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PERIAPICAL HEALING FOLLOWING ENDODONTIC TREATMENT IN PATIENTS RECEIVING BISPHOSPHONATES: IMPLICATIONS FOR MEDICATION-RELATED OSTEONECROSIS OF THE JAW

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ABSTRACT

Background

Medication-related osteonecrosis of the jaw (MRONJ) is a clinically important complication associated with antiresorptive therapy, particularly bisphosphonates. Tooth extraction is a major local risk factor, while persistent odontogenic infection and apical periodontitis may also contribute to local conditions associated with MRONJ.

Aims

This narrative review aimed to evaluate evidence on periapical healing after endodontic treatment in patients receiving bisphosphonates and to clarify the potential relevance of infection control and tooth preservation to MRONJ risk management.

Materials and Methods

A narrative literature review was performed. PubMed, Scopus, and Google Scholar were searched for English-language publications published from 2003 to 14 July 2026 concerning bisphosphonates, MRONJ, apical periodontitis, periapical healing, and endodontic treatment outcomes. Evidence was summarized thematically.

Results

Forty-one publications were included, but only a small number directly evaluated endodontic outcomes in patients receiving bisphosphonates. Available evidence suggests that satisfactory periapical healing and tooth retention can be achieved, particularly in patients treated for osteoporosis, whereas outcomes may be less predictable during prolonged intravenous zoledronate therapy. Apical periodontitis and chronic odontogenic infection may sustain local inflammation relevant to MRONJ, but their causal role remains unproven.

Conclusions

Non-surgical root canal treatment may be a reasonable tooth-preserving option when the tooth is restorable and predictable infection control can be achieved. However, current evidence does not demonstrate that endodontic treatment prevents MRONJ. Clinical decisions should distinguish patients with osteoporosis receiving oral bispho-

sphonates from oncology patients receiving prolonged intravenous therapy and should be individualized according to the patient's overall MRONJ risk.

Keywords: bisphosphonates; medication-related osteonecrosis of the jaw; MRONJ; endodontic treatment; root canal treatment; apical periodontitis; periapical healing; antiresorptive therapy; osteoporosis; tooth preservation

INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is a potentially serious adverse event associated with antiresorptive and antiangiogenic medications. The condition became widely recognized after early reports of jaw necrosis related to pamidronate and zoledronate, followed by broader descriptions of bisphosphonate-induced exposed bone lesions and their clinical consequences [1-3]. Contemporary position papers and clinical guidelines define MRONJ using the presence of exposed bone, or bone that can be probed through a fistula, persisting for more than eight weeks in patients exposed to relevant medications and without previous radiation therapy to the jaws [1,4-7].

The pathogenesis of MRONJ remains incompletely understood and is generally considered multifactorial. Proposed mechanisms include suppression of bone remodeling, local inflammation, infection, altered angiogenesis, immune dysregulation, and tissue trauma [8-10]. These mechanisms are particularly relevant in the jaws, where bone is exposed to the oral microbiome, frequent microtrauma, and high remodeling demands associated with dental disease and treatment.

Bisphosphonates are widely used for osteoporosis, metastatic bone disease, multiple myeloma, and other skeletal disorders. Risk differs substantially according to indication, route of administration, cumulative dose, treatment duration, and coexisting systemic factors. Patients treated with oral bisphosphonates for osteoporosis generally have a much lower MRONJ risk than oncology patients receiving high-dose intravenous bisphosphonates or denosumab [1,5,11-13]. This distinction is important when interpreting endodontic outcomes and formulating clinical recommendations.

Tooth extraction remains one of the most consistently reported local triggering events for MRONJ, particularly in cancer patients exposed to high-potency antiresorptive regimens [1,14-16]. However, increasing evidence indicates that infection and inflammation may not simply be secondary findings. Periapical disease, periodontal inflamma-

tion, and other chronic odontogenic infections may create local biological conditions that favor osteonecrosis, especially when bone turnover is suppressed [17-21].

Endodontic treatment is clinically relevant in this context because it may eliminate intracanal infection, support periapical healing, and preserve restorable teeth without direct surgical injury to alveolar bone. Earlier endodontic reviews proposed that non-surgical root canal treatment may be preferable to extraction in selected patients at risk of MRONJ, but they also emphasized the limited evidence base and the need for careful procedural technique [22,23].

