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Review article

Risk assessment and drug interruption guidelines for dentoalveolar surgery in patients with osteoporosis receiving anti-resorptive therapy

Ling-Ying Wei [a,b], Ching-Ming Chiu [c], Sang-Heng Kok [a,d], Hao-Hong Chang [a,d], Shih-Jung Cheng [a,d], Hung-Ying Lin [a,d], Wei-Yih Chiu [e], Jang-Jaer Lee [a,d*]

[a] *Department of Dentistry, School of Dentistry, College of Medicine, National Taiwan University, Taipei, Taiwan*
[b] *Department of Dentistry, National Taiwan University Hospital, Bei-hu Branch, Taipei, Taiwan*
[c] *Department of Internal Medicine, National Taiwan University Cancer Center, Taipei, Taiwan*
[d] *Division of Oral and Maxillofacial Surgery, Department of Dentistry, National Taiwan University Hospital, Taipei, Taiwan*
[e] *Division of Endocrinology and Metabolism, Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan*

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Risk assessment

Abstract Medication-related osteonecrosis of the jaw (MRONJ) is a rare and challenging complication of anti-resorptive therapy. This review addresses the critical issue of risk management in patients with osteoporosis who require dentoalveolar surgery while undergoing anti-resorptive therapy. Dental practitioners should be aware of these risks; however, they should not refuse treatment based solely on them. This review discusses the risks through five major factors: invasive dentoalveolar surgeries, concomitant oral infection, type of medication, duration of medication, and preoperative drug discontinuation. Additionally, we discussed the local factors associated with dental practices. Our review underscored the importance of personalized risk assessment, considering each patient's unique drug history and oral condition. Based on a comprehensive literature review and clinical evidence, we proposed specific guidelines for preoperative drug interruption tailored to different anti-resorptive agents. These recommendations aimed to balance osteoporosis management by minimizing the risk of MRONJ during oral surgical interventions and bridging the knowledge gap in managing patients with osteoporosis requiring dental care. This review will allow

* Corresponding author. Department of Dentistry, School of Dentistry, College of Medicine, National Taiwan University, No. 1, Chang-De Street, Taipei 10048, Taiwan.
E-mail address: leejj@ntuh.gov.tw (J.-J. Lee).

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clinicians to improve their practice and optimize patient outcomes by providing evidence-based strategies.

Introduction

With increasing life expectancy, the global elderly population is also increasing, leading to an increase in osteoporosis cases.[1] According to data from Taiwan's National Health Insurance system, the prevalence of osteoporosis among individuals aged 50 years and older has exhibited a substantial increase, increasing from 17.4 % in 2001 to 25.0 % in 2011.[2,3] However, the actual prevalence may have been underestimated because osteoporosis often remains asymptomatic and undiagnosed. This finding emphasizes the critical need for enhanced awareness, early detection, and proactive intervention strategies in this demographic group. Patients with osteoporosis have an elevated risk of severe fractures owing to decreased bone mineral density and compromised structural integrity.[4] In Taiwan, elderly patients with osteoporosis-related hip fractures exhibit significantly higher one-year mortality rates (11.2 % in women and 18.0 % in men) than their counterparts without fractures (2.8 % and 3.6 %, respectively).[5] Prolonged post-fracture immobilization can result in significant complications including compromised circulatory function and increased susceptibility to infections, which are major contributors to fracture-related mortality.[6] Early therapeutic intervention for osteoporosis is crucial to mitigate the risk of severe fractures and related mortality.

The primary treatment for osteoporosis involves medication,[7,8] such as anti-resorptive agents that inhibit osteoclast activity and anabolic agents that promote bone formation (Fig. 1A). In 2003, concerns were raised about the use of bisphosphonates (BPs), a class of anti-resorptive drugs such as zoledronate, pamidronate, and alendronate, owing to potential side effects that could lead to osteonecrosis of the jaw (Fig. 1B).[9] The American Association of Oral and Maxillofacial Surgeons (AAOMS) classified these conditions as medication-related osteonecrosis of the jaw (MRONJ) in 2014 and modified the definition in 2022 as understanding increases.[10,11] A staging system for MRONJ has also been introduced and modified using the AAOMS. The typical symptoms of MRONJ include pain, gingival swelling, paresthesia of the lower lip, suppuration, tooth loosening, and necrotic bone exposure, which are signs of infection. Radiographic images may reveal osteolysis, osteosclerosis, sequestral formations, and pathological fractures (Fig. 2).

