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Clinical characteristics of osteonecrosis of the jaw related to denosumab: a 5-year retrospective cohort study

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Abstract (J Korean Assoc Oral Maxillofac Surg 2026;52:18-26)

Objectives: This study aimed to investigate the clinical characteristics, treatment outcomes, and factors influencing treatment success in patients with denosumab (Dmab)-related osteonecrosis of the jaw (DRONJ).

Patients and Methods: This retrospective cohort study included the patients who were diagnosed with DRONJ and treated at the authors' affiliated hospital, between August 2019 and August 2024. The patients were divided into the three groups; Group 1, low-dose Dmab; Group 2, transition from bisphosphonates (BPs) to low-dose Dmab; Group 3, high-dose Dmab. Differences in clinical characteristics among the groups were compared. Surgical outcomes were classified into three categories: complete healing, partial healing, and no healing. "Treatment success" was defined as the combined proportion of complete and partial healing.

Results: A total of 178 DRONJ patients were included in this study. Most of DRONJ occurred in osteoporosis patients. In patients treated with low-dose Dmab, prior BP use resulted in the development of MRONJ within a shorter period after Dmab administration but did not affect disease severity or treatment outcomes. Overall postoperative healing outcomes were favorable at 3 months after DRONJ treatment. The overall treatment success rate was 81.5%; Group 1, 85.0%; Group 2, 82.8%; Group 3, 53.8%, P=0.027). Multiple regression analysis demonstrated that Dmab dosage was a significant factor influencing treatment success, whereas age, treatment duration, lesion location, and DRONJ stage were not (odds ratio, 5.13; 95% confidence interval, 1.19-22.14; P=0.028).

Conclusion: The earlier onset in the BP to Dmab transition group may be attributable to the cumulative duration of antiresorptive therapy. Patients treated with high-dose Dmab demonstrated poorer prognosis and more frequent recurrence after MRONJ treatment compared with those treated with low-dose Dmab or BP to Dmab transition therapy. herefore, these findings need to be considered for treatment of DRONJ.

Key words: Denosumab, Osteonecrosis, Bisphosphonate-associated osteonecrosis of the jaw, Osteoporosis

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I. Introduction

Bisphosphonates (BPs) and denosumab (Dmab) are the most commonly used drugs for treating osteoporosis[1]. Dmab was developed based on an understanding of the receptor activator of nuclear factor kappa B/receptor activator of nuclear factor kappa B ligand (RANK/RANKL) pathway starting in the 1990s and was approved by the U.S. Food and Drug Administration (FDA) as Prolia, and Xgeva in June and November 2010, respectively, for treatment of bone loss associated with osteoporosis and malignancy. BPs are analogues of inorganic pyrophosphate that inhibit pyrophosphate-dependent enzymes involved in bone resorption[2]. Dmab is a fully human monoclonal immunoglobulin G2 (IgG2) antibody that targets RANKL[3]. By inhibiting the interaction between RANKL and its receptor RANK, which is expressed on the surface of osteoclasts, Dmab suppresses the formation, function, and survival of osteoclasts, thereby reducing bone resorption and increasing bone density[3]. Although both BPs and Dmab reduce bone resorption, their mechanisms of action differ. BPs inhibit osteoclast differentiation and maturation and induce osteoclast apoptosis[2], whereas Dmab, as a monoclonal antibody against RANKL, inhibits osteoclast differentiation and

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function[3]. Unlike BPs, Dmab does not bind to bone, and its effects on bone remodeling are largely diminished within 6 months after treatment cessation. In addition, BPs have low gastrointestinal absorption and require strict dosing regimens, including fasting and postural restrictions, whereas Dmab is administered as a subcutaneous injection once every 6 months, offering greater convenience and patient compliance. Compared with BPs, Dmab has been reported to be associated with a relatively lower risk of severe side effects, such as osteonecrosis of the jaw (ONJ). For these reasons, Dmab is increasingly recommended as first-line therapy for osteoporosis. Consequently, reports of Dmab-related osteonecrosis of the jaw (DRONJ) have increased in recent years.