A recent scoping review by Zavalloni et al. mapped available evidence on endodontic treatment and MRONJ risk in patients receiving antiresorptive therapy [24]. The present narrative review differs from that work by focusing more specifically on periapical healing after endodontic treatment, by distinguishing evidence from osteoporosis patients receiving oral bisphosphonates from evidence involving oncology patients receiving intravenous therapy, and by integrating clinical outcome data with the biological role of apical periodontitis and persistent odontogenic infection. This focus is intended to clarify what can and cannot be inferred from the current literature regarding endodontic treatment, periapical healing, and MRONJ prevention.

AIM

The aim of this narrative review was to evaluate the available evidence on periapical healing after non-surgical endodontic treatment in patients receiving bisphosphonates.

RESEARCH OBJECTIVES

1. To summarize the clinical evidence on periapical healing and tooth survival after endodontic treatment in patients receiving bisphosphonates.
2. To compare outcomes in patients receiving oral bisphosphonates for osteoporosis with those in oncology patients receiving intravenous bisphosphonates.
3. To examine the relationship between apical periodontitis, odontogenic infection, and factors associated with MRONJ.
4. To assess the clinical implications and limitations of endodontic tooth-preserving strategies in patients at risk of MRONJ.

MATERIALS AND METHODS

This manuscript is a narrative review. The Scale for the Assessment of Narrative Review Articles (SANRA) was used as a quality assessment and self-assessment tool for the narrative review; it was not treated as a methodological guideline for conducting the review [29].

A literature search covering publications from 2003 to 14 July 2026 was performed in PubMed, Scopus, and Google Scholar. The search strategy included combinations of the following terms: “bisphosphonates”, “medication-related osteonecrosis of the jaw”, “MRONJ”, “bisphosphonate-related osteonecrosis of the jaw”, “endodontic treatment”, “root canal treatment”, “apical periodontitis”, “periapical healing”, “odontogenic infection”, “osteoporosis”, “zoledronate”, “denosumab”, and “antiresorptive therapy”.

English-language publications were considered eligible when they provided direct clinical evidence on endodontic treatment, periapical healing, or periapical status in patients receiving bisphosphonates or other antiresorptive medications. Reviews, position papers, consensus guidelines, case reports, case series, mechanistic studies, and experimental studies were also included when they provided relevant evidence on MRONJ pathogenesis, odontogenic infection, apical periodontitis, or the clinical management of patients at risk of MRONJ. Landmark publications from the early development of the MRONJ literature were included when they provided essential historical or conceptual context.

Publications were excluded when they were unrelated to antiresorptive therapy, MRONJ, odontogenic infection, endodontic treatment, or periapical disease. Non-English publications and reports that did not provide sufficient information for interpretation were also excluded.

Search results were screened by title and abstract, and potentially relevant publications were assessed in full text. Reference lists of key articles were also reviewed to identify additional relevant publications. Forty-one publications were included in the narrative synthesis.

The evidence was organized into four domains: (1) MRONJ pathogenesis and local risk factors, (2) apical periodontitis and chronic odontogenic infection, (3) periapical healing and tooth survival after endodontic treatment in patients receiving bisphosphonates, with separate consideration of osteoporosis patients receiving oral bisphosphonates and oncology patients receiving intravenous therapy, and (4) clinical impli-

cations and limitations of tooth-preserving strategies in patients at risk of MRONJ. The synthesis focused on separating direct clinical outcome data from biological rationale and expert-based clinical interpretation.

RESULTS

Evidence base and characteristics of directly relevant studies

The number of clinical studies directly evaluating periapical healing or endodontic outcomes in bisphosphonate-exposed patients was small. The most directly relevant evidence consisted of retrospective clinical studies, one prospective study with long-term follow-up, and observational studies evaluating periapical status in osteoporosis cohorts [24-28,30,31]. Table 1 summarizes the main clinical studies and review-level evidence directly relevant to endodontic treatment outcomes or periapical status in patients receiving antiresorptive therapy.

Table 1. Key studies and reviews addressing endodontic treatment outcomes or periapical status in patients receiving antiresorptive therapy