Approximately half of the MRONJ cases are associated with invasive dental procedures, such as dental extraction and implant placement, performed during anti-resorptive therapy (ART),[12,13] which is a finding that has caused considerable concern and apprehension among dentists. Dental practitioners may be reluctant to provide care for patients receiving ART owing to the paucity of standardized clinical protocols, even for simple dental procedures, resulting in potentially unnecessary specialist referrals. Such clinical hesitancy may compromise the timely intervention and optimal management of oral health conditions in this patient population. Conversely, owing to an insufficient understanding of MRONJ, some dentists may perform invasive dental surgeries, such as extractions and implant placements, without implementing adequate preventive strategies during ART, potentially leading to unnecessary MRONJ cases. This paradox of excessive precaution and knowledge-based neglect reflects the current challenges faced by dental practitioners in managing patients with osteoporosis receiving ART. In response to this knowledge gap, this review sought to provide evidence-based guidance for dental practitioners to optimize their clinical management protocols.

Risk assessment and prevalence of medication-related osteonecrosis of the jaw in patients with osteoporosis

The prevalence of MRONJ among patients with osteoporosis receiving ART ranged from 0.02 % to 0.3 % across all pharmacological agents, with a potential tenfold increase in risk following dentoalveolar surgical interventions (Fig. 3).[11] Current evidence indicates that patients with osteoporosis receiving ART have a low incidence of MRONJ, with risk stratification varying significantly among the different dental treatments. Fig. 3 illustrates the spectrum of invasive dental procedures that warrant particular attention in clinical risk assessments by dental practitioners. This article discusses five major risk factors and minor factors associated with dental practice for MRONJ.

First factor: invasive dentoalveolar procedures

Dentoalveolar surgical procedures, specifically tooth extraction and implant placement, are recognized as primary risk factors for MRONJ development owing to their associated alveolar trauma. Epidemiological studies have demonstrated that tooth extraction represents a significant precipitating event in MRONJ cases, with reported data indicating an approximately nine-fold increase in the incidence of MRONJ.[14] A nationwide retrospective cohort analysis utilizing Taiwan's National Health Insurance Research Database aligned with these findings, demonstrating that patients with osteoporosis receiving alendronate therapy who underwent tooth extraction experienced a 9.6-fold higher risk of MRONJ than their non-extraction

