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Systematic review

Bisphosphonates in Total Joint Arthroplasty: A Review of Their Use and Complications

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ABSTRACT

Background: Considerable interest has been expressed in the use of bisphosphonates to treat periprosthetic osteoporosis with the clinical goals of reducing periprosthetic fractures and prolonging implant survival.
Methods: A systematic review was performed with the goal of identifying both basic science and clinical studies related to the risks and benefits of bisphosphonate use in total joint arthroplasty.
Results: Studies have shown that bisphosphonates may increase early bony ingrowth, decrease the postoperative loss of bone mineral density, and increase the longevity of implants by reducing the need for revisions secondary to aseptic loosening. Continuing bisphosphonates for 1 year postoperatively seems to provide the greatest benefit, with only marginal benefit being shown by continuing therapy for up to 2 years. Current data present some concerns for an increased risk of periprosthetic fractures especially in younger patients, and prolonged therapy is not recommended due to the potential risk of atypical femur fractures. Patients should be counseled regarding the risk of side effects of bisphosphonates, including the risk of osteonecrosis of the jaw, which is a rare but serious side effect. They should also be counseled on the risk of atypical femur fractures and gastrointestinal intolerance.
Conclusions: Orthopedic surgeons could consider bisphosphonates for up to 1 year postoperatively regardless of the patient's prior bone mineral density, after discussion regarding the risks and benefits with the patient.

Introduction

Consistent with risk-reduction strategies in total joint arthroplasty (TJA), considerable interest has been expressed in the use of bisphosphonates to treat periprosthetic osteoporosis with the clinical goals of reducing periprosthetic fractures and prolonging implant survival. This critical review assesses available data on the role of bisphosphonates including advantages and disadvantages of therapy after TJA.

Osteoporosis is a common comorbidity observed in patients undergoing TJA and may contribute to periprosthetic fractures, implant loosening, and shorter implant survival [1-3]. Periprosthetic bone loss is highly undesirable in TJA and is a common culprit for implant loosening or failure prompting the need for revision surgery [4-7]. Bone loss in arthroplasty patients is primarily driven by 2 processes: stress shielding and osteolysis. Stress shielding is caused by alterations in the loading patterns in the bone surrounding implants, as loads are transferred along the implant to the diaphysis, bypassing the proximal femur, for example, following total hip arthroplasty (THA) [8] (Fig. 1). Differences in the metal stiffness of press-fit femoral implants as well as changing the location of porous coating to the metaphyseal region have attempted to address this issue by decreasing osteolysis at the metaphyseal region, thereby decreasing stress shielding at the diaphyseal region. Osteolysis occurs due to macrophage uptake of wear particles, activating osteoclast-mediated osteolysis resulting in subsequent aseptic loosening of the implant [9,10] (Figs. 2 and 3).

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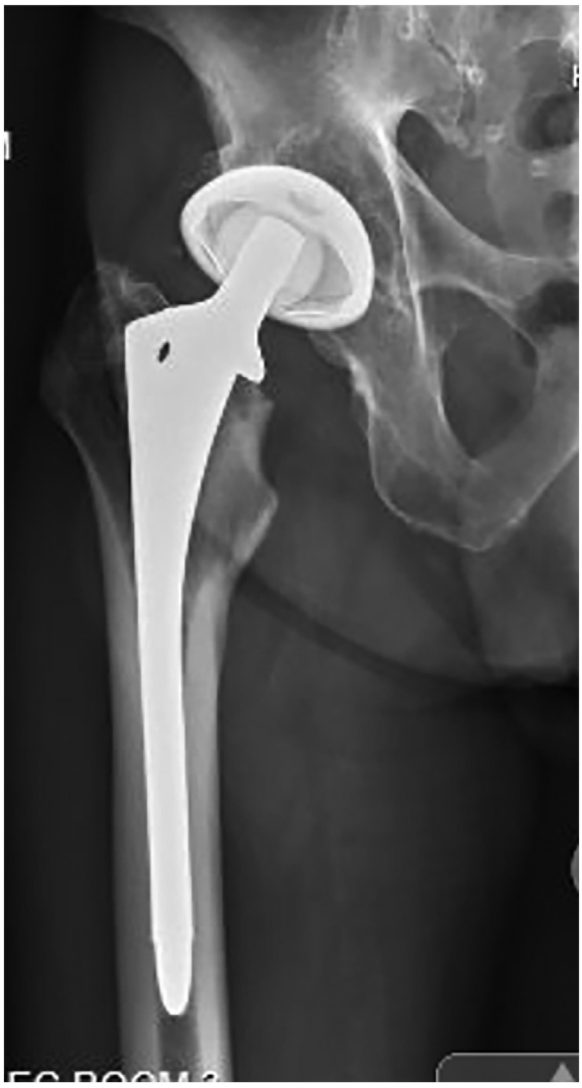

Figure 1. Stress shielding in the proximal femur as a result of load transfer to the femoral diaphysis in a fully-porous coated total hip arthroplasty stem.