STUDY	DESIGN AND POPULATION	MEDICATION	FOLLOW-UP AND ASSESSMENT	PRINCIPAL NUMERICAL FINDINGS
Hsiao et al. 2009 [25]	Retrospective study; 34 teeth with preoperative radiolucencies in patients taking oral bisphosphonates; 38 control teeth	Oral bisphosphonates	Mean follow-up 14 months; clinical and radiographic healing of periradicular lesions	Healing in 73.5% of bisphosphonate-exposed teeth and 81.6% of controls; difference not statistically significant
Zamparini et al. 2021 [26]	Prospective clinical study; 65 patients with 109 treated teeth at baseline; 57 patients and 96 root canal treatments analyzed at 60 months; control group 46 patients and 102 root canal treatments	Bisphosphonates, predominantly for non-oncologic indications	60 months; survival, clinical signs, and radiographic success	Survival 85% in bisphosphonate group and 88% in controls; success 76% and 73%, respectively; no significant difference
Dereci et al. 2016 [27]	Retrospective study; 24 patients and 37 teeth with apical periodontitis in patients receiving intravenous zoledronate	Intravenous zoledronate	12 months; clinical and radiographic healing categories	More non-healed or incompletely healed lesions in patients exposed to zoledronate for more than one year; association significant at $p < 0.05$
Cadoni et al. 2022 [28]	Retrospective clinical study; 76 patients with osteoporosis and 76 controls	Antiresorptive therapy including bisphosphonates and denosumab	Cross-sectional periapical status assessment	Apical periodontitis prevalence 42.1% in osteoporosis group and 47.4% in controls; apical periodontitis more frequent in root canal-treated teeth in osteoporosis patients
Zavalloni et al. 2025 [24]	Scoping review; 15 articles and 133 patients	Oral and intravenous bisphosphonates	Variable; evidence mapping of root canal treatment and MRONJ risk	Seven MRONJ cases after or around endodontic treatment, corresponding to 5.3% of patients in the collected literature; cases occurred in oncologic patients

Abbreviations: MRONJ, medication-related osteonecrosis of the jaw.

The table shows that the most favorable data come from patients receiving oral bisphosphonates or mixed non-oncologic antiresorptive therapy, whereas less favorable healing was observed in patients exposed to prolonged intravenous zoledronate. It also shows that available studies used different outcome definitions, different follow-up durations, and different populations, which limits direct comparison [24-28].

Medication-related osteonecrosis of the jaw and odontogenic infection

The general MRONJ literature supports a multifactorial model in which medication-related suppression of bone remodeling interacts with systemic risk factors, oral trauma,

and infection [1,4-10]. In this model, tooth extraction remains a major local event, but pre-existing infection may contribute to the local tissue environment before and after extraction [14-19].

Experimental and clinical studies support the relevance of local inflammatory conditions. Increased bisphosphonate uptake has been described in areas of tooth extraction or periapical disease, and removal of pre-existing periodontal inflammation reduced MRONJ-like lesions in an animal model [17,18]. A national cohort-based study also reported that pulp and periapical disease may be associated with increased risk of osteonecrosis of the jaw [19].

Table 2 summarizes the conceptual relationship between apical periodontitis, endodontic treatment, and factors associated with MRONJ. This table should be interpreted as a biological framework rather than evidence of causality.

Table 2. Conceptual relationship between apical periodontitis, endodontic treatment, and factors associated with MRONJ

CLINICAL OR BIOLOGICAL FACTOR	POTENTIAL RELEVANCE	STRENGTH OF SUPPORT
Apical periodontitis	Persistent local inflammation and periapical bone changes	Supported by general endodontic and MRONJ biological literature
Chronic odontogenic infection	Continuous microbial and inflammatory stimulation	Supported by mechanistic and observational evidence
Tooth extraction	Surgical trauma and bone exposure in susceptible patients	Strongly supported as a local risk factor
Non-surgical endodontic treatment	Infection control while avoiding direct surgical bone trauma	Supported by limited clinical studies and expert interpretation
Periapical healing	Reduction of inflammatory burden after infection control	Supported by endodontic outcome studies, but limited in antiresorptive-exposed populations
Tooth preservation	Possible reduction in need for extraction	Biologically plausible, but not proven to prevent MRONJ

Note: This table presents a conceptual model derived from the reviewed literature and does not imply causality [1,8,17-22].

Periapical healing following endodontic treatment in patients receiving bisphosphonates

Hsiao et al. retrospectively evaluated 34 teeth with preoperative periradicular radiolucencies in patients taking oral bisphosphonates and compared them with 38 teeth in non-exposed controls. Healing was reported in 73.5% of bisphosphonate-exposed teeth and 81.6% of control teeth, with no statistically significant difference. Although limited by sample size and retrospective design, this study suggested that oral bis-

phosphonate therapy does not necessarily prevent satisfactory healing after non-surgical root canal treatment [25].

