

## Medication-Related Osteonecrosis of The Jaws, Surgical or Non-Surgical Treatment: The Retrospective Study

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### ABSTRACT

**Objectives:** Radiation (ORNJ) and bisphosphonate-related (BRONJ) osteonecrosis of the jaw represent challenging entities to treat, with many patients requiring segmental resection and reconstruction with microvascular free tissue transfer (MFTT) in the setting of failed conservative therapy.

**Materials and methods:** Every lesion was identified and categorized in accordance with the 2014 AAOMS Position Paper's guidelines. The primary disease diagnosis, antiresorptive or anti-angiogenic regimen and schedule, existence of comorbidities or other risk reasons, time to MRONJ onset, potential relationship with dental practices & manifestation of pain and/or other symptoms were all gathered from each patient's medical history. To ascertain the existence and extent of bone exposure, soft tissue edema, pus discharge, and tooth movement, each patient received a clinical examination. To further identify the extent and boundaries of the lesions, radiological examinations were also carried out, such as orthopantomography (OPG) & improved multiline spiral computed tomography (EMS-CT) with 3D reconstruction.

**Results:** The current study comprised 20 individuals in total who had 34 MRONJ lesions. Group A comprised 15 patients with 27 lesions (average age 62.1 years, 9 males, 6 females) who had surgery. Group B includes 5 patients with 7 lesions (average age 61 years, 3 males, 2 females) who had non-surgical therapy. Table 1 reports the clinical characteristics of the lesions in both groups. Both Group A and B patients had recurring follow-up, with a mean follow-up duration of 1.6 years (range: 12–28 months). A retrospective comparative cohort study found that 88.9% of lesions healed with surgery, compared to 0% with non-surgical care. treatment choice was based on AAOMS stage severity, with outcomes assessed by a blinded examiner.

**Conclusion:** The results reinforce the significance of early detection, customized therapeutic approaches, and continued exploration of innovative strategies to enhance MRONJ management and patient outcomes.

**Keywords:** Bisphosphonates, MRONJ, American Association of Oral & Maxillofacial Surgery.

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### 1. INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is a relatively recent condition affecting the head and neck area. It was first described by Marx (2003)<sup>1</sup> and Carter et al.<sup>2</sup> MRONJ is defined as an avascular necrosis of the maxillofacial bones that does not heal following bisphosphonate (BP) therapy.<sup>3</sup> Initially, this condition was known as bisphosphonate-related osteonecrosis of the jaws (BRONJ) and could occur after intravenous or oral BP therapy.<sup>4</sup> However, in the last ten

years, it has been shown that denosumab and other anti-angiogenic medications can also cause MRONJ through a mechanism similar to BPs.<sup>5</sup> This discovery led to the 2015 American Association of Oral & Maxillofacial Surgery (AAOMS) definition of MRONJ: "exposure of necrotic bone in the oral cavity lasting more than 8 weeks, in patients treated with anti-resorptive or anti-angiogenic drugs, without prior head and neck radiotherapy, and without bone metastases in the maxillofacial region." MRONJ can significantly impact a patient's health and quality of life. Common symptoms include pain, swelling, bone sequestration, and in severe cases, fistulae and pathological fractures. Importantly, the lower jaw is more frequently affected than the upper jaw.<sup>5</sup> The pathophysiology of MRONJ is likely more complex than initially thought. For example, since the mandible has less vascularization than the maxilla, it would receive a lower concentration of bisphosphonates. Therefore, one would expect the lower jaw to have fewer MRONJ cases than the upper jaw. However, clinical findings show the opposite, with the mandible being more commonly affected.<sup>6</sup>

The AAOMS classifies MRONJ into four stages (0 to III). For the early stages (0–I), medical management is recommended, while surgical treatment is preferred for the later stages (II–III). This stage-specific approach allows for a more standardized treatment plan in early phases. However, patients in the later stages require individual evaluation.<sup>7</sup> Although surgery is generally advised for advanced stages, the extent of surgical intervention remains debated. Treatment options range from basic conservative care to sequestrectomy and removal of all affected bone, potentially including reconstruction with a microvascular free flap if necessary or feasible.<sup>8,9</sup>

To inform stage-consistent decision-making, we compared surgical versus non-surgical outcomes using AAOMS 2014 criteria with blinded assessment and predefined endpoints. This retrospective research aimed to characterize the course of treatment and results for 20 MRONJ patients.

