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Original Article

Bisphosphonates and Fractures of the Subtrochanteric or Diaphyseal Femur

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Background

A number of recent case reports and series have identified a subgroup of atypical fractures of the femoral shaft associated with bisphosphonate use. A population-based study did not support this association. Such a relationship has not been examined in randomized trials.

Methods

We performed secondary analyses using the results of three large, randomized bisphosphonate trials: the Fracture Intervention Trial (FIT), the FIT Long-Term Extension (FLEX) trial, and the Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly (HORIZON) Pivotal Fracture Trial (PFT). We reviewed fracture records and radiographs (when available) from all hip and femur fractures to identify those below the lesser trochanter and above the distal metaphyseal flare (subtrochanteric and diaphyseal femur fractures) and to assess atypical features. We calculated the relative hazards for subtrochanteric and diaphyseal fractures for each study.

Results

We reviewed 284 records for hip or femur fractures among 14,195 women in these trials. A total of 12 fractures in 10 patients were classified as occurring in the subtrochanteric or diaphyseal femur, a combined rate of 2.3 per 10,000 patient-years. As compared with placebo, the relative hazard was 1.03 (95% confidence interval [CI], 0.06 to 16.46) for alendronate use in the FIT trial, 1.50 (95% CI, 0.25 to 9.00) for zoledronic acid use in the HORIZON-PFT trial, and 1.33 (95% CI, 0.12 to 14.67) for continued alendronate use in the FLEX trial. Although increases in risk were not significant, confidence intervals were wide.

Conclusions

The occurrence of fracture of the subtrochanteric or diaphyseal femur was very rare, even among women who had been treated with bisphosphonates for as long as 10 years. There was no significant increase in risk associated with bisphosphonate use, but the study was underpowered for definitive conclusions.

Source Information

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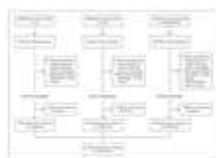


Figure 1

Figure 1. Process for Review of Hip and Femur Fractures from Three Clinical Trials.

FIT denotes Fracture Intervention Trial, FLEX FIT Long-Term Extension (ClinicalTrials.gov number, NCT00398931), and HORIZON-PFT Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly Pivotal Fracture Trial (NCT00049829).

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