The first case of ONJ, reported by Marx[4] in 2003, was caused by pamidronate and zoledronate. It occurred in cancer patients who received high-dose of BP through intravenously. Subsequent cases were also reported in patients treated with oral BPs[5]. In 2007, The American Association of Oral and Maxillofacial Surgeons (AAOMS) proposed a formal definition for BP-related osteonecrosis of the jaw (BRONJ)[6]. Taylor et al.[7] first reported DRONJ cases, and since then, DRONJ has been increasingly recognized. In 2014, the AAOMS recommended changing the terminology from BRONJ to medication-related osteonecrosis of the jaw (MRONJ)[8]. MRONJ is defined by following criteria: (1) Current or previous treatment with antiresorptive therapy alone or in combination with immune modulators or antiangiogenic medications, (2) exposed bone or bone that can be probed through an intraoral or extraoral fistula(e) in the maxillofacial region that has persisted for more than 8 weeks, (3) no history of radiation therapy to the jaw or metastatic disease to the jaws. This revised definition explicitly includes Dmab as a causative medication. Several studies have reported the clinical characteristics and treatment outcomes of DRONJ[9-12]. However, the most previous were limited to small case series and predominantly involved patients receiving high-dose Dmab for malignant disease, making it difficult to draw definitive conclusions applicable to clinical practice. In recent years, Dmab has been widely prescribed for osteoporosis, and DRONJ has become a substantial proportion of MRONJ cases[13,14]. Therefore, a comprehensive analysis of the clinical characteristics of DRONJ based on a larger patient population is warranted.

The objective of this study was to retrospectively analyze DRONJ cases treated at a single institution and to evaluate: (1) The clinical characteristics of DRONJ, with particular attention to differences among low-dose Dmab, high-dose Dmab, and sequential BP and Dmab therapy, (2) treatment outcomes following surgical treatments, (3) factors influencing treatment success in patients with DRONJ.

II. Patients and Methods

1. Study population

This retrospective cohort study included patients diagnosed as DRONJ who treated at the authors' affiliated institute, from August 2019 to August 2024. The definition and staging of affected patients were defined according to 2022 AAOMS position paper for MRONJ[15].

The inclusion criteria were as follows: (1) Patients with MRONJ after Dmab administration for osteoporosis treatment (low-dose Dmab, 60 mg/6 months; Prolia) or cancer treatment (high-dose Dmab, 120 mg/4 weeks; Xgeva), (2) history of Dmab treatment or switch to Dmab after BPs administration (alendronate, ibandronate, pamidronate, risedronate, or zoledronate), (3) minimum 3-months follow-up after conservative or surgical treatments.

The exclusion criteria were as follows: (1) History of radiation therapy to the oral and maxillofacial area, (2) patients whose medication history is not accurate or accessible, (3) patients who refuse treatment or were not followed up for more than 3 months after treatments.

2. Data collection

Patients were divided into 3 groups: Group 1, low-dose Dmab; Group 2, transition from BP to low-dose Dmab (BP to Dmab); Group 3, high-dose Dmab. Clinical and demographic data collected for each patient include age, sex, comorbidities, Dmab or BP therapy (dosage, duration), symptom at first visited, MRONJ stage, preceding event, location, the type of MRONJ treatment (conservative vs. surgical), number of surgical intervention(s), healing states, and number of recurrences were investigated retrospectively.

3. Evaluation of treatment outcomes

1) Primary outcomes: clinical healing

We investigated soft tissue healing status of individual patients at 3 months postoperatively. Definition of the outcomes after the surgery was divided into 3 categories according to the following clinical findings at least 3 months after conservative or surgical treatment; "complete", "partial," or "no

healing", which modified from a previous literature[16].

① Complete healing: Absence of exposed necrotic bone or bone that can be probed through fistula, absence of purulent discharge, absence of edema or pain, and complete mucosal coverage at the surgical site.

② Partial healing: Clinical evidence of MRONJ stage improvement compared to the stage of the initial diagnosis, but did not show complete mucosal coverage.

③ No healing: Unchanged or worsening of stage compared to the stage of initial diagnosis.

The "treatment success" was defined as the combined proportion of "complete healing" and "partial healing".

2) Secondary outcomes: DRONJ recurrence

Recurrence was defined as the reappearance of exposed necrotic bone or bone that could be probed through a fistula, persisting for more than 8 weeks after an area had been previously classified as "complete healing".