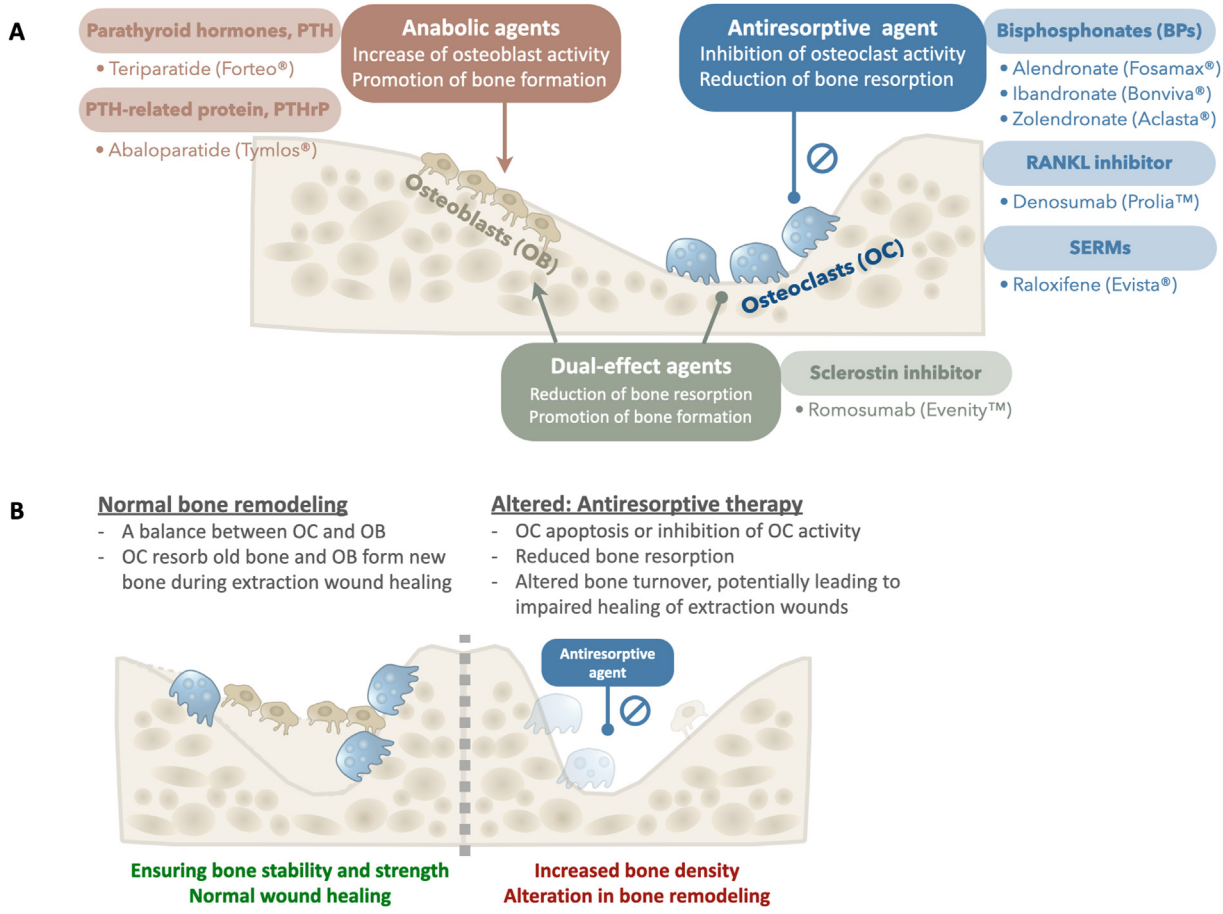


Figure 1 Medications for osteoporosis and their effects on bone remodeling. (A) The diagram outlines the different classes of medications used to manage osteoporosis. Anabolic agents like parathyroid hormone (PTH) and PTH-related protein (PTHrP) stimulate osteoblast (OB) activity to promote bone formation. In contrast, antiresorptive agents such as bisphosphonates (BPs), receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitors, and selective estrogen receptor modulators (SERMs) inhibit osteoclast (OC) activity to reduce bone resorption. Dual-effect agents can both decrease OC-mediated resorption and enhance OB-driven bone formation. (B) Effects on bone remodeling. Normal bone remodeling involves a balance between OC and OB activity. By inhibiting OC activity and reducing bone resorption, antiresorptive agents can lead to decreased bone turnover. This alteration in bone remodeling may potentially impair the healing of extraction wounds and lead to medication-related osteonecrosis of jaws.

counterparts.[15] Additionally, 52–61 % of MRONJ-affected sites have previously undergone tooth extraction.[16–21] In the following paragraphs, the most common invasive dentoalveolar procedures performed in dental clinics are discussed.

Dental extractions

For patients undergoing ART, minimizing elective dentoalveolar surgery is recommended where clinically feasible. However, dentoalveolar surgery should not be considered an absolute contraindication. In the presence of active dental infections, prompt therapeutic intervention is essential to prevent the progression to severe infections and potential MRONJ development. When clinical manifestations of infection are present, and tooth preservation through conservative measures is not feasible, surgical extraction remains the recommended therapeutic approach. The following precautions should be taken when extracting teeth:

1. Administer prophylactic antibiotics 1 h preoperatively.
2. Use minimal flap design with periosteal preservation to maintain blood supply.
3. Minimize bone removal with copious saline irrigation.
4. Limit extractions to fewer than three teeth per quadrant.
5. Achieve primary soft tissue closure to minimize bone exposure.
6. Avoid bone graft materials to prevent foreign body reactions.
7. Prescribe postoperative antibiotics and chlorhexidine mouth rinse.

Dental implantations

According to the MRONJ position paper published by AAOMS in 2014, the risk of developing MRONJ following dental implant procedures is similar to that associated with tooth extraction.[10] While the current evidence suggests that ART

	Stage 0	Stage 1	Stage 2	Stage 3
Exposed bone	• No exposed bone	• Exposed bone • Necrotic bone	• Exposed bone • Necrotic bone	• Exposed bone • Necrotic bone
Patient symptom	• Non-specific • Odontalgia (not odontogenic cause) • Dull pain	• No symptom	• Symptomatic • Pain	• Symptomatic • Pain
Infection sign	• No infection	• No infection	• With infection • Erythema, pus	• With infection sign • ≥ 1 of following ✓ Extending beyond alveolar region ✓ Pathologic fracture ✓ Extraoral fistula ✓ Oroantral or oronasal communication ✓ Osteolysis extending to the inferior border of the mandible or sinus floor
Radiographic finding	Localized to the alveolar bone region			Beyond alveolar bone
	• Alveolar bone loss/resorption (not chronic periodontal disease) • Changes to trabecular pattern sclerotic bone and no new bone in extraction sockets • Osteosclerosis involving the alveolar bone and/or the surrounding basilar bone • Thickening of the lamina dura/decreased size of periodontal ligament (PDL) space			

Figure 2 Stage descriptions for medication-related osteonecrosis of the jaw based on key clinical features, including exposed bone, patient symptoms, infection signs, and radiographic findings.