It has been proposed that bisphosphonates may halt periprosthetic bone loss, a problem that has been estimated to result in more than 30,000 TJA revision procedures per year [11].

Bisphosphonates are currently the most widely used agents to treat diseases characterized by osteoclast-driven bone resorption, such as osteoporosis and Paget's disease [12]. More recently, these agents have been shown to be effective for other indications; researchers have begun to exploit the medications' ability to prevent the periprosthetic resorption of bone, increase the clinical survivorship of TJA implants, and decrease the rate of revision surgeries [7,13]. Revision TJA is associated with poorer clinical outcomes, increased length of stay, increased complications, and significant financial burden to the patient and health-care system [14]. Therefore, there is considerable interest in therapies to prolong the life span of total joint implants and potentially prevent the need for revision TJA.

The specific mechanisms by which bisphosphonates work is largely dependent on their chemical structures, which can be grouped into 2 classes; non-nitrogen-containing and nitrogen-containing. The earlier developed bisphosphonates, such as etidronate, possessed non–nitrogen-containing side chains and functioned by binding to bone after being metabolized into a cytotoxic adenosine triphosphate (ATP) analog. Osteoclasts subsequently absorb this bone-bisphosphonate complex, and the cytotoxic ATP inhibits osteoclast function and induces apoptosis [15]. The newer bisphosphonates contain amino groups and have been found to be up to 1000 times more potent than their predecessors. These agents act on the mevalonate pathway, which is better known for its role in cholesterol synthesis. In this pathway, it is believed bisphosphonates act primarily by preventing protein prenylation and subsequent GTPase formation, which is vital for the regulation of osteoclasts, including cell morphology, cytoskeleton production, and induction of apoptosis. Specifically, nitrogen-containing bisphosphonates act by inhibiting farnesyl diphosphate synthase [16]. The other mechanism by which these bisphosphonates have been demonstrated to work is through regulation of osteoblast-derived osteoclastogenic factors. For example, some studies have shown nitrogen-containing bisphosphonates decrease the expression of receptor activator of nuclear factor kappa-B ligand (RANKL) and upregulate the expression of osteoprotegerin, a RANKL decoy, thereby decreasing osteoclast-mediated bone loss [17].

While our understanding of bisphosphonate functioning in the setting of systemic diseases such as osteoporosis has increased, it is of paramount importance for further research to elucidate how bisphosphonates function specifically in arthroplasty patients to further optimize how and when we administer these drugs. There are currently no established guidelines or clinical recommendations on whom, when, and how these agents should be administered in the setting of TJA. Furthermore, it is unclear if these agents have the ability to reverse bone loss which has already occurred, rather than just prevent future loss.

Benefits of bisphosphonates in TJA

The potential benefits of bisphosphonates in TJA include increased radiographic/histological bony ingrowth, decreased osteolysis and implant loosening, and decreased risk of all-cause revision rate (Table 1).

Histological advantages of bisphosphonates

In examining the histologic changes that occur with bisphosphonate use, the main concerns revolve around osteoclast inhibition altering the ingrowth into a porous stem and the effect of wear debris on the histologic stability of the bone-implant interface. With regard to total knee arthroplasty (TKA), one study examined the effect of alendronate and zoledronic acid on rabbits at 6 and 12 weeks postoperatively [18]. Each rabbit had bilateral femoral condyles implanted with fiber-mesh-coated titanium-alloy plugs, with the left leg coated with submicron ultra-high-molecular-weight polyethylene debris during surgery to simulate wear-mediated osteolysis. They found that radiographic periprosthetic cortical thickness was increased with both bisphosphonates at 6 weeks (alendronate: +18%; zoledronate: +11%, $P < .0001$) and 12 weeks (alendronate: +17%; zoledronate: +19%, $P = .001$). They also observed histologically that bone volume was increased by 2-fold without any ultra-high-molecular-weight polyethylene wear debris present and more than 3-fold with UHMPE debris present. Finally, they observed histologically that osteoid thickness improved both in the absence of wear debris (alendronate: +132%, $P = .007$; zoledronate: +67%, $P = .51$) and in the presence of wear debris (alendronate: +134%, $P = .023$; zoledronate: +138%, $P = .016$). This study demonstrated that in a rabbit model of wear-mediated osteolysis, similar to total knee