4. Statistical analysis

Patient demographics are expressed as n (%) and mean± standard deviation. To analyze the difference between the groups, continuous variables such as duration of drug administration were investigated by the ANOVA followed by Tukey's post-hoc test. To compare the categorical variables, such as the MRONJ stage, Fisher's exact test or chi-square test were used. Multiple logistic regression analysis was used to determine factors independently associated with the dependent variable—success rate of DRONJ treatment. Covariates in this model were age, dosage and duration of Dmab, location of the lesion, stage of DRONJ and treatment methods; 95% confidence intervals (CIs) for estimated odds ratio (OR) approximating the relative risk are also given. Statistical significance was set at $P<0.05$. Statistical tests were performed using SPSS statistical software (IBM SPSS Statistics for Windows ver. 29.0; IBM).

5. Ethics statement

This study protocol was approved by the Kyungpook National University Dental Hospital Institutional Review Board (approval No. KNUDH-2024-11-04-00). In written informed consent from the patients were waived, because of the retrospective nature of the study and use of de-identified participant data. This study was performed in accordance with the Declaration of Helsinki.

III. Results

After screening patients with MRONJ, 193 patients with DRONJ were initially identified as eligible for this retrospective study. However, 15 patients refused treatment or were lost to follow-up and were subsequently excluded. A total of 178 patients with DRONJ were ultimately included in the analysis.

1. Demographics and clinical characteristics

Baseline characteristics of the study population, including age, sex, and comorbidities, are summarized in Table 1. Majority of DRONJ cases (92.7%) occurred in patients treated for osteoporosis; Group 1 (low-dose Dmab, n=60; 33.7%), Group 2 (transition from BP to low-dose Dmab, n=105; 59.0%), Group 3 (high-dose Dmab, n=13; 7.3%). The mean age was 77.4±6.7 years in Group 1, 76.6±7.2 years in Group 2, and 63.5±8.9 years in Group 3 (ANOVA, $P<0.001$). Patients in Group 3 were significantly younger than those in the osteoporosis groups (Groups 1 and 2). The mean duration of Dmab administration before MRONJ development was 23.2±15.3 months in Group 1, 16.0±11.3 months in Group 2, and 27.9±18.8 months in Group 3. In Group 2, BPs had been administered for a mean duration of 56.7±46.4 months prior to Dmab treatment.

Overall, tooth extraction was the most common precipitating factor, accounting for 81 cases (45.5%), followed by periodontal disease (25 cases, 14.0%), peri-implantitis (22 cases, 12.4%), denture-related trauma (17 cases, 9.6%), implant surgery (11 cases, 6.2%), apical lesions (4 cases, 2.2%), and dentoalveolar surgery (2 cases, 1.1%). Idiopathic cases accounted for 16 patients (9.0%). Tooth extraction was the most frequent preceding event in all three groups, with no statistically significant difference among groups ($P=0.656$). Among the 178 patients, 31 (18.0%) were diagnosed with stage 1 MRONJ, 108 (60.7%) with stage 2, and 38 (21.3%) with stage 3. There were no statistically significant differences in MRONJ stage distribution among the groups ($P=0.552$).

Regarding lesion location, the mandible was the most commonly affected site overall (107, 60.1%), followed by the maxilla (62 cases, 34.8%) and involvement of both jaws (9 cases, 5.1%), with no significant intergroup difference ($P=0.261$). The mandible was the predominant site in all three groups, with prevalence of 56.7%, 59.0%, and 84.6%, respectively. The posterior mandible was the most frequently affected subsite, accounting for 100 cases (49.5%). Single-site

Table 1. Demographic characteristics of DRONJ and clinical variables

Variable	Total	Osteoporosis		Cancer	*P*-value
		Group 1 (Low-dose Dmab)	Group 2 (BP to Dmab switching)	Group 3 (High-dose Dmab)	
Sample size	178	60 (33.7)	105 (59.0)	13 (7.3)	
Female	153 (86.0)	51 (85.0)	93 (88.6)	9 (69.2)	0.163
Age (yr)	75.9±8.0	77.4±6.7[1]	76.6±7.2[1]	63.5±8.9[2]	<0.001
Drug administration (mo)					
Dmab	19.3±14.0	23.2±15.3[1]	16.0±11.3[2]	27.9±18.8[1]	<0.001
BP			56.7±46.4		
Preceding events					0.656
Extraction	81 (45.5)	25 (41.7)	51 (48.6)	5 (38.5)	
Trauma from prosthesis	17 (9.6)	4 (6.7)	11 (10.5)	2 (15.4)	
Peri-implantitis	22 (12.4)	6 (10.0)	16 (15.2)	0 (0)	
Implant surgery	11 (6.2)	4 (6.7)	6 (5.7)	1 (7.7)	
Periodontitis	25 (14.0)	12 (20.0)	10 (9.5)	3 (23.1)	
Apical lesion	4 (2.2)	2 (3.3)	1 (1.0)	1 (7.7)	
Dentoalveolar surgery	2 (1.1)	1 (1.7)	1 (1.0)	0 (0)	
Idiopathic	16 (9.0)	6 (10.0)	9 (8.6)	1 (7.7)	
Stage					0.552
1	31 (18.0)	10 (16.7)	18 (17.1)	4 (30.8)	
2	108 (60.7)	38 (63.3)	65 (61.9)	5 (38.5)	
3	38 (21.3)	12 (20.0)	22 (21.0)	4 (30.8)	

