Healing Time and Complications in Surgically Treated Atypical Femur Fractures Associated With Bisphosphonate Use: A Multicenter Series

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Background/Purpose: Atypical femur fractures associated with bisphosphonate use have been reported to have high nonunion rates and delayed healing. However, published trials have had small patient numbers limiting their conclusions. The purpose of this study is to characterize the demographics, rate of union, healing time, and complications of a large series of surgically treated atypical bisphosphonate femur fractures as well as the natural history of the contralateral femur.

Methods: All bisphosphonate-related fractures as defined by the ASBMR (American Society for Bone and Mineral Research) task force document from 15 centers were reviewed in detail. To be included, patients had to have been treated with bisphosphonates for at least 12 months. Fractures had to be operatively treated and followed for at least 6 months or to union or revision. Average follow-up was 16 months. Data collected included demographics, medication history, prodromal history, injury and surgery characteristics, complications, revision surgery, and time to union. Information about the contralateral limb, when available, was recorded including prodromal symptoms, radiographic signs of stress, and subsequent fracture.

Results: There were 196 patients, 178 women and 18 men, average age 73 years (range, 32-96) and average BMI (body mass index) 27.5; 77% had at least one additional medical risk factor including diabetes, rheumatoid arthritis, thyroid disease, or smoking. 20% of patients had a prior history of fragility fracture, 34% had prodromal pain in the extremity, and 19 of 135 that had clear documentation had pain in the contralateral extremity. 98% percent

See pages 91 - 132 for financial disclosure information.

were ambulatory, 28% with an assistive device, and 85% were living independently prior to the fracture. Patients averaged 79 (range, 12-192) months of bisphosphonate use prior to injury and 51% of patients discontinued bisphosphonates at the time of surgery. 27% had radiographic changes suggesting stress reaction prior to injury and 10% of fractures were periprosthetic. Surgical fixation was with cephalomedullary nail (50%), antegrade nail (37%), retrograde nail (5%), or plate (8%). Complications included pneumonia (4), death (4), pulmonary embolism (3), superficial or deep wound infection (7), hematoma (2), and screw removal (3). 18 patients (9%) underwent revision surgery at an average of 13 months after the initial procedure, most commonly with a cephalomedullary nail. Excluding those who required revision surgery, the average union time was 5.2 months (6.4 for plates and 5.1 for nails) for those whose time to union was clearly discernable based on visit intervals. 22% of patients took >6 months to heal. For the patients who had revision surgery, union occurred at an average of 10 months after secondary intervention, although 5 were lost to follow-up. Continuation or discontinuation of bisphosphonates did not have an effect on time to union ($P = 0.85$) or the need for revision surgery ($P = 0.51$). After fracture fixation patients achieved full ambulation at an average of 4 months, and 92% were living in their homes at the time of final follow-up (25% with help). 9% had a non-femur fragility fracture during follow-up. 20% of patients sustained a contralateral femur fracture, 23 months on average after their index procedure; 45% of these had discontinued bisphosphonate treatment at the time of their index procedure. Of those with information available, 23% had prodromal pain and 35% had a stress reaction on radiography prior to their contralateral fracture.

Conclusion: In this large, multicenter series, atypical bisphosphonate femur fractures occurred primarily in an independently living and ambulatory population. Surgery had a 9% failure rate requiring revision surgery and 22% took greater than 6 months to heal. 20% of patients developed contralateral femur fractures within 2 years, underscoring the need to evaluate the contralateral extremity for stress reactions. Most importantly, 92% were living at home and only 8% were in facilities at final follow-up. This patient population is distinctly different than osteoporotic hip fracture patients and had only a 2% mortality rate at average 16 months.

- The FDA has not cleared this drug and/or medical device for the use described in this presentation (i.e., the drug or medical device is being discussed for an "off label" use). For full information, refer to page 496.