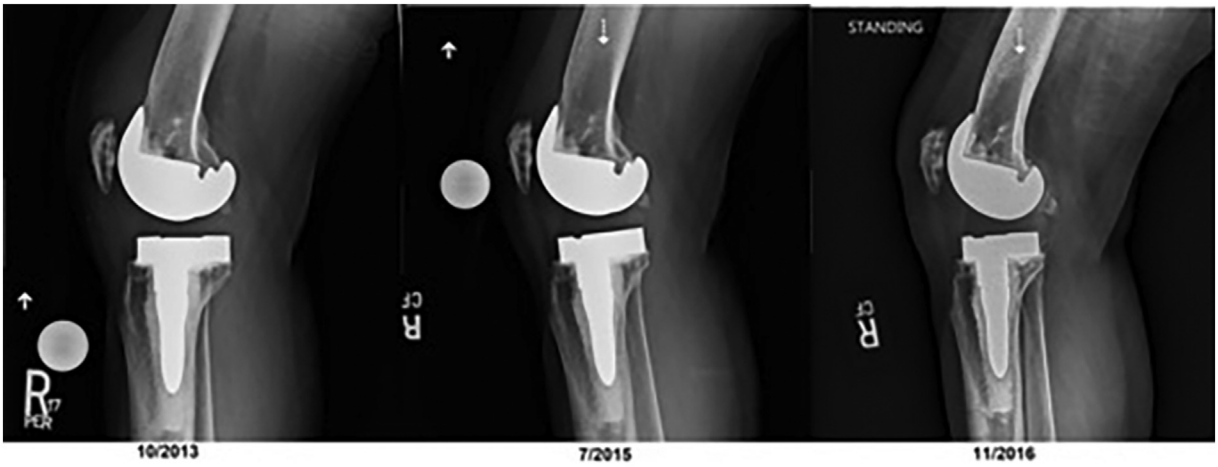

Figure 2. Progressive osteolysis of the distal femur after total knee arthroplasty (arrows).

replacements, bisphosphonates are effective in increasing cortical thickness, bone volume, and osteoid thickness both in the presence and absence of wear debris. This supports the finding that bisphosphonates can both help initial stability and decrease the deleterious effects of osteolysis.

A noninferiority study examined if alendronate inhibited bony ingrowth into hydroxyapatite-coated cementless THA stems at 4 and 24 weeks postoperatively in 12 canines (24 hips) [19]. First, they radiographically compared the control subjects to alendronate subjects and found no significant difference in cortical thickness or radiographic fixation of the femoral component. In a histomorphometric analysis, they found that the linear extent of the hydroxyapatite coating decreased significantly among both the control and alendronate groups from 4 to 24 weeks. However, they found no difference between either group in bony ingrowth of cementless hydroxyapatite-coated implants at both 4 and 24 weeks. Thus, in total hip models, there does not appear to be deleterious effects of bisphosphonates in the early postoperative period, allowing for adequate ingrowth on cementless stems as well as increasing histomorphometric bone volume and osteoid thickness.

Bone mineral density benefits of bisphosphonates in TJA

The effects of bisphosphonates must be evaluated with regard to their role in periprosthetic bone mineral density (BMD) in TJA. In THA, Gruen zones (Fig. 4) have been used to examine the effects of bisphosphonates in BMD on different regions of the femur, with the argument that the more proximal Gruen zones are more clinically relevant for femoral stem stability in cementless total hip stem constructs. In one meta-analysis examining the effects of risedronate on 275 cementless THAs, the authors demonstrated that in comparison to the control group, patients taking risedronate had increased BMD in all Gruen zones as determined by software analysis ($P < .05$) at the 6- and 12-month follow-up periods [20]. This study also found higher Harris hip scores in the risedronate group, as well as higher bone alkaline phosphatase levels and lower urine N-telopeptide of type I collagen levels, indicating better functional outcomes as well as lower levels of bone resorption in the bisphosphonate group.