(DRONJ: denosumab-related osteonecrosis of the jaw, BP: bisphosphonate, Dmab: denosumab)
Values are presented as number only, number (%), or mean±standard deviation.
[1,2]Same letters are not statistically significant by Tukey test. Fisher's exact test or chi-square test were used for categorical variables.
Inter-group differences were analyzed with ANOVA and Tukey test.
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Table 2. Clinical data concerning DRONJ location

Location	Total	Osteoporosis		Cancer
		Group 1 (Low-dose Dmab)	Group 2 (BP to Dmab switching)	Group 3 (High-dose Dmab)
Location				
Maxilla	62 (34.8)	24 (40.0)	37 (35.2)	1 (7.7)
Mandible	107 (60.1)	34 (56.7)	62 (59.0)	11 (84.6)
Maxilla & Mandible	9 (5.1)	2 (3.3)	6 (5.7)	1 (7.7)
No. of DRONJ sites				
Single site				
Maxilla	59 (33.1)	23 (38.3)	35 (33.3)	1 (7.7)
Mandible	99 (55.6)	33 (55.0)	55 (52.4)	11 (84.6)
Multiple sites				
Maxilla	3 (1.7)	1 (1.7)	2 (1.9)	0 (0)
Mandible	8 (4.5)	1 (1.7)	7 (6.7)	0 (0)
Both				
Maxilla+mandible	9 (5.1)	2 (3.3)	6 (5.7)	1 (7.7)

(DRONJ: denosumab-related osteonecrosis of the jaw, BP: bisphosphonate, Dmab: denosumab)
Values are presented as number (%).
There was no statistically significant difference among the groups on location of the lesions (P=0.261) or number of the sites (P=0.099) by chi-square test.
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involvement was observed in 158 patients (88.7%), whereas 20 patients (11.3%) exhibited multiple-site involvement. No significant differences were observed among groups regarding the number of involved sites (P=0.099).(Table 2)

2. Treatment outcomes

A total of 32 patients (18.0%) received conservative treatment, including antibiotic therapy, chlorhexidine gargling, incision and drainage, or minimal removal of necrotic bone. Surgical treatment, such as sequestrectomy and/or surgical curettage, was performed in 146 patients. The mean number

Table 3. Treatments of DRONJ

Methods and number of surgeries	Total	Osteoporosis		Cancer
		Group 1 (Low-dose Dmab)	Group 2 (BP to Dmab switching)	Group 3 (High-dose Dmab)
Method of treatment				
Conservative treatment	32 (18.0)	13 (21.7)	17 (16.2)	2 (15.4)
Surgical intervention	146 (82.0)	47 (78.3)	88 (83.8)	11 (84.6)
No. of surgical intervention				
Surgical intervention 1 time	118 (66.3)	40 (66.7)	72 (68.6)	6 (46.2)
Surgical intervention 2 times	23 (12.9)	6 (10.0)	12 (11.4)	5 (38.5)
Surgical intervention 3 times	5 (2.8)	6 (10.0)	4 (3.8)	0 (0)
Average number of the surgeries	1.23±0.50	1.17±0.50	1.23±0.52	1.45±0.52

(DRONJ: denosumab-related osteonecrosis of the jaw, MRONJ: medication-related osteonecrosis of the jaw, BP: bisphosphonate, Dmab: denosumab)
Values are presented as mean±standard deviation or number (%).
There was no statistically significant difference among the groups on method of treatment for MRONJ (P=0.657, chi-square test) and the average number of surgical intervention (P=0.231, ANOVA).
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Table 4. Treatment outcomes for patients

