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Original Article

MEDICATION-RELATED OSTEONECROSIS OF THE JAWS, SURGICAL OR NON-SURGICAL TREATMENT: THE RETROSPECTIVE STUDY

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ABSTRACT

Objectives: *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.*

Materials and Methods: *Every lesion was identified and categorized in accordance with the 2014 AAOMS Position Paper's guidelines.5 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.*

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

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INTRODUCTION

A relatively recent condition affecting the head and neck area is medication-related osteonecrosis of the jaw (MRONJ)[1]. Marx (2003)[2] and Carter et al. described the first examples. They defined MRONJ as an avascular necrosis of the maxillofacial bones

that did not recover following bisphosphonate (BP) therapy[3]. Therefore, this condition was once known as bisphosphonate-related osteonecrosis of the jaws (BRONJ), and it may be brought on by intravenous or oral BP therapy[4]. It has been demonstrated in the last ten years, however, that denosumab and other anti-angiogenic medications may also produce MRONJ by a mechanism akin to that of BPs[5]. This discovery ultimately paved the way for the 2015 American Association of Oral & Maxillofacial Surgery (AAOMS) definition of MRONJ, which is "an exposure of necrotic bone in the oral cavity that lasts more than 8 weeks, in patients treated with anti-resorptive or anti-angiogenic drugs, without previous head and neck radiotherapy, and without bone metastases in the maxillofacial region." MRONJ has the potential to seriously harm a patient's health and well-being. Pain, swelling, bone sequestrate, & in more severe instances, fistulae and pathological fractures, are common symptoms. Crucially, the lower jaw is more affected by the illness than the upper jaw[5]. The pathophysiology, however, is probably more intricate than previously believed. For instance, a lesser concentration of bisphosphonates would be transmitted to the mandibular bone as opposed to the maxillary bone since the mandible has less vascularization than the maxilla. Consequently, it makes sense to believe that the lower jaw should experience fewer MRONJ instances than the upper jaw. On the other hand, clinical findings revealed the reverse[6].

• Alveolar osteitis (dry socket): recent extraction; resolves within weeks; MRONJ persists >8 weeks.

• Chronic suppurative osteomyelitis: infectious source; responds to culture-directed therapy; MRONJ linked to antiresorptive exposure.

• Osteoradionecrosis: prior head-neck radiotherapy; excluded by MRONJ definition.

• Periodontitis/periapical pathology: tooth-centered radiolucencies; MRONJ shows non-healing exposed bone with cortical breach.

• Sinusitis-related osteitis: sinonasal symptoms and CT mucosal thickening; MRONJ may secondarily involve the sinus but has oral bone exposure.

• Jaw metastasis: radiographic lesions with primary cancer; biopsy distinguishes; excluded by definition.

The AAOMS classified MRONJ into four phases, which are stages 0 through III. For the initial phases (stages 0–I), the AAOMS has recommended medical care; for the later stages (stages II–III), surgical approaches are preferred[7]. In the early phases, a more uniform treatment strategy is made possible by this stage-specific approach. However, each patient must be evaluated individually for the latter stages[8]. The degree of surgical therapy is still up for debate, even though it is usually advised for the latter stages. Among the available treatment options are the most basic conservative measures, as well as, if required or practical, a sequestrectomy and bony excision of all impacted bone, either with or without reconstruction using a microvascular free flap[9].

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.

MATERIALS AND METHODS

Twenty patients with MRONJ visited the hospital's oral surgery unit between March 2020 and August 2024 as part of the current study, which was performed in the surgical department with institutional ethical permission, and written consent was taken from each patient included in the study. Every lesion was identified and categorized in accordance with the 2014 AAOMS Position Paper's guidelines[5]. 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. Ultimately, each patient's treatment plan was customized based on what was considered clinically suitable. The patients were therefore split into two clusters: Group A (GA), which included those who could undergo surgical treatments without risk, and Group B (GB), which

included those for whom non-surgical management was necessary because surgery was not thought to be entirely safe or because they were unable to stop their cancer-related therapies. GA patients were treated by stopping blood pressure medication and antiresorptive/anti-angiogenic medications at least three months before surgery (other chemotherapeutic agents or corticosteroids were stopped three to five days before surgery and continued until the wound healed); administering at least three rounds of antibiotics before surgery, which included ceftriaxone (1 g/i.m.daily) and metronidazole (500 mg/per os twice a day) for eight days with a 10-day break between each cycle; surgically removing the necrotic bone, typically under general anaesthesia; & closing the wound without using a mucoperiosteal flap. The surgical strategy varied based on the lesions' stage and extent; for minor MRONJ, it included simple surgical debridement; for larger lesions, it involved substantial bone resection. As previously stated, all surgical specimens were sent for histological analysis to confirm the diagnosis of MRONJ. Following OPG, weekly periodic clinical follow-up was instituted throughout the first month. Patients only resumed BPs, antiresorptive, and anti-angiogenic therapies if required following clinic radiological wound healing. Treatment of GB patients involved monthly low-level laser therapy, which involved irradiating the necrotic bone with a diode laser with a fiber of 320 μm, a wavelength of 800 ± 10 nm, at a power of 0.5–1 W; using an antiseptic mouth rinse (chlorhexidine); routine dental examinations; and administering systemic antibiotics (ceftriaxone 1 g/i.m. daily and metronidazole 500 mg/per os twice a day for seven days once a month).