Another study examined the role of zoledronic acid on reducing BMD loss in 51 patients undergoing cementless THA with injections

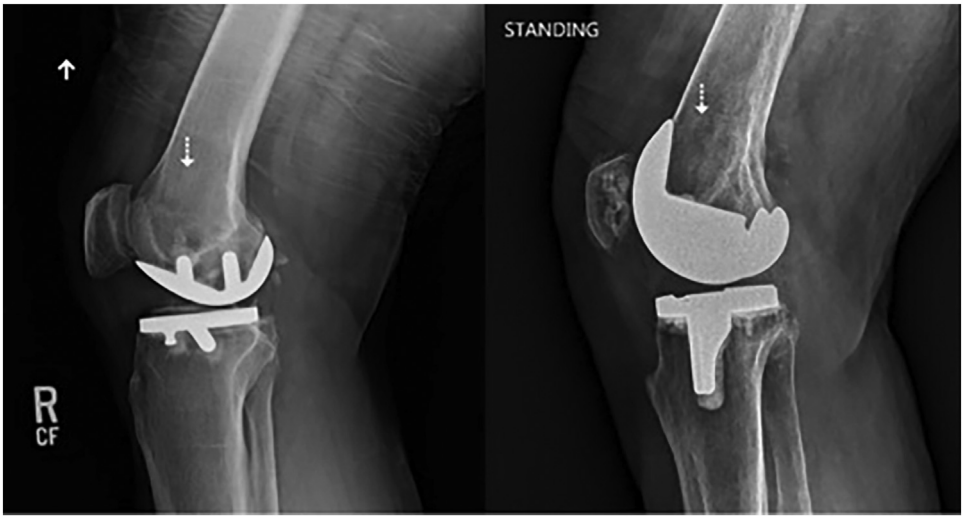

Figure 3. Loss of trabecular texture and bone mineral density after conversion of a unicompartmental implant to a total knee arthroplasty (arrows).

Table 1
List of studies examining bisphosphonates in total joint arthroplasty.

Article	Type of study	Patients (n)	THA/TKA	Bisphosphonate used	Outcome measure
von Knoch et al. [18]	Preclinical	36	TKA	Alendronate/Zoledronic acid	Cortical thickness, bone volume, osteoid thickness
Mochida et al. [19]	Preclinical	24	THA	Alendronate	Early bony ingrowth
Li et al. [20]	Meta-analysis	275	THA	Risedronate	Bone mineral density, Harris hip score, bony resorption
Aro et al. [21]	Retrospective	51	THA	Zoledronic acid	Bone mineral density
Gao et al. [22]	Meta-analysis	185	THA	Zoledronic acid	Bone mineral density
Shi et al. [23]	Meta-analysis	1163	THA/TKA	All bisphosphonates	Bone mineral density
Wang et al. [24]	Prospective RCT	91 women	TKA	Alendronate	Bone mineral density
Bhandari et al. [25]	Retrospective	290	THA/TKA	All bisphosphonates	Bone mineral density
Namba et al. [26]	Meta-analysis	34,116	TKA	All bisphosphonates	Aseptic revision rate
Ro et al. [27]	Meta-analysis	56,043 THA 331,660 TKA	THA/TKA	All bisphosphonates	All-cause revision rate
Prieto-Alhambra et al. [28]	Case-control meta-analysis	10,524	THA/TKA	All bisphosphonates	All-cause revision rate
Yang [29]	Meta-analysis of RCTs	198	THA	Risedronate	Bone mineral density
Teng [30]	Meta-analysis	31,293	THA/TKA	All bisphosphonates	All-cause revision rate
Zhou et al. [31]	RCT	40	THA	Zoledronic acid	Bone mineral density
Khatod et al. [32]	Retrospective	12,878	THA	All bisphosphonates	All-cause revision, periprosthetic fracture

RCT, randomized controlled trial.

at 2 weeks postoperatively and 1 year postoperatively [21]. In total, zoledronic acid was more effective than placebo at preventing BMD loss at both 1 year (+0.80% vs −6.03%, $P < .0001$) and 2 years (−0.16% vs −7.13%, $P < .0001$). They found that it was particularly more effective in the more proximal Gruen zones. Other studies have shown that alendronate is effective in reducing perioperative bone loss after total joint replacement [24,33]. This effect has been shown to result in a 50% decrease in revision rate when bisphosphonates are used after total knee replacement, as well as a 2-fold greater median survival time in both TKA and THAs [28]. Zhou et al. concluded that, specifically in osteoporotic women, 5 mg of zoledronic acid given intravenously (in conjunction with calcium and calcitriol) significantly reduced the amount of periprosthetic bone loss throughout zones 1, 2, 4, 6, and 7 after THA at 1 year postoperatively [31].