Zamparini et al. provided the strongest prospective clinical evidence. The study included 65 patients with 109 root canal-treated teeth at baseline, and 57 patients with 96 root canal treatments were analyzed after 60 months. A control group of 46 patients with 102 root canal treatments was also evaluated. Tooth survival was 85% in bisphosphonate-exposed patients and 88% in controls, while success rates were 76% and 73%, respectively. These findings indicate that long-term retention and radiographic success can be achieved in many bisphosphonate-exposed patients when non-surgical treatment and restorative management are performed predictably [26].

Dereci et al. evaluated a higher-risk group of 24 patients with 37 teeth and apical periodontitis who were receiving intravenous zoledronate. After 12 months, patients exposed to zoledronate for more than one year showed more non-healed or incompletely healed lesions than patients treated for shorter periods. The difference was statistically significant, suggesting that medication potency, intravenous administration, duration of exposure, and systemic disease context may influence periapical healing [27].

Cadoni et al. evaluated 76 patients affected by osteoporosis and 76 control subjects. Overall apical periodontitis prevalence was similar between groups, but apical periodontitis was more frequent in root canal-treated teeth among patients with osteoporosis. More recent cross-sectional and systematic review evidence has also suggested that osteoporosis and antiresorptive exposure may be associated with altered periapical status, although causality and the independent effect of medication remain uncertain [28,30,31].

Overall, direct clinical evidence suggests that many patients receiving oral bisphosphonates for osteoporosis can achieve satisfactory periapical healing after non-surgical root canal treatment. In contrast, evidence involving oncology patients receiving high-dose intravenous bisphosphonates is limited and less reassuring. These two populations should not be interpreted as clinically equivalent [24-28].

Reported complications, case reports, and procedural considerations

In addition to clinical outcome studies, the literature includes case reports and reviews describing MRONJ diagnosed after endodontic failure, rubber dam clamp trauma, persistent periapical infection, or endodontic treatment in medically complex patients

[24,32-38]. These reports do not prove that root canal treatment causes MRONJ. Rather, they suggest that MRONJ-like lesions may occur in high-risk patients when endodontic disease persists, local trauma occurs, or infection is not fully controlled.

The scoping review by Zavalloni et al. identified seven MRONJ cases among 133 patients described in the available endodontic literature, corresponding to 5.3% of collected cases; importantly, these cases occurred in oncologic patients and were largely derived from case reports or case series, which are prone to publication bias [24]. Therefore, these data should not be interpreted as an incidence rate applicable to all bisphosphonate-exposed patients.

General endodontic considerations remain relevant in this setting. Adequate infection control, avoidance of unnecessary soft tissue trauma, careful working length control, and limitation of apical extrusion are prudent, particularly in patients receiving high-dose antiresorptive therapy [22-24,32-38]. However, the current evidence base does not support a universal rule that endodontic treatment prevents MRONJ.

DISCUSSION

This narrative review evaluated evidence on periapical healing after endodontic treatment in patients receiving bisphosphonates. The main finding is that favorable outcomes are achievable in many patients, especially those receiving oral bisphosphonates for osteoporosis, but the evidence base remains small and heterogeneous [24-28]. The review also confirms that direct evidence demonstrating prevention of MRONJ by endodontic treatment is absent.

A key issue is the distinction between patient populations. Patients receiving oral bisphosphonates for osteoporosis generally represent a lower-risk group, and the studies by Hsiao et al. and Zamparini et al. suggest that periapical healing and long-term tooth retention may be similar to outcomes in non-exposed controls [25,26]. In contrast, oncology patients receiving high-dose intravenous zoledronate or other potent antiresorptive regimens represent a substantially higher-risk group. The findings of Dereci et al. and the cases summarized by Zavalloni et al. indicate that outcomes in this group require more cautious interpretation [24,27].

The biological rationale for conservative dental treatment remains plausible. Persistent apical periodontitis may maintain local inflammatory burden, and local infection has been increasingly discussed as a factor in MRONJ pathogenesis [17-22].

Successful non-surgical root canal treatment may remove intracanal infection and reduce the need for extraction. Nevertheless, this is a biologically plausible clinical strategy rather than a proven MRONJ-preventive intervention.

The present review differs from the 2025 scoping review by Zavalloni et al. in emphasis and presentation. Zavalloni et al. mapped the literature on endodontic treatment and MRONJ risk across patients receiving antiresorptive therapy [24]. The present review focuses specifically on periapical healing, numerical outcomes from the main clinical studies, and the distinction between osteoporosis-related oral bisphosphonate exposure and oncology-related intravenous exposure. This distinction is important because broad conclusions about endodontic safety can be misleading when risk groups are combined.