## 2. METHODOLOGY

Twenty patients with MRONJ were treated at the hospital's oral surgery unit between **March 2022 and August 2026** as part of this study, conducted with institutional ethical approval and written patient consent. Lesions were identified and classified following the **2014 AAOMS Position Paper** guidelines. Patient data collected included:

- Primary disease diagnosis
- Antiresorptive or anti-angiogenic treatment regimen and schedule
- Presence of comorbidities or other risk factors
- Time to MRONJ onset
- Possible links to dental procedures
- Symptoms such as pain

Each patient underwent a clinical examination assessing bone exposure, soft tissue swelling, pus discharge, and tooth mobility. Radiological evaluations included orthopantomography (OPG) and enhanced multiline spiral CT (EMS-CT) with 3D reconstruction to determine lesion extent and boundaries. Treatment plans were individualized based on clinical findings.

Patients were divided into two groups:

- Group A (GA): Patients eligible for surgical treatment without risk.
- Group B (GB): Patients requiring non-surgical management because surgery was unsafe or they could not pause cancer-related therapies.

**GA Treatment Protocol:**

- Discontinued blood pressure and antiresorptive/anti-angiogenic medications at least 3 months before surgery.
- Other chemotherapeutic agents or corticosteroids stopped 3–5 days before surgery and continued until wound healing.
- Administered at least three rounds of antibiotics before surgery, including:
  - Ceftriaxone (1 g intramuscular daily)
  - Metronidazole (500 mg orally twice daily for 8 days, with 10-day breaks between cycles).
- Surgically removed necrotic bone, usually under general anesthesia.
- Wound closure without a mucoperiosteal flap.
- Surgical approach varied by lesion stage:
  - Minor MRONJ: simple surgical debridement.
  - Larger lesions: extensive bone resection.
- All surgical specimens underwent histological analysis to confirm MRONJ.
- Post-surgery, weekly clinical follow-ups with orthopantomography (OPG) for the first month.
- Resumption of BPs, antiresorptive, and anti-angiogenic therapies only after clinical and radiological wound healing.

**GB Treatment Protocol:**

- Monthly low-level laser therapy using a diode laser:

- Fiber size: 320  $\mu\text{m}$
- Wavelength: 800  $\pm$  10 nm
- Power: 0.5–1 W
- Use of antiseptic mouth rinse (chlorhexidine).
- Routine dental check-ups.
- Systemic antibiotics monthly:
  - Ceftriaxone (1 g intramuscular daily)
  - Metronidazole (500 mg orally twice daily for 7 days).

#### Treatment Outcome Categories:

- **Complete Healing:** Oral mucosa fully covers previously exposed bone.
- **Partial Healing:** Lesion size decreases per **AAOMS criteria**.
- **Stable Disease:** No change in lesion clinical stage during observation.
- **Continuing Disease:** Lesion grows during observation.

#### Study Design:

- **Type:** Retrospective comparative cohort (March 2022 – August 2026).
- **Sampling:** Consecutive eligible patients to reduce selection bias.
- **Allocation:** Based on **AAOMS 2014 staging**; surgery offered when medically and anatomically feasible; non-surgical care for contraindications or inability to pause therapy.
- **Independent Examiner:** Senior oral and maxillofacial surgeon (OMFS), blinded to treatment, verified baseline stage and healing at follow-ups; calibration and adjudication of disagreements performed.

#### Staging and Treatment:

- Stages **I–III** assigned using clinical and radiographic criteria.
- Treatment tailored by stage:
  - Early disease: conservative care  $\pm$  sequestrectomy/debridement.
  - Advanced disease: resection/debridement with closure.
- Stage transitions (up/down-staging) documented to guide ongoing care.

#### Statistical Analysis:

- Analysis using **Fisher's exact test** and **relative risk (RR)** with 95% confidence interval (CI) applying Haldane–Anscombe correction.
- GA (surgical group) healing 95% CI (Wilson): **0.72–0.96**.
- Significance level:  $\alpha = 0.05$  (**two-sided**).

### 3. RESULTS

The study included 20 patients with a total of 34 MRONJ lesions:

- Group A (Surgical): 15 patients with 27 lesions
  - Average age: 62.1 years
  - Gender: 9 males, 6 females
- Group B (Non-surgical): 5 patients with 7 lesions
  - Average age: 61 years
  - Gender: 3 males, 2 females

Both groups had recurring follow-ups with a mean duration of 1.6 years (range: 12–28 months).

#### Outcomes (per AAOMS staging):

- Group A:
  - 100% of stage I and II lesions achieved complete healing.
  - 70% of stage III lesions fully healed.
  - 30% of stage III lesions exhibited partial healing and were down-staged to stage I.
- Group B:
  - Patients unable to stop chemotherapy, corticosteroids, or antiresorptive drugs showed only partial healing.
  - Some lesions down-staged (one stage II to I; two stage III to II), four lesions remained stable, and one lesion up-staged from II to III.
  - No lesions showed complete healing in Group **B**.