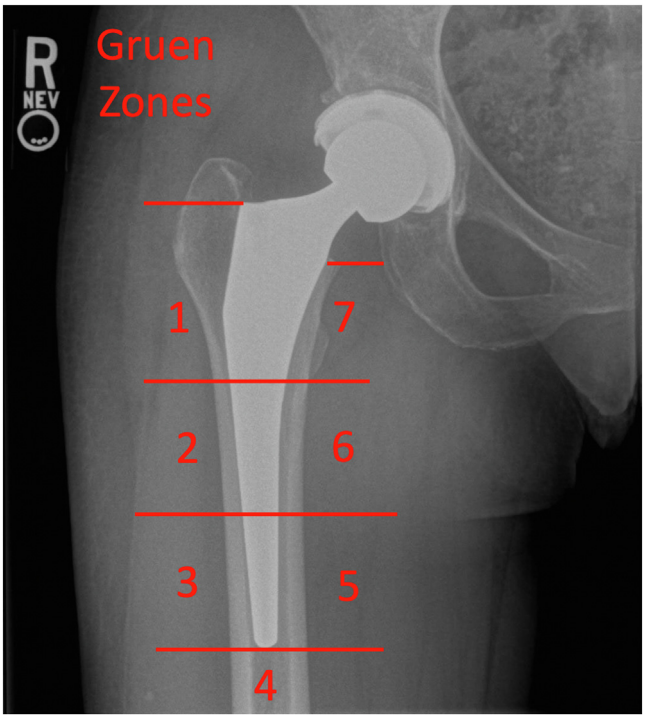

Figure 4. The Gruen zones of the hip.

In one meta-analysis of zoledronic acid including 185 patients with follow-ups of 1-2.8 years, the authors found that BMD was higher in the proximal Gruen zones (Gruen zones 1 [standardized mean difference (SMD) = 0.752, $P = .000$], 2 [SMD = 0.524, $P = .000$], 4 [SMD = 0.400, $P = .008$], 6 [SMD = 0.893, $P = .000$], and 7 [SMD = 0.988, $P = .000$]) [22]. In a multicenter prospective cohort study, Fu et al. found that patients who had osteoporosis and took zoledronic acid had an increase in BMD of 16% over 1 year after THA, compared with patients with osteopenia who lost 10% of their BMD in Gruen zone 1 over the same time period [34]. Similarly, Yang performed a meta-analysis of 198 THAs followed up for up to 6 months from the index surgery to evaluate the efficacy and safety of oral risedronate on BMD after THA [29]. These authors concluded that, in an uncemented femoral component, risedronate significantly reduces periprosthetic bone loss up to 6 months after THA, and no severe adverse events occurred. A second meta-analysis of 198 patients found that compared with placebo, risedronate significantly reduces bone resorption, especially in proximal Gruen zones, without any adverse effects [35].

Another meta-analysis examined the BMD at 3 months through 5-10 years after THA in 1163 patients [23]. They found that at all time points after surgery, the use of bisphosphonate therapy resulted in a higher total BMD than controls. Additionally, they noted that Gruen zones 1 and 7 had significantly higher BMD scores at all time points than controls, and cemented arthroplasty components had significantly greater increases in BMD than cementless components. They observed that second- and third-generation bisphosphonates were more effective than first-generation bisphosphonates in increasing BMD after TJA.

With regard to changes in BMD after TKA, Wang et al. examined 96 women who underwent TKA, with half receiving alendronate for 6 months and half in the control group [24]. They noted that in the distal femur, the control group lost 13.8% ($P < .001$) and 7.8% ($P = .03$) of BMD after 6 and 12 months, respectively. This was in comparison to the alendronate group, which gained 10.0% ($P = .010$) and 1.9% ($P = .049$) of BMD after 6 and 12 months, respectively. In the proximal tibia, the control group lost 6.5% ($P = .002$) and 3.6% ($P = .141$) of BMD after 6 and 12 months, respectively. In the alendronate group, the patients gained 9.4% ($P < .001$) and 5.4% ($P = .032$) of

BMD at 6 and 12 months, respectively, with overall statistical significance between the 2 groups in both the distal femur ($P = .033$) and proximal tibia ($P = .011$).