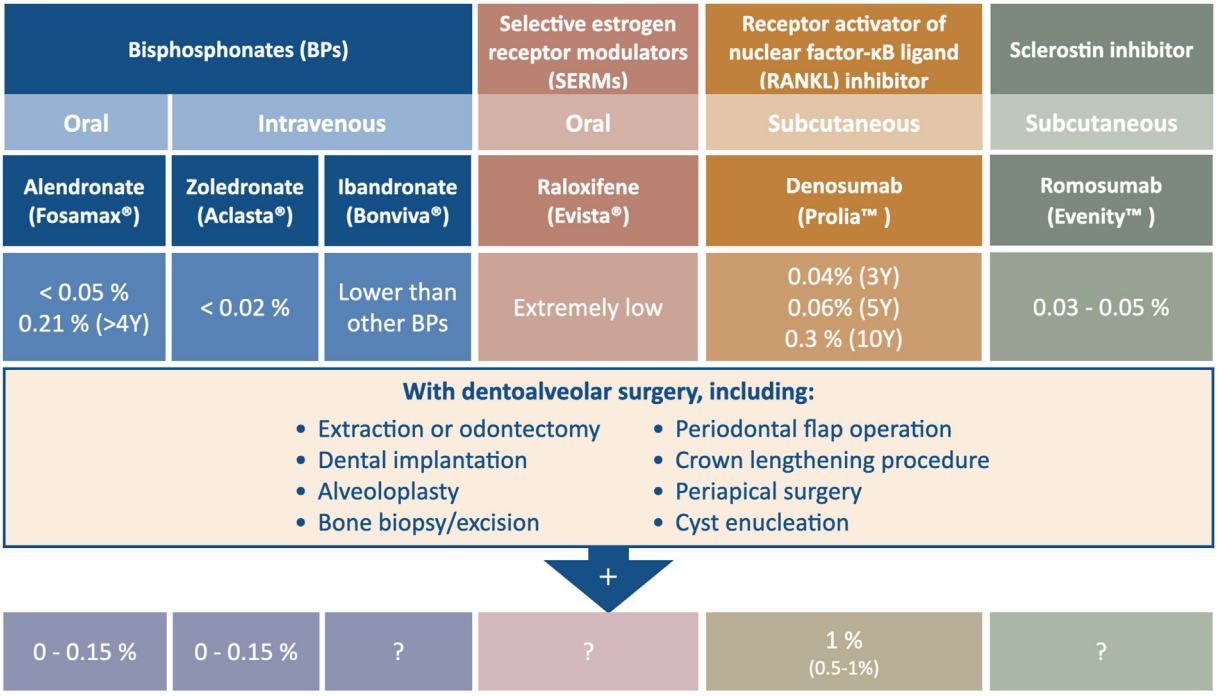


Figure 3 Prevalence of medication-related osteonecrosis of jaws (MRONJ) associated with different antiresorptive agents. It has been reported the prevalence of MRONJ increases when patients underwent dentoalveolar surgeries, such as tooth extractions or apical surgeries.

does not significantly affect dental implant success rates, dental practitioners should remain aware that implant placement procedures carry an inherent risk of MRONJ, which may compromise implant survival.[22–24] Thus, comprehensive patient counseling regarding potential risks is essential before implant therapy. The following protocol is recommended for implant placement:

1. Administer prophylactic antibiotics 1 h preoperatively.
2. Apple aseptic and minimally invasive techniques (flapless or mini-flap approaches).
3. Maintain copious saline irrigation during osteotomy preparation.
4. Avoid bone grafts or regenerative materials.
5. Select a two-stage submerged implant protocol over one-stage surgery.
6. Ensure primary soft tissue closure.
7. Prescribe postoperative antibiotics and chlorhexidine mouth rinse.
8. Implement regular monitoring at 3–6 month intervals.

Successfully implanted dental implants carry the risk of developing MRONJ, which can be categorized into early- and late-onset osteonecrosis of the jaw.[25] Early-onset MRONJ, also known as early implant surgery-triggered osteonecrosis, is often associated with the surgical procedure itself and typically occurs 2–10 months after implant placement, leading to implant failure. In contrast, late-onset MRONJ referred to as late implant presence-triggered necrosis, is caused by the long-term use of the implant due to improper force distribution or peri-implantitis.[26] Moreover, the soft tissue toxicity associated with BPs increases the incidence and treatment complexity of peri-implantitis.[27] Therefore, patients receiving ART require more rigorous post-implantation monitoring than the standard protocols, to minimize inflammatory complications and subsequent MRONJ development.

Second factor: concomitant oral infection

The second most significant risk factor for MRONJ was concomitant oral infection. Notably, 50 % of the MRONJ cases were not associated with the previously discussed invasive dentoalveolar procedures. However, they rather originated from inflammatory conditions such as periodontitis, apical periodontitis, and peri-implantitis.[28,29] The key strategies for MRONJ prevention include maintaining oral health and carefully assessing surgical requirements during ART. Regular dental checkups and early treatment of oral problems reduce the need for tooth extraction during ART.[30] Furthermore, regular dental examinations (every 6 months) and maintenance of optimal oral hygiene reduce the incidence of MRONJ from 4.6 % to 0.8 %, representing an 83 % reduction.[31]

Third factor: types of medication

The third major risk factor for MRONJ is the pharmacokinetic differences among drugs, which requires consideration of the potency of anti-resorptive agents and their bone-binding ability. A higher drug potency correlates with enhanced therapeutic efficacy against osteoporosis; however, it corresponds to an increased risk of developing MRONJ.[32,33] The skeletal distribution of drugs is determined by their binding affinities. High-affinity agents exhibit longer half-lives, increased MRONJ incidence, and prolonged healing periods following the onset of MRONJ.[34,35] The subsequent discussion addresses two major categories of anti-resorptive agents: BPs and denosumab (DMB).