Treatment outcome	Total	Osteoporosis		Cancer
		Group 1 (Low-dose Dmab)	Group 2 (BP to Dmab switching)	Group 3 (High-dose Dmab)
Healing states (complete healing)	138 (77.5)	48 (80.0)	83 (79.0)	7 (53.8)
Partial healing	7 (3.9)	3 (5.0)	4 (3.8)	0 (0)
No healing	10 (5.6)	2 (3.3)	5 (4.8)	3 (23.1)
Recurrence	23 (12.9)	7 (11.7)	13 (12.4)	3 (23.1)
Treatment success (complete and partial healing)	145 (81.5)	51 (85.0)	87 (82.8)	7 (53.8)

(MRONJ: medication-related osteonecrosis of the jaw, BP: bisphosphonate, Dmab: denosumab)
Values are presented as number (%).
Complete healing, complete mucosal coverage at least 3 months after treatment; Partial healing, better stage than the one of the first diagnosis; No healing, unchanged or worsening of stage than initial diagnosis; Recurrence, showing clinical evidence of MRONJ after "complete healing" status. There was no statistically significant difference in each group on treatment outcomes (P=0.102 by chi-square test). Treatment success was significant different between the groups (P=0.027 by chi-square test).
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of surgical interventions was highest in Group 3. However, there were no statistically significant differences among groups in treatment modality (P=0.657, chi-square test) or in the mean number of surgical procedures (P=0.231, ANOVA). (Table 3)

Treatment outcomes were evaluated on all 178 patients. Complete healing was achieved in 138 patients (77.5%), partial healing in 7 patients (3.9%), no healing in 10 patients (5.6%), and recurrence occurred in 23 patients (12.9%). Complete healing was more frequently observed in osteoporosis patients (Group 1, 80.0%; Group 2, 79.0%) than in cancer patients treated with high-dose Dmab (Group 3, 53.8%). The overall recurrence rate was 12.9% (Group 1, 11.7%; Group 2, 12.4%; Group 3, 23.1%). Although differences in individual outcome categories were not statistically significant among groups (P=0.102), treatment success rates differed significantly. Treatment success was observed in 85.0% of Group 1 and 82.8% of Group 2 patients, compared with 53.8% in Group 3 (P=0.027).(Table 4)

When outcomes were stratified by treatment modality, complete healing was achieved in 78.8% of patients who underwent surgical treatment and in 71.9% of those who received conservative treatment, with no statistically significant difference between the two approaches (P=0.657).(Table 5)

3. Factors influencing treatment success after DRONJ treatment

To identify factors associated with treatment success following DRONJ management, multiple logistic regression analysis was performed. Dmab dosage was identified as a significant independent predictor of treatment success (OR, 5.13; 95% CI, 1.19-22.14; P=0.028), whereas age, duration of Dmab therapy, lesion location, MRONJ stage, and treatment modality were not significant predictors. These findings indicate that patients treated with low-dose Dmab for osteo-

Table 5. Treatment outcomes for patients according to treatment method

Healing state	Complete healing	Partial healing	No healing	Recurrence
Total cases (n=178)				
Conservative treatment (n=32)	23 (71.9)	4 (12.5)	5 (15.6)	0 (0)
Surgical intervention (n=146)	115 (78.8)	3 (2.1)	5 (3.4)	5 (15.8)
Group 1 (n=60)				
Conservative treatment (n=13)	9 (69.2)	2 (15.4)	2 (15.4)	0 (0)
Surgical intervention (n=47)	39 (83.0)	1 (2.1)	0 (0)	7 (14.9)
Group 2 (n=105)				
Conservative treatment (n=17)	13 (76.5)	2 (11.8)	2 (11.8)	0 (0)
Surgical intervention (n=88)	70 (79.5)	2 (2.3)	3 (3.4)	13 (14.8)
Group 3 (n=13)				
Conservative treatment (n=2)	1 (50.0)	0 (0)	1 (50.0)	0 (0)
Surgical intervention (n=11)	6 (54.5)	0 (0)	2 (18.2)	3 (27.3)

Values are presented as number (%).
Statistically significance was evaluated with by chi-square test (P=0.657).
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Table 6. Results of multiple logistic regression analysis examining the significant contributing factors on success rate after DRONJ treatment