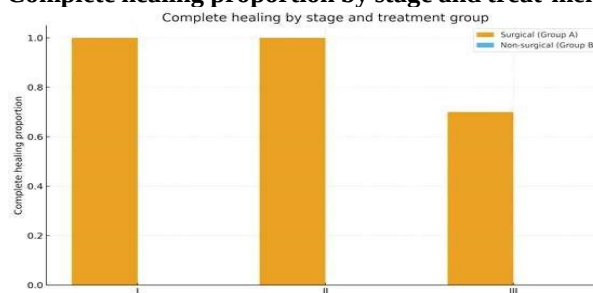
**Table 1: Clinical characteristics of surgical and nonsurgical treatment**

| Clinical features                     | Group A (27 lesions) | Group B (7 lesions) |
|---------------------------------------|----------------------|---------------------|
| Site                                  |                      |                     |
| Upper Jaw                             | 9                    | 3                   |
| Lower Jaw                             | 18                   | 4                   |
| Stage                                 |                      |                     |
| I                                     | 2                    | 1                   |
| II                                    | 15                   | 2                   |
| III                                   | 10                   | 4                   |
| Primary disease                       |                      |                     |
| Oncologic                             | 21                   | 5                   |
| Non-oncologic                         | 6                    | 2                   |
| Trigger Event                         |                      |                     |
| Spontaneous                           | 15                   | 6                   |
| Oral Surgery                          | 12                   | 1                   |
| Antiresorptive/anti-angiogenic agents |                      |                     |
| Denosumab                             | 9                    | 4                   |
| Bisphosphonates                       | 16                   | 2                   |
| Both                                  | 2                    | 1                   |

**Table 2: Healing outcome by stage and group (lesion-level):**

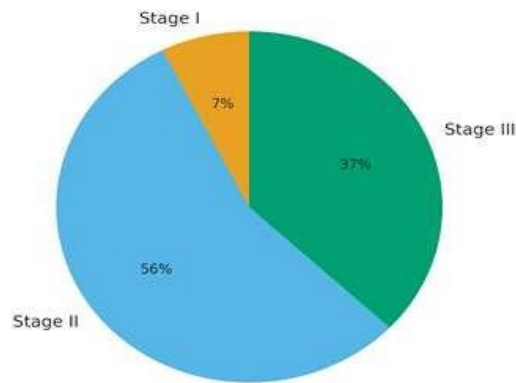
| Stage | Group A: Complete | Group A: Not complete | Group B: Complete | Group B: Not complete |
|-------|-------------------|-----------------------|-------------------|-----------------------|
| I     | 2                 | 0                     | 0                 | 1                     |
| II    | 15                | 0                     | 0                 | 2                     |
| III   | 7                 | 3                     | 0                 | 4                     |

**Fig 1: Complete healing proportion by stage and treatment group**



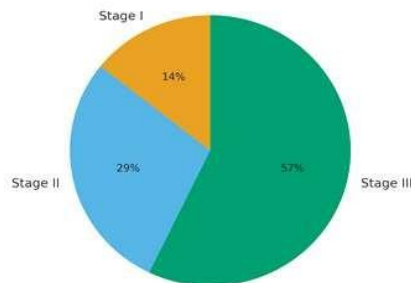
**Fig 2: Stage distribution within Group A**

Stage distribution — Group A (surgical)

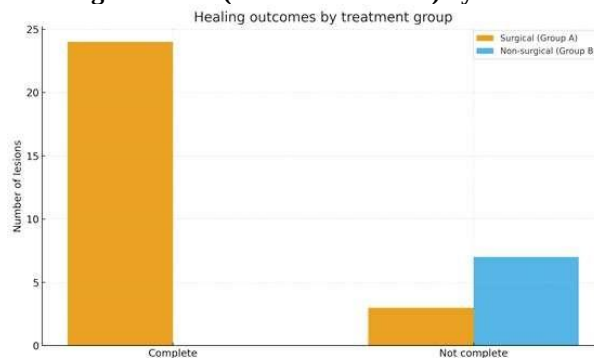


**Fig 3: Stage distribution within Group**

Stage distribution — Group B (non-surgical)



**Fig 4: Healing outcomes (number of lesions) by treatment group.**



#### 4. DISCUSSION

Stage-guided surgery yielded substantially higher complete-healing than conservative care in our cohort, supporting selective early surgical inter-vention. Blinded verification of AAOMS staging and outcomes strengthens the inference, but lesion-level analysis and small non-surgical sample introduce bias and limit generalizability. Future prospective, adequately powered, drug-stratified studies should evaluate patient-centered outcomes and durability.