Clinical recommendations should therefore be cautious. Non-surgical root canal treatment may be considered for restorable teeth when predictable infection control and restoration are achievable, especially in lower-risk patients treated for osteoporosis. In high-risk oncology patients receiving intravenous bisphosphonates, treatment planning should be individualized and preferably discussed with oral surgery and the medical team. Extraction, endodontic treatment, and observation may each be appropriate in different circumstances depending on restorability, symptoms, infection severity, systemic risk, and patient preference [1,5-7,24,39-41].

Table 3 summarizes cautious clinical implications derived from the reviewed literature. The statements are intentionally formulated as considerations rather than universal recommendations because the current evidence does not permit definitive treatment algorithms.

Table 3. Cautious clinical implications for endodontic management of patients receiving bisphosphonate therapy

CLINICAL SCENARIO	POSSIBLE MANAGEMENT CONSIDERATION	IMPORTANT CAUTION
Restorable tooth with pulpitis	Non-surgical root canal treatment may be considered when long-term restoration is predictable	Decision should consider individual MRONJ risk profile
Restorable tooth with apical periodontitis	Root canal treatment may be considered to control infection and avoid extraction when feasible	Healing should be monitored clinically and radiographically
Persistent periapical lesion after treatment	Follow-up, retreatment, or referral may be considered according to symptoms and risk	Persistent infection should not be ignored in high-risk patients
Oncology patient receiving intravenous bisphosphonates	Individualized interdisciplinary planning is advisable	Evidence is limited and risk is higher than in osteoporosis patients
Consideration of endodontic surgery	Non-surgical options may be preferable when technically feasible	Surgical procedures require careful risk assessment
Non-restorable tooth	Extraction may be unavoidable in selected cases	Risk mitigation and specialist involvement may be needed
Active odontogenic infection	Prompt diagnosis and infection control are important	Choice of intervention should be individualized

Note: These statements are not intended as universal recommendations. Management should be individualized according to medication type, indication for therapy, duration of exposure, dental restorability, infection severity, and interdisciplinary clinical judgment [1,5-7,22-24,39-41].

The evidence base is therefore clinically useful but not definitive. It supports the feasibility of endodontic treatment in selected bisphosphonate-exposed patients, particularly those treated orally for osteoporosis, and it supports infection control as an important clinical objective. It does not support the claim that root canal treatment prevents MRONJ, nor does it justify a universal recommendation to prefer endodontic treatment over extraction in all patients.

LIMITATIONS OF THE REVIEW

This review has several limitations. First, only a small number of directly relevant clinical studies have evaluated periapical healing or endodontic outcomes in patients receiving bisphosphonates. Most available evidence comes from retrospective studies, observational cohorts, reviews, and case reports [24-28,32-38].

Second, the included studies differ substantially in patient characteristics, medication indication, route of administration, duration of exposure, follow-up time, diagnostic criteria, and outcome assessment methods. These differences limit direct comparison across studies and prevent quantitative synthesis.

Third, only English-language publications were included. Relevant data published in other languages may therefore have been missed. Fourth, although the search strategy and selection principles were described, this was not a systematic review. The source selection process was not registered, a PRISMA flow diagram was not prepared, and formal risk-of-bias assessment was not performed.

Fifth, most favorable clinical evidence relates to oral bisphosphonate therapy in osteoporosis patients, whereas evidence in oncology patients receiving high-dose intravenous bisphosphonates remains limited. Finally, direct evidence demonstrating that endodontic treatment reduces the incidence of MRONJ is absent. Any relationship between infection control, periapical healing, tooth preservation, and reduced MRONJ risk should therefore be regarded as plausible but unproven.

CONCLUSIONS

Available clinical evidence indicates that satisfactory periapical healing and long-term tooth retention after non-surgical endodontic treatment can be achieved in selected patients receiving bisphosphonates. The most favorable outcomes have been reported in patients with osteoporosis receiving oral bisphosphonates. Evidence concerning oncology patients receiving prolonged intravenous bisphosphonate therapy remains limited and suggests less predictable healing.

Apical periodontitis and chronic odontogenic infection may sustain local inflammation and create conditions potentially associated with MRONJ. However, the causal role of these factors, as well as the effect of infection control on the risk of developing MRONJ, has not been established.

Non-surgical endodontic treatment may be considered a tooth-preserving option when the tooth is restorable and reliable infection control can be achieved. However, the available evidence does not confirm that endodontic treatment prevents MRONJ or that it should be preferred to tooth extraction in all cases.