Four categories were assigned to treatment outcomes: Complete healing is when the oral mucosa completely covers the previously exposed bone; partial healing is when the lesion shrinks in accordance with the AAOMS criteria; stable disease is when the lesion's clinical stage remains unchanged during observation; & continuing disease is when the lesion grows during observation.

Design: Retrospective comparative cohort (March 2020–August 2024). Sampling: consecutive eligible patients to minimize selection bias. Allocation: AAOMS 2014 stage-guided; surgery offered when medically/anatomically feasible; non-surgical care for contraindications or therapy-interruption constraints. Independent examiner: senior OMFS, blinded to modality, verified baseline stage and healing at follow-ups; calibration performed; disagreements adjudicated.

Stages I–III assigned per clinical/radiographic criteria. Treatment pathways were stage-stratified (conservative ± sequestrectomy/debridement for early disease; resection/debridement with closure for advanced disease). Stage transitions (down/up-staging) were documented and guided subsequent care.

Primary endpoint: complete healing (yes/no) per lesion. Fisher's exact test; RR with 95% CI (Haldane–Anscombe correction). GA healing 95% CI (Wilson): 0.72–0.96. α=0.05 (two-sided). Secondary: stage-wise outcomes; site and drug distributions.

Non-surgical group was underpowered. Approximately 5 lesions per group are required for 80% power at α=0.05 to detect rates comparable to those observed (surgical ≈ 89% vs non-surgical ≈ 10%). Future studies should target these numbers and use patient-level models to handle clustering.

RESULT

TThe 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). According to the AAOMS staging method, all (100%) of the Group A patients' stage I and II lesions and 7 (70%) of their stage III lesions exhibited full healing, while 3 (30%) of their stage III lesions showed partial healing and were downstaged from stage III to stage I. Oncologic patients who were unable to stop receiving chemotherapy, corticosteroids, and/or antiresorptive medications because of their general illnesses showed all partial healings. Although one stage II lesion and two stage III lesions underwent a downstaging to stage I and II, respectively, four lesions showed stable disease, and one lesion displayed an upstaging from stage II to III during surveillance, none of the lesions in Gb patients showed full recovery.

Complete healing: 24/27 lesions in Group A vs 0/7 in Group B (Fisher's exact p=0.0000; RR=14.00, 95% CI 0.95–205.73). Treatment choices mirrored clinical severity and AAOMS criteria. Outcome assessors were blinded. Follow-up averaged 1.6 years with zero losses.

Lesions with complete mucosal coverage showed no recurrence through 12–28 months. Down-staged lesions remained clinically and radiographically stable.

Given small strata, formal testing by drug class was not performed; descriptive distributions are shown, and stratified analyses are recommended in larger cohorts

Approximately 5 lesions per group are needed for 80% power; the present Group B (n=7) is underpowered for inferential testing.

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

Note: "Not complete" includes partial healing, stable disease, and up-staging events.

DISCUSSION

Stage-guided surgery yielded substantially higher complete-healing than conservative care in our cohort, supporting selective early surgical intervention. 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)[2], 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[10]. 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[11] that the gold standard for managing MRONJ is nonsurgical treatment, 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[12]. A 90% success rate with stable mucosal closure was reported by Bensi et al[13] and Basile for MRONJ patients having surgery. According to Şahin et al[14] 70% of lesions had decreased staging following surgery, and 43% of treated patients experienced full healing of their lesions.

According to research by He et al[15], surgery was the gold benchmark for managing MRONJ, with non-surgical methods reserved for individuals who couldn't have surgery due to certain medical conditions. We compared the surgical & non-surgical management results of MRONJ and a total of 27 le-

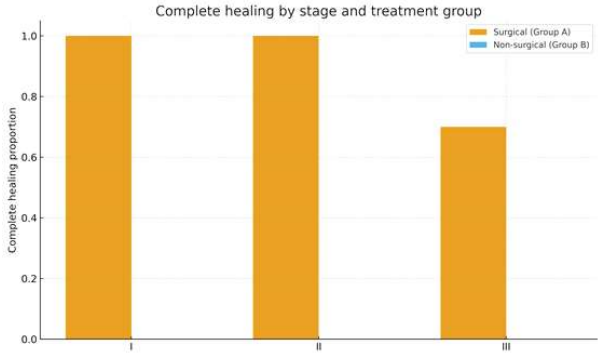

Fig 1: Complete healing proportion by stage and treatment group.