MRONJ has been controversial since it was originally described in 2003 (Marx, 2003)<sup>2</sup>, and there is still much disagreement on how to manage MRONJ patients. Several writers have suggested various therapy options: surgical debridement, ozone therapy, laser therapy, antibiotic therapy, hyperbaric oxygen, and extensive surgery According to the AAOMS position document, prevention is the most crucial factor in managing MRONJ. However, if MRONJ has occurred, the aim of treatment is to alleviate pain & manage soft tissue infection & disease development<sup>10</sup>.

Furthermore, the AAOMS document states that only individuals with stage III lesions should have surgical therapy; those with stage I and II lesions are not advised to receive it. Other authors agreed with Kün-Darbois et al<sup>11</sup> that the gold standard for managing MRONJ is nonsurgical treat-ment, which includes antimicrobial mouthwash and antibiotic medication. In these trials, stable wound conditions or MRONJ downstaging, as defined by the AAOMS staging

system, were thought to be the objectives of treatment rather than the full healing of the lesions. On the other hand, higher MRONJ healing rates after surgical procedures were reported by some writers<sup>12</sup>. A 90% success rate with stable mucosal closure was reported by Bensi et al<sup>13</sup> and Basile for MRONJ patients having surgery. According to Şahin et al<sup>14</sup> 70% of lesions had decreased staging following surgery, and 43% of treated patients experienced full healing of their lesions.

## 5. CONCLUSION

Surgical management under AAOMS 2014 staging achieved markedly higher complete healing and durable stability at ~1.6 years. These findings support timely surgery when feasible and individualized conservative care when not, pending larger confirmatory studies.

## 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. *Journal of oral and maxillofacial surgery*. 2022 May 1;80(5):920-43.
2. Marx RE. Pamidronate (Aredia) and zoledronate (Zome-ta) induced avascular necrosis of the jaws: a growing epidemic. *Journal of oral and maxillofacial surgery*. 2003 Sep 1;61(9):1115-7.
3. Byrne H, O'reilly S, Weadick CS, Brady P, Ríordáin RN. How we manage medication-related osteonecrosis of the jaw. *European Journal of Medical Research*. 2024 Aug 2;29(1):402.
4. Tetradis S, Allen MR, Ruggiero SL. Pathophysiology of Medication-Related Osteonecrosis of the Jaw—A Minireview. *Journal of Bone and Mineral Research Plus*. 2023 Aug 1;7(8):e10785.
5. Ruan HJ, Li MY, Zhang ZY, Ma HL, He Y. Medication-related osteonecrosis of the jaw: a retrospective single center study of recurrence-related factors after surgical treatment. *Clinical Oral Investigations*. 2024 Oct;28(10):1-2.
6. Kwon YD, Jo H, Kim JE, Ohe JY. A clinical retrospective study of implant as a risk factor for medication-related osteonecrosis of the jaw: surgery vs loading?. *Maxillofacial Plastic and Reconstructive Surgery*. 2023 Sep 14;45(1):31.
7. Ruan HJ, Li MY, Zhang ZY, Ma HL, He Y. Medication-related osteonecrosis of the jaw: a retrospective single center study of recurrence-related factors after surgical treatment. *Clinical Oral Investigations*. 2024 Oct;28(10):1-2.
8. AlDhalaan NA, BaQais A, Al-Omar A. Medication-related osteonecrosis of the jaw: a review. *Cureus*. 2020 Feb;12(2).
9. Lobekk OK, Dijkstra W, Pedersen TØ. Surgical vs conservative treatment of medication-related osteonecrosis of the jaw: A complex systematic review and meta-analysis. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2021 Dec 1;132(6):671-9.
10. Choi NR, Lee JH, Park JY, Hwang DS. Surgical treatment of medication-related osteonecrosis of the jaw: a retrospective study. *International journal of environmental research and public health*. 2020 Dec;17(23):8801.
11. Kün-Darbois JD, Fauvel F. Medication-related osteonecrosis and osteoradionecrosis of the jaws: Update and current management. *Morphologie*. 2021 Jun 1;105(349):170-87.
12. Wick A, Bankosegger P, Otto S, Hohlweg-Majert B, Steiner T, Probst F, Ristow O, Pautke C. Risk factors associated with onset of medication-related osteonecrosis of the jaw in patients treated with denosumab. *Clinical oral investigations*. 2022 Mar 1:1-4.
13. Bensi C, Giovacchini F, Lomurno G, Eramo S, Barraco G, Tullio A. Quality of life in patients affected by medication-related osteonecrosis of the jaws: A systematic review. *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*. 2021 Aug 1;132(2):182-9.
14. Şahin O, Akan E, Tatar B, Ekmekcioğlu C, Ünal N, Odabaşı O. Combined approach to treatment of advanced stages of medication-related osteonecrosis of the jaw patients. *Brazilian Journal of Otorhinolaryngology*. 2022 Aug 15;88(4):613-20.