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## Should Patients Who Have Periprosthetic Fractures Around the Hip or Knee Be Screened and Treated for Osteoporosis?



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## Should patients who have periprosthetic fractures around the hip or knee be screened, and treated, for osteoporosis?

**Response/Recommendation:** While it is well established that patients who have osteopenia or osteoporosis face a heightened risk of periprosthetic fractures (PPFs) around the hip or knee, current literature lacks conclusive evidence demonstrating that screening and treating these underlying bone conditions markedly reduces the incidence of PPF.

**Level of Evidence:** moderate.

**Expert Vote:** agree 75.9%, disagree 18.1%, and abstain 6%

## Rationale

Periprosthetic fractures (PPFs) can occur at any age following total hip arthroplasty and total knee arthroplasty, but their incidence is notably higher in postmenopausal women and men over the age of 50 years, likely due to the increased prevalence of osteoporosis in these populations [1]. Based on this, the Bone

Health and Osteoporosis Foundation advocates for the prevention, risk assessment, diagnosis, and treatment of osteoporosis in postmenopausal women and men aged 50 years and older [2]. Several studies have focused on the prevention of PPF after total hip arthroplasty and total knee arthroplasty, with some suggesting that a low T-score on dual-energy X-ray absorptiometry scans and reduced bone density around implants may predict the likelihood of PPF [3,4]. Furthermore, the prophylactic use of antiosteoporotic medications, such as bisphosphonates, which are Food and Drug Administration-approved, has been explored. These agents have demonstrated promising results in enhancing bone density around implants in multiple studies [5,6].

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We conducted a comprehensive review of the literature, thoroughly screening and analyzing studies published from 2000 onwards. A total of 16 studies were included in our systematic review, comprising eight randomized controlled trials (RCTs) and eight cohort studies [3,4,7–18]. Larger cohort studies, which incorporated data from smaller cohorts, were prioritized for final analysis to reduce the potential for data overlap. To further explore the effect of prophylactic bisphosphonate use, we performed four separate meta-analyses.

In the first set of studies, two meta-analyses were conducted to compare the rate of PPF between treatment and control groups in RCTs and cohort studies. The analysis of RCTs revealed no statistically significant difference in PPF rates (relative risk (RR) = 1.08, 95% confidence interval (CI): [0.15 to 7.66],  $P = 0.94$ ). Interestingly, in cohort studies involving over 126,000 patients, the PPF rate was unexpectedly higher in the treatment group compared to the control group, although this difference was not statistically significant (relative risk [RR] = 2.56, 95% confidence interval [CI]: [0.73 to 9.03],  $P = 0.14$ ). In the second set of studies, two meta-analyses examined the rate of PPF in relation to the timing of bisphosphonate prophylaxis, comparing preoperative to postoperative administration. Similar to the first analysis, no significant differences in PPF rates were found in either the preoperative prophylaxis group (RR = 2.56, 95% CI: [0.72 to 9.03],  $P = 0.14$ ) or the postoperative prophylaxis group (RR = 1.08, 95% CI: [0.15 to 7.66],  $P = 0.94$ ).

Although PPF can occur at various intervals following surgery, they most frequently arise within the first two years post-operatively. In a study conducted by Namba et al., which included over 34,000 patients aged 40 years and older, the mean time to PPF was reported to be 1.8 years [15]. Additionally, atypical femur fractures, characterized by unusual radiologic features and occurring with minimal trauma, are more prevalent among patients on long-term bisphosphonate therapy [19]. However, the exact incidence of atypical femur fractures was not clearly defined in the studies reviewed, and the distinction between insufficiency fractures and atypical fractures was not established. Importantly, most patients included in the analysis had been on bisphosphonate treatment for a relatively short duration, typically up to six months.

In conclusion, although bisphosphonates have been shown to enhance bone mineral density, their effect on reducing the incidence of PPF remains unproven. Patients receiving prophylactic bisphosphonate treatment appear to experience a similar rate of PPF as those receiving only calcium supplements at a dose of 500 mg. The existing literature indicates that the rate of PPF, particularly around the hip, is affected by the use of uncemented components, both in the early postoperative period and later on by contributing to stress shielding and a subsequent reduction in bone mineral density [20,21].

#### CRedit authorship contribution statement

**Seyed Mohammad Javad Mortazavi:** Writing – review & editing, Project administration, Investigation, Data curation. **Seyed Hadi Kalantar:** Investigation, Data curation. **Shiro Kajiyama:** Writing – review & editing. **David Choon:** Writing – review & editing, Conceptualization. **Antony Palmer:** Writing – review & editing, Conceptualization. **Henrique Cabrita:** Writing – review & editing, Validation. **Riccardo Compagnoni:** Writing – review & editing, Validation. **Jiri Gallo:** Writing – review & editing. **Ali Sol-tani Farsani:** Writing – original draft, Investigation, Formal analysis, Data curation.

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