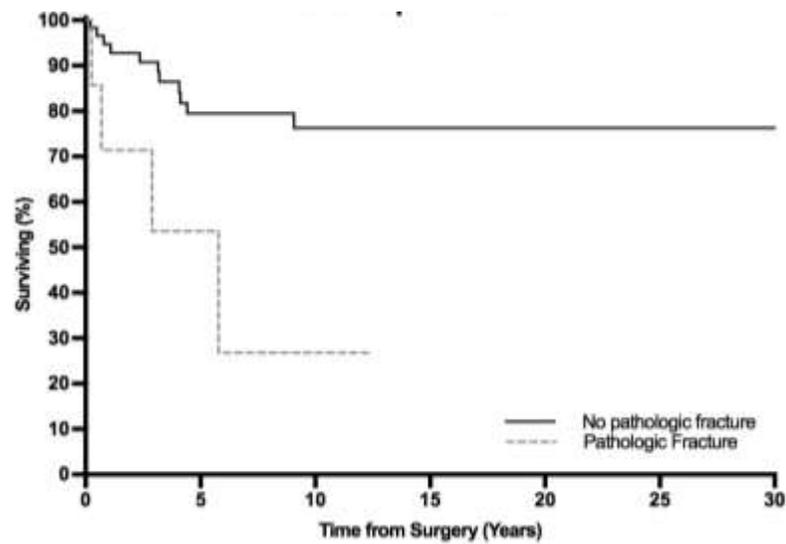
**Results:** 17 patients (5.6%) with OS and 7 patients (10.1%) with CS had a PF prior to limb salvage surgery. In the OS cohort, there were no differences in age (24.7 vs 22.4 yrs;  $p=0.52$ ), sex (52.9% vs 57.1% male;  $p=0.73$ ), disease stage (11.8%/76.5%/11.8% vs 8.3%/80.2%/11.5% stage I/II/III;  $p=0.88$ ), or percent tumor necrosis (74.7% vs 69.5%;  $p=0.46$ ) in patients with and without a PF. In OS, there were no differences in disease-specific patient survival (0.80) (Figure 1A), metastases (35.2% vs 38.3%;  $p=0.80$ ), or local recurrence (17.6% vs 9.4%;  $p=0.27$ ). In CS, PF patients were older (65.0 vs 50.5 years;  $p<0.001$ ) and more likely to have high grade IIA/IIB tumors (28.6%/71.4%/0% I/II/III vs 53.2%/40.3%/6.5%;  $p=0.32$ ) and dedifferentiated disease (42.9% vs 19.4%;  $p=0.15$ ). PF patients with CS had worse disease-specific patient survival ( $p=0.0004$ ) (Figure 1B) and higher rates of metastases (85.7% vs 21.0%;  $p<0.001$ ) and local recurrence (57.1% vs 12.9%;  $p=0.003$ ). For patients with dedifferentiated CS, 100% of patients with a PF developed distant metastases versus 26.3% of patients without a PF ( $p<0.001$ ). Survival to both distant metastases and local recurrence was significantly diminished in CS with a PF ( $p<0.001$  for both) (Figure 2A-B). There was no significant difference in survival of limb salvage between patients with and without PF (100% vs 89.6% at 25 years;  $p=0.55$ ). Overall implant survival was 26.0% at 30 years and did not differ significantly between patients with and without PF (52.3% vs 24.8%,  $p=0.40$ ).

**Conclusions:** In OS, the presence of a PF did not significantly influence disease prognosis. In CS, the presence of a PF in patients who undergo limb salvage surgery was a poor prognostic factor, and a larger proportion of patients with PF had dedifferentiated disease. For patients who undergo endoprosthetic reconstruction, implant survival does not appear to be affected by the presence of a PF.

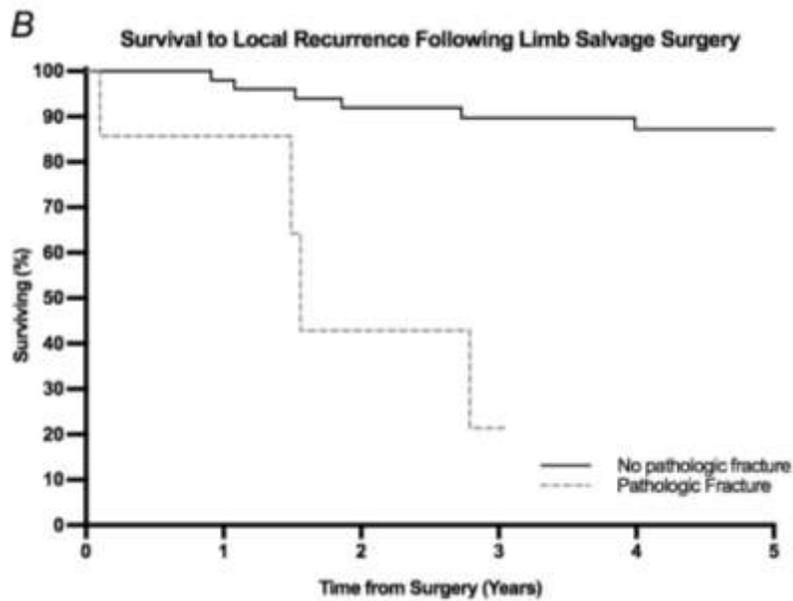
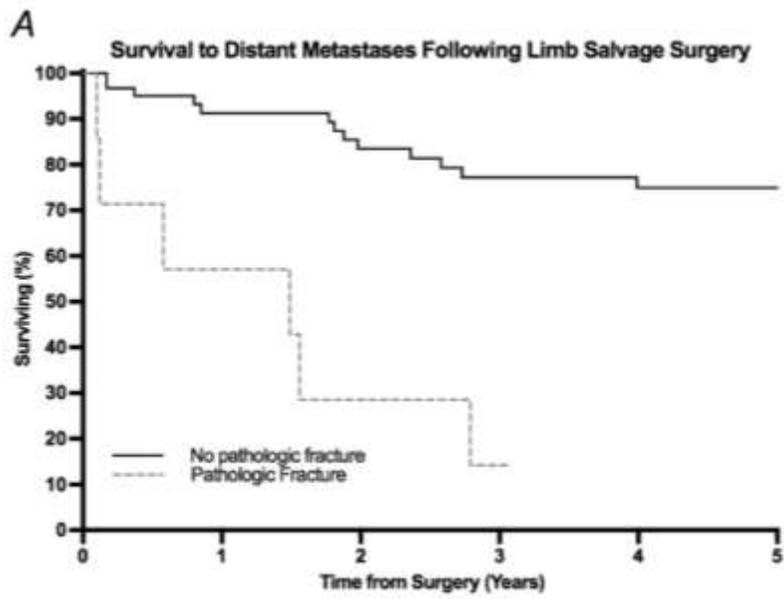
A



B



**Figure 1A-B:** Disease-specific survival following limb salvage surgery was not significantly different between patients with and without a pathologic fracture in osteosarcoma (**Figure 1A**) ( $p=0.80$ ), but was significantly lower in the presence of a pathologic fracture in patients with chondrosarcoma (**Figure 1B**) ( $p=0.004$ ).



**Figure 2A-B:** Following limb salvage surgery for chondrosarcoma, patients with a pathologic fracture had decreased survival to distant metastases (**Figure 2A**) and local recurrence (**Figure 2B**) ( $p < 0.001$  for both).