Bisphosphonates

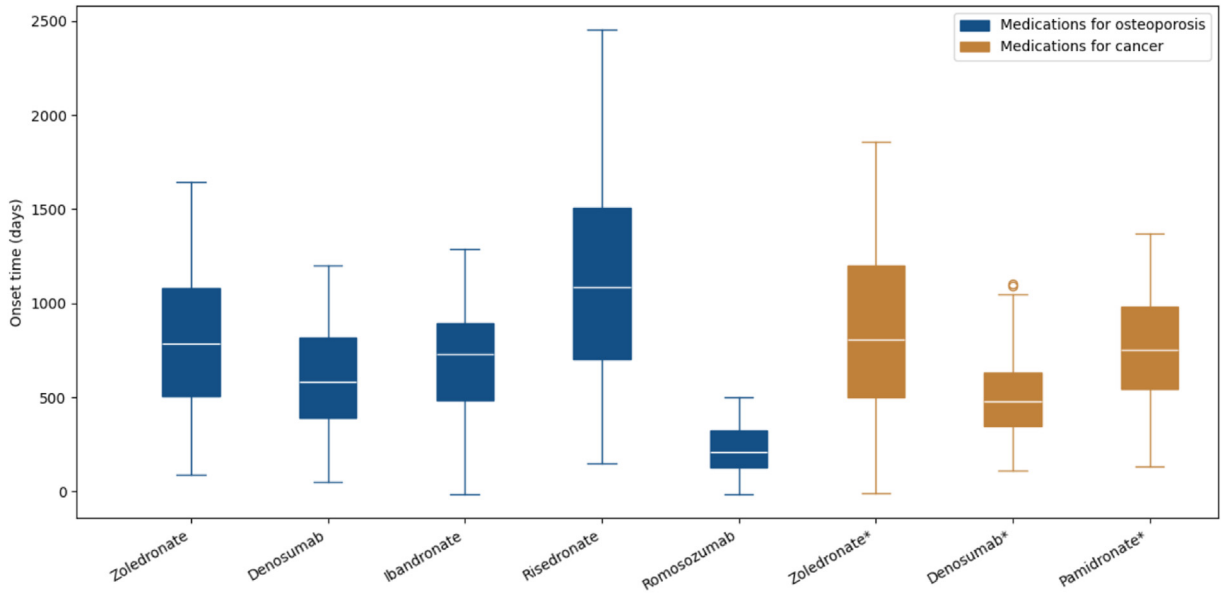
Upon entering the body, BPs establish strong bonds with the bone matrix, which enables their release during osteoclastic bone resorption. This results in BPs entering osteoclasts and interfering with their metabolic functions, ultimately causing osteoclast dysfunction or apoptosis.[36,37] Furthermore, BPs demonstrate remarkable skeletal stability and resistance to metabolic degradation.[38] For example, alendronate has a half-life exceeding 10 years, suggesting that temporary drug discontinuation has a minimal effect on systemic drug concentration. Regarding bone binding affinity, zoledronate was ranked as the strongest, followed by alendronate and ibandronate.[39] Regarding potency, zoledronate exhibited the highest efficacy and was approximately ten times more potent than ibandronate and one hundred times more potent than alendronate.[40]

Denosumab

The monoclonal antibody DMB, a receptor activator of nuclear factor kappa-B ligand (RANKL), primarily acts on the bloodstream rather than on the bone. Under normal physiological conditions, RANKL binds to its receptors on pre-osteoclasts and activates them into mature osteoclasts.[41] DMB functions by binding to RANKL, rendering it ineffective, and thereby reducing the production of mature osteoclasts.[42] Notably, the potency of DMB is comparable to that of zoledronate, making it a considerably potent drug.[43,44] Since DMB does not bind to bone and has a half-life in the blood of 25–30 days,[45] the effects of DMB on bone turnover are fully reversible after discontinuation.[46] Consequently, alterations in bone remodeling and wound healing were restored if DMB was discontinued for 2–3 months.[47,48]