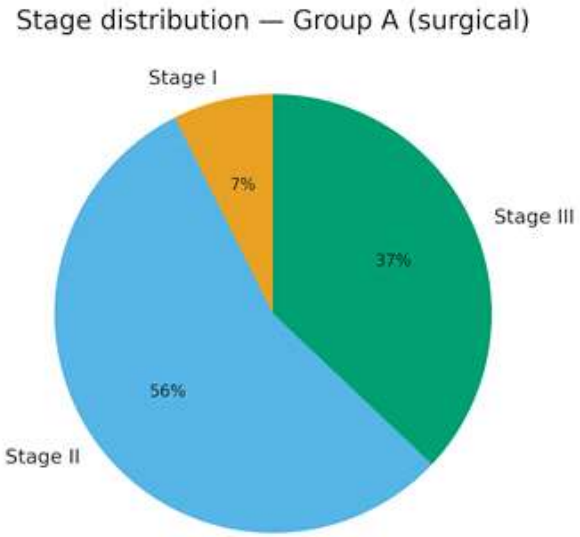

Fig 2: Stage distribution within Group A

sions from 15 patients in the current study; however, statistical analyses were inappropriate because of the small sample size of non-surgical GB patients (5 individuals with 7 lesions). However, some conclusions can be made. During the radiological follow-up, we found that all stage I and II lesions in GA, as well as 80% of stage III lesions, had fully healed, had a sustained absence of bone exposure, and showed no signs of MRONJ persistence or recurrence. The quality of life for patients was enhanced when only 20% of stage III lesions did not mend & instead suffered a drop in staging to stage I, which is defined by exposed and necrotic bone without any indication of infections or symptoms. On the other hand, 90% of GB patients' lesions remained constant, one exhibited upstaging from stage II to III, and just two lesions improved, with downstaging from stage II to I and from stage III to II, respectively. These patients never shown full healing of their lesions.

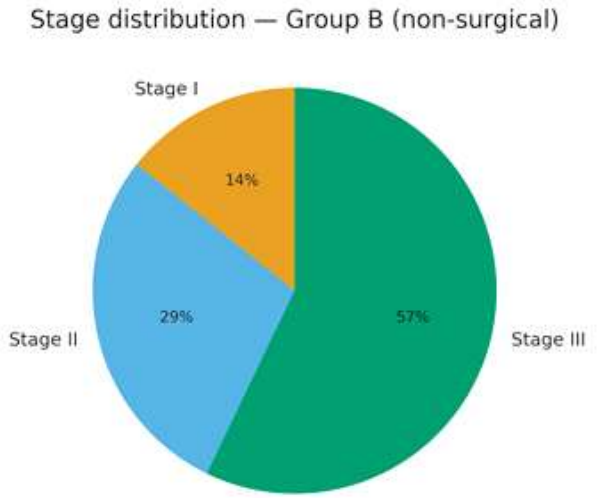

Fig 3: Stage distribution within Group B

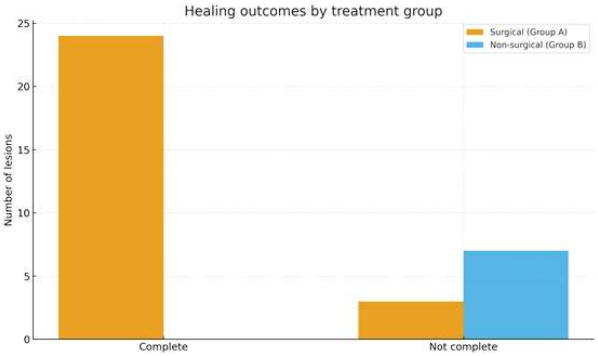

Fig 4: Healing outcomes (number of lesions) by treatment group.

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.

The findings underscore the efficacy of surgical interventions, particularly for stage I & II lesions and a significant proportion of stage III lesions, with notable rates of complete healing and improved quality of life. Non-surgical treatments, while valuable for patients unable to undergo surgery, yielded limited improvement, emphasizing the need for individualized treatment plans. The results reinforce the significance of early detection, customized therapeutic approaches, and continued exploration of innovative strategies to enhance MRONJ management and patient outcomes.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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AUTHORS' CONTRIBUTION

The following authors have made substantial contributions to the manuscript as under:

Conception or Design:	HJ, SUS, MU, MUJ, SY, RMD
Acquisition, Analysis or Interpretation of Data:	HJ, SUS, MU, MUJ, SY, RMD
Manuscript Writing & Approval:	HJ, SUS, MU, MUJ, SY, RMD

All the authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.