Treatment decisions should be individualized and should take into account the indication for bisphosphonate therapy, route of administration, duration of treatment, the patient's general condition, the level of MRONJ risk, tooth restorability, and the severity of odontogenic infection. In high-risk patients, particularly those receiving intravenous bisphosphonates for oncologic indications, treatment decisions should preferably be made in consultation with an oral surgeon and the treating physician.

DISCLOSURE

Author Contributions

Conceptualization: Zuzanna Galicka. Literature search and selection: Zuzanna Galicka, Jakub Artur Czapkiewicz, Maja Witek, Weronika Kwaśnica, Katarzyna Raczek, Justyna Polko, Zuzanna Jeziorska, Izabela Migdał, Bartosz Szymajda, Tomasz Horodniczy. Manuscript drafting: Zuzanna Galicka. Critical revision of the manuscript: Jakub Artur Czapkiewicz, Maja Witek, Weronika Kwaśnica, Katarzyna Raczek, Justyna Polko, Zuzanna Jeziorska, Izabela Migdał, Bartosz Szymajda, Tomasz Horodniczy. Final manuscript preparation: Zuzanna Galicka.

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Conflict of Interest

The authors declare no conflict of interest.

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REFERENCES

1. Ruggiero SL, Dodson TB, Aghaloo T, Carlson ER, Ward BB, Kademani D. American Association of Oral and Maxillofacial Surgeons' Position Paper on Medication-Related Osteonecrosis of the Jaws: 2022 Update. J Oral Maxillofac Surg. 2022;80(5):920-943. https://doi.org/10.1016/j.joms.2022.02.008
2. Marx RE. Pamidronate (Aredia) and zoledronate (Zometa) induced avascular necrosis of the jaws: a growing epidemic. J Oral Maxillofac Surg. 2003;61(9):1115-1117. https://doi.org/10.1016/S0278-2391(03)00720-1
3. Marx RE, Sawatari Y, Fortin M, Broumand V. Bisphosphonate-induced exposed bone osteonecrosis/osteopetrosis of the jaws: risk factors, recognition, prevention, and treatment. J Oral Maxillofac Surg. 2005;63(11):1567-1575. https://doi.org/10.1016/j.joms.2005.07.010

4. Ruggiero SL, Dodson TB, Fantasia J, Goodday R, Aghaloo T, Mehrotra B, et al. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw: 2014 update. J Oral Maxillofac Surg. 2014;72(10):1938-1956. https://doi.org/10.1016/j.joms.2014.04.031
5. Khan AA, Morrison A, Hanley DA, Felsenberg D, McCauley LK, O'Ryan F, et al. Diagnosis and management of osteonecrosis of the jaw: a systematic review and international consensus. J Bone Miner Res. 2015;30(1):3-23. https://doi.org/10.1002/jbmr.2405
6. Yarom N, Shapiro CL, Peterson DE, Van Poznak CH, Bohlke K, Ruggiero SL, et al. Medication-related osteonecrosis of the jaw: MASCC/ISOO/ASCO clinical practice guideline. J Clin Oncol. 2019;37(25):2270-2290. https://doi.org/10.1200/JCO.19.01186
7. Bedogni A, Mauceri R, Fusco V, Bertoldo F, Bettini G, Brandi ML, et al. Italian position paper (SIPMO-SICMF) on medication-related osteonecrosis of the jaw (MRONJ). Oral Dis. 2024;30(6):3679-3709. https://doi.org/10.1111/odi.14887
8. Allen MR, Burr DB. The pathogenesis of bisphosphonate-related osteonecrosis of the jaw: so many hypotheses, so few data. J Oral Maxillofac Surg. 2009;67(5 Suppl):61-70. https://doi.org/10.1016/j.joms.2009.01.007
9. Chang J, Hakam AE, McCauley LK. Current understanding of the pathophysiology of osteonecrosis of the jaw. Curr Osteoporos Rep. 2018;16(5):584-595. https://doi.org/10.1007/s11914-018-0474-4
10. Bassan Marinho Maciel G, Marinho Maciel R, Linhares Ferrazzo K, Cademartori Danesi C. Etiopathogenesis of medication-related osteonecrosis of the jaws: a review. J Mol Med (Berl). 2024;102(3):353-364. https://doi.org/10.1007/s00109-024-02425-9
11. Hernlund E, Svedbom A, Ivergard M, Compston J, Cooper C, Stenmark J, et al. Osteoporosis in the European Union: medical management, epidemiology and economic burden. Arch Osteoporos. 2013;8:136. https://doi.org/10.1007/s11657-013-0136-1
12. Limones A, Saez-Alcaide LM, Diaz-Parreno SA, Helm A, Bornstein MM, Molinero-Mourelle P. Medication-related osteonecrosis of the jaws (MRONJ) in cancer patients treated with denosumab vs. zoledronic acid: a systematic review and meta-analysis. Med Oral Patol Oral Cir Bucal. 2020;25(3):e326-e336. https://doi.org/10.4317/medoral.23324
13. Saad F, Brown JE, Van Poznak C, Ibrahim T, Stemmer SM, Stopeck AT, et al. Incidence, risk factors, and outcomes of osteonecrosis of the jaw: integrated analysis from three blinded active-controlled phase III trials in cancer patients with bone metastases. Ann Oncol. 2012;23(5):1341-1347. https://doi.org/10.1093/annonc/mdr435
14. McGowan K, McGowan T, Ivanovski S. Risk factors for medication-related osteonecrosis of the jaws: a systematic review. Oral Dis. 2018;24(4):527-536.