Fourth factor: duration of medication

The fourth major risk factor for MRONJ is the duration of drug use. According to the U.S. Adverse Event Reporting System of the Food and Drug Administration, the median interval between the initiation of drug therapy and the onset of MRONJ ranges from 5 months to approximately 2 years (Fig. 4).[49] Therefore, the prevalence of MRONJ in patients with osteoporosis undergoing ART is low, with no statistically significant difference observed between BPs and DMB.[11] Nevertheless, the prolonged use of BPs, characterized by their long half-life, results in a cumulative dose effect, consequently leading to a significant increase in MRONJ risk over time.[50] In contrast, DMB exhibited a more consistent MRONJ risk profile despite long-term administration owing to its shorter half-life and the absence of the pronounced accumulation effect observed with BPs.[51] The risk of MRONJ significantly increases with



The onset time for medication-related osteonecrosis of the jaw			
Medication	Brand name	Median (days)	Q1, Q3
Medications for osteoporosis			
Zoledronate	**Aclasta®**	730	368, 1268
Denosumab	**Prolia™**	489.5	236.3, 909.8
Ibandronate	**Bonviva®**	722.5	314, 1055
Risedronate	**Reosteo®**	761	368, 1720
Romosozumab	**Evenity™**	153	50, 346
Medications for cancer			
Zoledronate	**Zometa®**	680.5	255.3, 1283
Denosumab	**Xgeva®**	488	245, 851
Pamidronate	**Aredia®**	696.5	347, 1087

Figure 4 Median interval between the initiation of drug therapy and the onset of MRONJ.

extended use, such as when alendronate is used for >4 years or DMB is used for >10 years, with the risk increasing to 0.21 %[52] and 0.3 %,[53] respectively (Fig. 3). Moreover, the risk of MRONJ persists even after the discontinuation of osteoporosis treatment owing to the prolonged residual effects of BPs in the bone.[54]

Fifth factor: drug discontinuation

The fifth major risk factor of MRONJ is the lack of appropriate drug discontinuation before invasive dentoalveolar procedures. However, the necessity of preoperative drug discontinuation remains controversial.[10,11,33,55] However, based on pharmacokinetic reasoning, temporarily discontinuing the use of anti-resorptive agents before dentoalveolar surgery to reduce their concentration in the body should reduce the occurrence of MRONJ.[56,57] Drug discontinuation has emerged as the primary modifiable factor within the dentist's control, highlighting the critical role of interdisciplinary collaboration in patient care. The recommended discontinuation intervals for individual medications before dentoalveolar surgery are shown in Fig. 5. Supporting evidence for these recommendations is discussed below.

Bisphosphonates: alendronate

In 2022, the AAOMS recommended that patients with 4 or more years of alendronate exposure or those who were exposed to alendronate for less than 4 years and in combination with steroids or anti-angiogenic medications should discontinue alendronate 2 months before tooth

Treatment of osteoporosis		Discontinuation of medication before dental procedure			
Medication (Brand name)	**Route/ Frequency**	**Non-invasive**	**Invasive- tooth extraction**	**Invasive- dental implantation**	**Resume timing**
Anabolic agents (Promoting bone formation)					
Teriparatide (Forteo®)	Subcutaneous, daily (For 1.5Y)	Continued	Continued	Continued	-
Antiresorptive agents (Reducing bone resorption)					
Bisphosphonates, BPs					
Alendronate (Fosamax®)	Oral, daily	Continued	• <4Y: continued • <4Y + steroid or antiangiogenic medications: discontinued 2M • >4Y: discontinued 2M		• Post-extraction 1M • Post-implantation 3M
Ibandronate (Bonviva®)	Intravenous, Q3M		• Continued • 3M after last dose		
Zoledronate (Aclasta®)	Intravenous, annual		• 3M after last dose		
Receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor					
Denosumab (Prolia™)	Subcutaneous, Q6M	Continued	• 3M after last dose		• Post-extraction 1M • Post-implantation 3M
Selective estrogen receptor modulators (SERMs)					
Raloxifene (Evista®)	Oral, daily	Continued	Continued	Continued	-
Dual-effect agents (anabolic + antiresorptive)					
Romosumab (Evenity™)	Subcutaneous, monthly (For 1 year)	Continued	• Continued • After 3 doses		As scheduled
Sequential treatment (2 or more medication in succession)					
Any	-	Continued	Follow the current medication		

Figure 5 Recommended discontinuation intervals for individual medications before dentoalveolar surgery. The timing for resuming medication after dentoalveolar surgery is also listed in the figure.

extraction.[11] This recommendation can be attributed to the fact that a fraction of alendronate remains unbound in the bloodstream with a half-life of 28 days,[58] potentially impeding epithelial healing owing to its soft tissue toxicity, thereby increasing the risk of exposing the underlying alveolar socket.[59] Therefore, the temporary discontinuation of alendronate may reduce its systemic concentration and potentially mitigate its adverse effects on extraction wound healing.