In another study that retrospectively reviewed 290 patients over 1 year with regard to differences in BMD loss between patients who had received bisphosphonates and controls, they found that at 3 (3.3%, $P < .01$), 6 (4.5%, $P < .001$), and 12 months (4.2%, $P = .03$), bisphosphonates were more effective than controls at preventing BMD loss in both hip and knee replacements [25]. They noted in their review that there was no difference between different types of bisphosphonates in their ability to prevent BMD loss in hip or knee replacements.

Clinical significance of bisphosphonates in TJA

Based upon observations of histologic and radiographic benefits of bisphosphonates, several large retrospective reviews and meta-analyses have examined their clinical significance with regard to revision rates in hip and knee arthroplasty.

Khatod et al. performed a retrospective review of a large database to evaluate for revisions and periprosthetic fractures in THA patients [32]. These researchers found a significantly lower risk of aseptic revision as well as all-cause revision in patients taking bisphosphonates (hazard ratio (HR) 0.53 and 0.50, respectively). However, there was a higher risk of periprosthetic fractures in patients on bisphosphonates (HR 1.92, 95% CI 1.13–3.27), which was more profound in patients younger than 65 years (HR 4.55, 95% CI 1.05-19.6) and those with normal bone quality. These researchers concluded that patients who used bisphosphonates were at lower risk for revision surgery overall; however, younger patients with normal bone quality were at higher risk for periprosthetic fractures. Thus, it is important to consider preoperative BMD and patient age to optimize the use of bisphosphonates in THA.

In one meta-analysis of 34,116 patients who underwent primary TKA, with 6692 of these patients receiving bisphosphonates, they found that the overall aseptic revision rate was lower in the bisphosphonate group (0.5%) than that in the nonbisphosphonate group (1.6%) [26]. This study also examined the effect of preoperative BMD (normal, osteopenia, and osteoporosis) on the effect of bisphosphonates and still found that across all levels of BMD, bisphosphonates were still more effective than controls at reducing the need for aseptic revisions among normal (HR 0.24, $P = .16$), osteopenic (HR 0.34, $P < .001$), and osteoporotic (HR 0.11, $P < .001$) patients. They also found that the effect was age-independent, with patients younger than 65 years (HR 0.35, $P < .001$) benefiting as much as patients older than 65 years (HR 0.26, $P < .001$) when taking bisphosphonates compared with controls. Importantly, they did find the risk of periprosthetic fracture after TKA was increased in patients on bisphosphonates, which must be thoroughly considered by the patient and surgeon when prescribing. More research into this association in TKA is imperative to further elucidate this finding.

Another meta-analysis also examined the rate of revisions in patients who underwent TKA (331,660 patients) and THA (56,043 patients) [27]. These patients were followed up between 4 and 14 years. The researchers found that the TKA revision rate was 1.4% for bisphosphonate users and 2.9% for nonbisphosphonate users ($P < .001$). They also found that the THA revision rate was 2.8% for bisphosphonate users and 5.3% for nonbisphosphonate users ($P < .001$) over the same time period. Additionally, they examined the role of continued bisphosphonate use for greater than 1 year and observed that continued bisphosphonate use beyond 1 year resulted in a further decreased rate of revision (TKA HR 0.472, $P < .001$; THA HR 0.490, $P = .041$). Similarly, a 2015 meta-analysis upon 4 observational studies in both THA and TKA concluded that long-term bisphosphonate use decreases the risk of revision in TJA. However, this author cautioned readers given the overall variable quality and quantity of available studies [30].

Finally, in a case-control meta-analysis of 1558 bisphosphonate users matched to 8966 bisphosphonate nonusers undergoing either THA or TKA, the use of bisphosphonates was correlated with a lower rate of revision with median follow-up duration of 2.61 years (1.73% vs 4.45%, respectively; HR 0.41) [36]. They also examined the effects of medication adherence and length of bisphosphonate administration. They identified a dose-dependent relationship between medication adherence and revision rate (HR 0.38). They found that taking bisphosphonates for 1 year further reduced the risk for revision compared with taking bisphosphonates for 6 months (HR 0.36, $P = .02$) but also that there was no further benefit in patients who took them for 1 year vs 2 years (HR 0.36 vs 0.35, respectively).