https://doi.org/10.1111/odi.12708

15. Vahtsevanos K, Kyrgidis A, Verrou E, Katodritou E, Triaridis S, Andreadis CG, et al. Longitudinal cohort study of risk factors in cancer patients of bisphosphonate-related osteonecrosis of the jaw. J Clin Oncol. 2009;27(32):5356-5362. https://doi.org/10.1200/JCO.2009.21.9584
16. Kyrgidis A, Vahtsevanos K, Koloutsos G, Andreadis C, Boukovinas I, Teleioudis Z, et al. Bisphosphonate-related osteonecrosis of the jaws: a case-control study of risk factors in breast cancer patients. J Clin Oncol. 2008;26(28):4634-4638. https://doi.org/10.1200/JCO.2008.16.2768
17. Cheong S, Sun S, Kang B, Bezouglaia O, Elashoff D, McKenna CE, et al. Bisphosphonate uptake in areas of tooth extraction or periapical disease. J Oral Maxillofac Surg. 2014;72(12):2461-2468. https://doi.org/10.1016/j.joms.2014.07.004
18. Kim T, Kim S, Song M, Lee C, Yagita H, Williams DW, et al. Removal of pre-existing periodontal inflammatory condition before tooth extraction ameliorates medication-related osteonecrosis of the jaw-like lesion in mice. Am J Pathol. 2018;188(10):2318-2327. https://doi.org/10.1016/j.ajpath.2018.06.019
19. Baek HJ, Lee H, Lee JR, Park JC, Shin HS, Lee JH, et al. Pulp and periapical disease as a risk factor for osteonecrosis of the jaw: a national cohort-based study in Korea. J Periodontal Implant Sci. 2024;54(2):65-74. https://doi.org/10.5051/jpis.2300120006
20. Nair PNR. On the causes of persistent apical periodontitis: a review. Int Endod J. 2006;39(4):249-281. https://doi.org/10.1111/j.1365-2591.2006.01099.x
21. Karamifar K, Tondari A, Saghiri MA. Endodontic periapical lesion: an overview on the etiology, diagnosis and current treatment modalities. Eur Endod J. 2020;5(2):54-67. https://doi.org/10.14744/eej.2020.42714
22. Moinzadeh AT, Shemesh H, Neirynck NAM, Aubert C, Wesselink PR. Bisphosphonates and their clinical implications in endodontic therapy. Int Endod J. 2013;46(5):391-398. https://doi.org/10.1111/iej.12018
23. Kyrgidis A, Arora A, Lyroudia K, Antoniades K. Root canal therapy for the prevention of osteonecrosis of the jaws: an evidence-based clinical update. Aust Endod J. 2010;36(3):130-133. https://doi.org/10.1111/j.1747-4477.2010.00280.x
24. Zavalloni G, Spinelli A, Coppini M, Mauceri R, Campisi G, Lenzi J, et al. Endodontic treatment and management of patients under antiresorptive treatment: a scoping review on MRONJ risk. Clin Oral Investig. 2025;29(10):466. https://doi.org/10.1007/s00784-025-06543-7
25. Hsiao A, Glickman GN, He J. A retrospective clinical and radiographic study on healing of periradicular lesions in patients taking oral bisphosphonates. J Endod.