Bisphosphonates: zoledronate

Zoledronate, a highly potent nitrogen-containing BP, is associated with MRONJ in patients with osteoporosis. Preclinical studies have demonstrated that zoledronate inhibits epithelial cell migration and bone healing following tooth extraction.[60,61] Following infusion, the bone resorption marker C-telopeptide (CTX) reached maximum suppression in 9–11 days and maintained this suppression for approximately 3 months before gradual recovery, whereas the bone formation marker P1NP showed maximum suppression at 3 months post-infusion.[62] Based on these pharmacological principles, dentoalveolar surgery should be considered at least 3 months after previous zoledronate administration. Our recent clinical investigation demonstrated that a 3-month drug interruption with zoledronate significantly reduced MRONJ risk, supporting this strategy.[63]

Bisphosphonates: ibandronate

Ibandronate, a high-potency BP characterized by its relatively low binding affinity for bone minerals, has a lower risk of inducing MRONJ than other BPs.[64] While the precise incidence has not been established, the literature currently contains only isolated case reports of ibandronate-associated MRONJ.[65–67] Moreover, no reported guidelines were observed for the discontinuation of ibandronate before dentoalveolar surgery. Given the pharmacokinetic profile of ibandronate, discontinuation of the medication may not be necessary before dentoalveolar procedures. However, if a drug interruption is deemed appropriate, we propose that dentoalveolar surgeries be scheduled approximately 3 months after the last ibandronate administration, aligning with the general recommendations for most anti-resorptive agents.

Receptor activator of nuclear factor kappa-B ligand inhibitor: denosumab

In 2022, the AAOMS also recommended that dentoalveolar surgeries be scheduled—3–4 months after the last dose of DMB, when the level of osteoclast inhibition is waning.[11] Emphasizing that while DMB has a relatively short half-life, and its discontinuation can effectively reduce its systemic concentration, prolonged or arbitrary cessation of therapy may precipitate a serious adverse event known as

rebound-associated multiple vertebral fractures.[68,69] Therefore, not delaying the subsequent dose by more than 1 month to maintain optimal therapeutic efficacy is recommended.[70] This highlights the importance of carefully managing DMB discontinuation to minimize potential risks to patients.

Selective estrogen receptor modulators: raloxifene
Raloxifene, a selective estrogen receptor modulator,[71] has a different mechanism of action from other anti-resorptive medications. It mimics the effects of estrogen and exerts limited inhibition of osteoclast activity, helping to maintain bone density at levels comparable to those observed in premenopausal women.[72–74] To date, reported MRONJ cases associated with raloxifene treatment are extremely rare.[75,76] Consequently, the current recommendations suggest that discontinuation of raloxifene before invasive dental procedures is unnecessary.

Anabolic agent: teriparatide
Teriparatide, a recombinant human parathyroid hormone, is prescribed as an anabolic agent for increasing the rate of bone formation.[77] Emerging evidence suggests that teriparatide may enhance post-extraction alveolar bone healing and promote the osseointegration of dental implants.[78,79] Therefore, discontinuing the medication preoperatively is not necessary.

Dual-effect agent: romosozumab
Romosozumab, with the dual effect of promoting bone formation and inhibiting bone resorption,[80] lacks specific guidelines for its discontinuation before dentoalveolar surgery owing to its recent introduction. Regarding pharmacological effects, the inhibitory effect of romosozumab on osteoclasts is relatively milder than that of DMB; however, both have comparable effects in promoting bone mineral density.[81] Analysis of bone resorption markers indicated a significant decrease in CTX levels within the first week following romosozumab injection, which gradually returned to baseline by the third month. These findings suggest that after three doses of romosozumab, the inhibitory effects on osteoclasts markedly decreased, with their activity approaching pretreatment levels.[82,83] Therefore, romosozumab discontinuation before dentoalveolar surgery was not deemed necessary. Alternatively, scheduling dentoalveolar procedures after the third monthly romosozumab injection may be considered a relatively safe approach.

Sequential use of two or more medications
An increasing number of patients with osteoporosis are receiving sequential therapy, which involves the administration of two or more medications in succession. For instance, current strategies initially employ anabolic agents followed by potent anti-resorptive agents. This combination effectively reduced the fracture risk rapidly and yielded substantial gains in bone mineral density.[84–86] The prolonged skeletal retention of BPs necessitates careful consideration when transitioning to DMB owing to potential pharmacological interactions, which is associated with a possible overlapping effect, resulting in dual osteoclastic inhibition. This may theoretically increase the risk of MRONJ. Furthermore, extended cumulative anti-resorptive exposure in sequential BP-to-DMB therapy could increase the risk of MRONJ during invasive dental procedures.[87] In principle, a drug discontinuation plan should be tailored to a patient's current medication regimen.

Timing for resuming anti-resorptive therapy after dentoalveolar surgery
For patients undergoing dentoalveolar surgery who have temporarily discontinued ART, an important consideration is the timing of ART resumption following the completion of these procedures. We recommend that for BPs and DMB, ART be resumed 1-month post-extraction and 3 months post-dental implantation to allow complete soft tissue healing and osseointegration.[88,89] A subsequent dose of romosozumab was administered according to a regular monthly schedule (Fig. 5).