Risks of bisphosphonates in TJA

With regard to the risks of bisphosphonate therapy, interest has been on both the general risk of this drug class and the specific risks associated with TJA. The main concern of bisphosphonate therapy is around the highly publicized osteonecrosis of the jaw. Studies have shown that the main risk for osteonecrosis of the jaw is seen in oncology patients, which confers a risk of approximately 5% [2,22,31,37]. In a review of 368 cases of osteonecrosis of the jaw secondary to bisphosphonate use, 353 patients were oncology patients, and of the 353 patients, 60% had undergone tooth extraction or other dental surgery. The other 40% of these cases happened spontaneously but were highly associated with the presence of dentures. Of the 5% of patients who suffer osteonecrosis of the jaw secondary to bisphosphonates, only 4% of those patients did not have malignancy, indicating a very low risk in this cohort of patients [22].

In a study of 185 patients who underwent TJA and received zoledronic acid, there were no cases of osteonecrosis of the jaw, and all adverse events were mild to moderate in severity and able to be managed with supportive care alone [22]. In another study of 49 patients receiving TJA and zoledronic acid with 1-year follow-up, there was no difference in the adverse effects in the zoledronic acid group compared with the control group (68.0% vs 70.8%, respectively) [21]. There was also no statistically significant difference between serious adverse events in either group (8.0% vs 12.5%, respectively). Researchers found that the most common side effect observed was low back pain (28.0% vs 37.5%) and was not related to bisphosphonate use. In regard to risedronate, Yang's meta-analysis also reported no severe adverse events in their study of THAs; however, the follow-up was short (6 months), and thus, monitoring for long-term adverse events must be a priority going forward [29].

In addition to the general concerns about bisphosphonates, specific concerns with respect to TJA have been atypical femur fractures, deep infections, hip dislocations, and periprosthetic fractures. In the 2 prior studies of zoledronic acid, [21,22] none of these complications were observed with a minimum follow-up of 1 year. However, multiple studies as mentioned above have demonstrated an increased risk of periprosthetic fractures, especially in younger patients, and this must be taken into consideration when considering bisphosphonate use in TJA [32,26].

It is important to note that atypical femur fractures have been generally associated with continuous bisphosphonate use over 5 years (Fig. 5). However, the half-life of these medications can be up to 10 years. Thus, even a year of taking these medications can lead to long-term trabecular network changes. In one study, atypical femur fractures were noted to occur approximately 5 years after taking bisphosphonates and commonly occurred in the

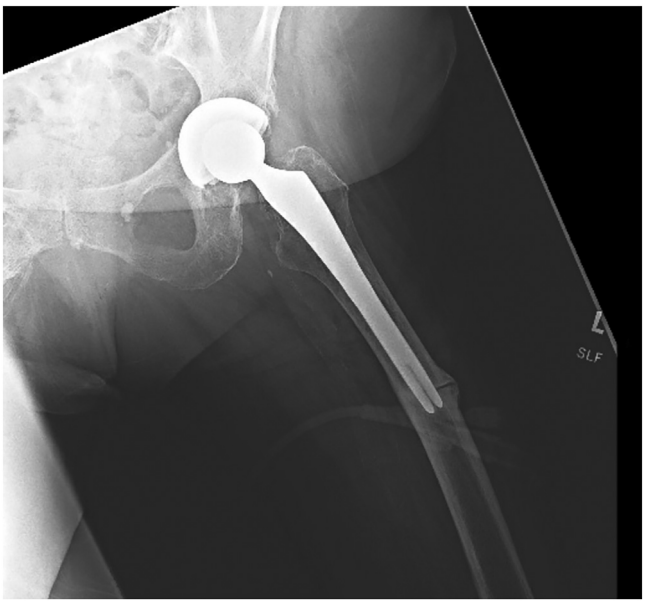

Figure 5. Radiograph of a patient previously treated with alendronate for osteoporosis who underwent THA, subsequently developed atraumatic thigh pain, and was found to have an atypical femur fracture. It was treated with open reduction and internal fixation.