2009;35(11):1525-1528. https://doi.org/10.1016/j.joen.2009.07.020

26. Zamparini F, Pelliccioni GA, Spinelli A, Gissi DB, Gandolfi MG, Prati C. Root canal treatment of compromised teeth as alternative treatment for patients receiving bisphosphonates: 60-month results of a prospective clinical study. Int Endod J. 2021;54(2):156-171. https://doi.org/10.1111/iej.13405

27. Dereci O, Orhan EO, Irmak O, Ay S. The effect of the duration of intravenous zolendronate medication on the success of non-surgical endodontic therapy: a retrospective study. BMC Oral Health. 2016;16:9. https://doi.org/10.1186/s12903-016-0163-6

28. Cadoni E, Ideo F, Marongiu G, Mezzena S, Frigau L, Mela Q, et al. Periapical status in patients affected by osteoporosis: a retrospective clinical study. Clin Exp Dent Res. 2022;8(5):1068-1075. https://doi.org/10.1002/cre2.604

29. Baethge C, Goldbeck-Wood S, Mertens S. SANRA: a scale for the quality assessment of narrative review articles. Res Integr Peer Rev. 2019;4:5. https://doi.org/10.1186/s41073-019-0064-8

30. Goker Kamali S, Turkaydin D. Endodontic and periapical status of patients with osteoporosis: a cross-sectional study with age- and sex-matched controls. J Am Dent Assoc. 2024;155(12):1022-1030. https://doi.org/10.1016/j.adaj.2024.09.010

31. Rodrigues Freitas G, Capitanio BL, Weissheimer T, Dotto SR, de Figueiredo JAP, Ferrazzo KL. Increased prevalence of periapical lesions in osteoporosis patients: a systematic review. Eur Endod J. 2025;10(2):94-103. https://doi.org/10.14744/eej.2024.98700

32. Tempesta A, Capodiferro S, Di Nanna S, Favia G, Limongelli L, Maiorano E. Medication-related osteonecrosis of the jaw triggered by endodontic failure in oncologic patients. Oral Dis. 2023;29(7):2799-2805. https://doi.org/10.1111/odi.14449

33. Gallego L, Junquera L, Pelaz A, Diaz-Bobes C. Rubber dam clamp trauma during endodontic treatment: a risk factor of bisphosphonate-related osteonecrosis of the jaw? J Oral Maxillofac Surg. 2011;69(6):e93-e95. https://doi.org/10.1016/j.joms.2010.06.197

34. Sarathy AP, Bourgeois SL Jr, Goodell GG. Bisphosphonate-associated osteonecrosis of the jaws and endodontic treatment: two case reports. J Endod. 2005;31(10):759-763. https://doi.org/10.1097/01.don.0000182737.09980.2c

35. Katz H. Endodontic implications of bisphosphonate-associated osteonecrosis of the jaws: a report of three cases. J Endod. 2005;31(11):831-834. https://doi.org/10.1097/01.don.0000186481.96169.cd

36. Kaptan F, Kazandag MK, Iseri U. Treatment of bisphosphonate related osteonecrosis following root canal therapy at the 1-year follow-up: report of two cases. Ther Clin Risk

Manag. 2013;9:477-482. https://doi.org/10.2147/TCRM.S52630

37. AlRahabi MK, Ghabbani HM. Clinical impact of bisphosphonates in root canal therapy. Saudi Med J. 2018;39(3):232-238. https://doi.org/10.15537/smj.2018.3.20923

38. Bermudez-Bejarano E, Martins A, Lorenzo A, Castro A, Lopez A. Implications of endodontic treatment in chemo-osteonecrosis of the maxillary jaw due to bisphosphonates. An updated review. Saudi Endod J. 2022;12(3):261. https://doi.org/10.4103/sej.sej_246_21

39. Nicolatou-Galitis O, Schiodt M, Mendes RA, Ripamonti C, Hope S, Drudge-Coates L, et al. Medication-related osteonecrosis of the jaw: definition and best practice for prevention, diagnosis, and treatment. Oral Surg Oral Med Oral Pathol Oral Radiol. 2019;127(2):117-135. https://doi.org/10.1016/j.oooo.2018.09.008

40. Kuroshima S, Sasaki M, Sawase T. Medication-related osteonecrosis of the jaw: a literature review. J Oral Biosci. 2019;61(2):99-104. https://doi.org/10.1016/j.job.2019.03.005

41. Hinchy NV, Jayaprakash V, Rossitto RA, Anders PL, Korff KC, Canallatos P, et al. Osteonecrosis of the jaw: prevention and treatment strategies for oral health professionals. Oral Oncol. 2013;49(9):878-886. https://doi.org/10.1016/j.oraloncology.2013.06.008

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