Other risk factors of medication-related osteonecrosis of the jaw

While numerous risk factors for MRONJ development have been identified, including systemic (such as diabetes, rheumatic arthritis, and cancer), demographic (such as age), and genetic variables (such as PPAR gamma and CYP2C8),[11] the following discussion primarily focuses on local factors associated with dental practices.

Tooth extraction site
Extraction of the posterior mandibular teeth poses a higher risk of MRONJ development than other extraction sites.[63] Several factors may have contributed to this increased risk. First, blood circulation in the mandible is less abundant than that in the maxilla, potentially compromising healing.[90] Secondly, the complex root structure of the lower posterior teeth often necessitates more invasive extraction procedures, making it challenging to perform atraumatic extractions.[91] Lastly, achieving primary wound closure in this region is often challenging and frequently requires additional alveolectomies and flap advancement procedures. Cases with primary closure after extraction have been reported to be less likely to develop MRONJ.[92]

Ill-fitted removable denture
Ill-fitted removable dentures may exert excessive pressure on the alveolar ridge, potentially leading to mucosal trauma and subsequent alveolar bone exposure,[93,94] thus elevating the risk of MRONJ.[17,20] Notably, MRONJ can develop in areas with dental problems and edentulous regions. Therefore, patients should undergo regular evaluations and denture adjustments to minimize the incidence of spontaneous MRONJ. This proactive approach to denture maintenance is crucial to mitigate the risk of MRONJ in patients undergoing ART.

Exostosis
Exostosis, a manifestation of bone overgrowth, is characterized by prominent protrusions that are typically observed at the midline of the hard palate and lingual aspect of the mandible.[95] The mucosal tissue overlying these exostoses is often attenuated, rendering it

susceptible to ulceration and bone exposure when subjected to mechanical stress during mastication, thereby increasing the risk of MRONJ.[96,97] Alveoloplasty, a dentoalveolar surgery, is contraindicated in patients undergoing ART; however, patient education focusing on careful mastication and avoidance of hard or sharp food items is essential to prevent mucosal trauma and subsequent complications. Furthermore, dental practitioners should minimize mechanical friction when obtaining impressions from prosthetic devices.

Differentiation between pre-existing medication-related osteonecrosis of the jaw and periodontitis

MRONJ without bone exposure may initially present solely as tooth mobility, potentially leading to misdiagnosis of periodontitis. This misdiagnosis could result in tooth extraction, which may subsequently be erroneously identified as extraction-induced MRONJ. Clinically, both conditions share features, such as deep periodontal pockets, tooth mobility, and localized abscesses.[98] However, distinctions can be observed in tooth vitality; teeth affected by periodontitis typically exhibit normal pulp responses, whereas those affected by MRONJ may demonstrate pulp necrosis.[99] A crucial differentiating factor lies in the pocket location: in periodontitis, the pocket forms between the alveolar bone and the root surface, whereas in MRONJ, it develops between the gingiva and the alveolar bone, reflecting the underlying osseous etiology.[11] Radiographically, periodontitis is characterized by alveolar bone resorption and a discontinuous lamina dura in the crestal bone. In contrast, MRONJ-affected teeth do not show bone resorption and may exhibit thickening of the lamina dura, a feature specifically observed in patients using BPs.[100,101] Understanding these features will enable dental practitioners to effectively identify preexisting MRONJ, facilitating more accurate risk assessment and informed clinical decision-making.

Conclusion

Clinical guidelines provide a general safety consensus; however, they cannot guarantee the prevention of MRONJ in all cases. While extended preoperative drug interruption may yield safer outcomes, it significantly disrupts osteoporosis treatment. Notably, current recommendations for drug discontinuation before dentoalveolar surgery are not based on comprehensive prospective clinical trials but on retrospective cohort studies and pharmacological inferences. Consequently, adherence to these guidelines does not ensure complete prevention of MRONJ. However, it serves to minimize its risk. Various uncontrollable factors persist, such as ART duration, concurrent therapy, anatomical site of intervention, and comorbidities, all of which may contribute to an increased risk of MRONJ. Dental practitioners should always inform patients of the risk of MRONJ before invasive dental procedures and provide alternative treatment options when feasible.

In conclusion, this review presents the first specific guidelines for preoperative drug discontinuation tailored to individual anti-resorptive agents in patients with osteoporosis undergoing dentoalveolar surgery. By identifying the significant risk factors for personalized assessment and offering applicable surgical precautions, this article aids dental practitioners in optimizing patient outcomes. We recommend temporarily discontinuing certain anti-resorptive agents before dentoalveolar surgery to minimize the risk of MRONJ.

Declaration of competing interest

The authors declare that they have no competing financial interests or personal relationships that may have influenced the work reported in this study.

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