subtrochanteric region or femoral diaphysis [38]. These authors recommend a drug holiday after this time to prevent the occurrence of atypical femur fractures with bisphosphonate use. Lee et al. further examined the role of bisphosphonates in periprosthetic femur fractures; they identified 10 women with 11 atypical peri-implant femur fractures associated with bisphosphonate use [39]. These fractures occurred at an average of 5 years of bisphosphonate therapy and an average of 4 years after their index surgery [39]. This further identifies the role of a drug holiday while on bisphosphonate therapy as well as close clinical monitoring in these patients for signs of impending fracture, including cortical thickening, lateral "beaking" (where the lateral femoral cortex juts out due to a cortical stress reaction, resembling a beak), horizontal lucencies through the subtrochanteric region, or an increase in thigh pain. However, clinical studies to date have limited bisphosphonate use in TJA to 1 year, making atypical femur fractures very unlikely.

In another cohort of 34,116 primary TKA patients, the overall rate of revision was found to be lower for bisphosphonate users (0.5% vs 1.6%), but the rate of periprosthetic fracture was higher among bisphosphonate users, although it was still an infrequent complication (0.6% vs 0.1%, $P < .05$) [26]. This seems to indicate that at least in initial studies, bisphosphonates may provide a protective benefit for all-cause revisions, but at the increased risk of periprosthetic fracture.

Summary and recommendations

Bisphosphonates are a class of medications that act to promote bone formation by osteoclast inhibition. Recently, attention has been on the role of bisphosphonates in TJA to aid in the initial fixation and longevity of implants and reduce the need for costly and morbid revision surgeries.

Recent data have shown that bisphosphonates are effective at increasing early bony ingrowth, decreasing the postoperative loss of BMD, and increasing the longevity of implants by reducing the need for revisions secondary to aseptic loosening. These data have been shown to be effective at all time points up to 2 years of follow-up and is effective in both THA and TKA. At this time, there does not appear to be any significant difference between different forms of bisphosphonates; however, adherence to the medication regimen is one of the largest factors in influencing implant survivorship. Thus, finding a regimen that is feasible for the patient is paramount in the postoperative period.

Regarding duration of bisphosphonate therapy, current data suggest that continuing bisphosphonates for 1 year postoperatively provides the greatest benefit, with only marginal benefit being shown by continuing therapy for up to 2 years. Prolonged therapy, particularly longer than 5 years, is not recommended due to the potential risk of atypical femur fractures.

Patients should be counseled regarding the risk of side effects of bisphosphonates. The most concerning risk is osteonecrosis of the jaw; however, this risk seems to be most significant in patients who have malignancy and undergo any dental procedure or have dentures. Apart from this subset of patients, the risk of jaw osteonecrosis is very low. Other potential side effects appear to be minor, such as nausea or gastrointestinal intolerance, and symptomatic management has been effective in treating all these common side effects.

Overall, bisphosphonates appear to be a relatively safe medication with current data supporting their use in primary TJA in the perioperative period to improve BMD, which may prevent revisions for aseptic loosening. Orthopedic surgeons can consider using them for up to 1 year postoperatively regardless of the patient's prior BMD following discussion regarding the risks and benefits with the patient. Surgeons should discuss the increased risk of periprosthetic fractures until further prospective studies determine the true risk profile of this class of medications. This risk may be additionally elevated in younger patients, and surgeons should be judicious in their use in this cohort. Additionally, osteoporosis is a common problem prior to TJA, with up to 25% of individuals being qualified to receive bisphosphonate medication prior to TJA based on osteoporosis criteria alone [38]. It is imperative that arthroplasty surgeons screen for osteoporosis and consider bisphosphonate therapy both for osteoporosis and for implant survival to decrease revisions. The greatest benefit would likely be in patients aged 65 years or older with a T-score less than −2.5 to help decrease the risk of periprosthetic fractures seen in younger patients and provide the greatest benefit in aiding bony ingrowth and preventing aseptic loosening. For patients who are already on bisphosphonates at the time of TJA, a conversation between the surgeon and patient should take place to discuss the length of therapy and the above risks, as well as the possibility for atypical femur fractures with prolonged use. In this scenario, shared decision-making may help both surgeon and patient feel comfortable with the decision to continue or stop bisphosphonate use. Currently, data regarding this topic have focused on basic science and retrospective cohort studies. Further high-quality prospective studies are necessary to further elucidate the potential benefits and risks of bisphosphonates and TJA to guide surgeons regarding the use of this important class of medications.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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