Variable	OR	95% CI for B	P-value
Age	1.02	0.96-1.07	0.564
Dosage of Dmab	5.13	1.19-22.14	0.028
Duration of Dmab	1.00	0.98-1.03	0.761
Location of DRONJ	1.21	0.59-2.49	0.612
Stage of DRONJ	1.51	0.79-2.87	0.212
Treatment (conservative/surgical)	1.02	0.34-3.05	0.976

(DRONJ: denosumab-related osteonecrosis of the jaw, Dmab: denosumab, OR: odds ratio, CI: confidence interval)
Age, duration and dosage of Dmab, location of the lesion, stage, and treatment methods were included in the models. Results were presented as ORs with 95% CIs.
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porosis (Groups 1 and 2) had significantly higher treatment success rates than those treated with high-dose Dmab for malignancy.(Table 6)

IV. Discussion

This study aims to clarify the clinical characteristics, possible risk factors, treatment modalities and outcomes of patients with DRONJ. An additional objective was to identify differences in clinical characteristics, risk factors, and treatment outcomes according to prior BP use in order to evaluate the impact of BP exposure on the development and prognosis of DRONJ. Although there were no significant differences were observed among groups with respect to DRONJ symptoms, disease stage, treatment modality, or overall treatment outcomes, significant differences were identified in the time to onset of DRONJ.

To date, relatively few studies have reported on DRONJ. Scoletta et al.[17], reported 37 patients treated between 2006 and 2007. Palla et al.[18] published a study on 108 patients treated from 2003 to 2009. A retrospective multicenter study conducted in Germany reported 69 DRONJ sites in 63 patients treated between 2011 and 2017[9]. More recently, Pautke et al.[12] reported on 132 patients treated between 2011 and 2019; after excluding 45 patients with BP-related ONJ, their analysis focused on 87 patients with DRONJ. In contrast, the present study evaluated the clinical characteristics and prognosis of DRONJ in a larger cohort of 178 patients treated over a 5-year period from 2019 to 2024.

Martins et al.[16] evaluated treatment outcomes in patients with MRONJ and categorized outcomes into five stages: healed, improved, stable, worsened, and relapse. Varoni et al.[19] further refined this system by dividing "healed" category into short-term healing and long-term healing, resulting in 6 outcome categories: short-term healing, long-term healing, stable, improved, worsened, and recurrence. In the present study, cases demonstrating unchanged or worsened disease stage after treatment were consolidated into a single category, "no healing," because no clinically meaningful differences were observed between these outcomes. In addition, as no significant distinction was identified between short-term healing and improved outcomes, these categories were combined

and analyzed as "partial healing." Consequently, treatment outcomes in this study were classified into four categories: complete healing, partial healing, no healing, and recurrence. Treatment success was defined as the combined proportion of cases achieving complete or partial healing.

In present study, females (86.0%) were affected more frequently than males, consistent with findings from most previous studies[9,19,20]. Earlier reports indicated that multiple myeloma or metastatic cancers such as breast or prostate cancer, were the most common primary disease in DRONJ, accounting for 42%-62%[9,19,20]. In contrast, de Oliveira et al.[21] indicated that osteoporosis and osteopenia were the most frequent primary disease (47%), with only 5.9% of patients having breast cancer. In our study, an even higher proportion of patients had osteoporosis as the primary disease (92.7%). This difference likely reflects the dosing indications: high-dose Dmab (120 mg) is typically used for oncological purposes, whereas low-dose Dmab (60 mg) is indicated for osteoporosis and osteopenia. Consequently, unlike previous studies, we observed a high rate of MRONJ associated with low-dose Dmab. Several factors may explain the differences between our study and prior reports. First, increasing age is a well-established risk factor for osteoporosis, and rising life expectancy has led to a growing number of osteoporosis patients. Second, in South Korea, Dmab was covered by insurance for osteoporosis treatment beginning in 2016, leading to an increase in Dmab use and a corresponding decrease in BP use. This shift is likely contributing to the rising number of ONJ cases related to Dmab.

The mandible is at higher risk for developing MRONJ due to its denser structure and lower vascularization, which hinders the healing process[17]. The posterior mandible is particularly susceptible, as it is exposed to higher masticatory forces, resulting in continuous remodeling of the alveolar bone[21]. In agreement with these previous studies[17,21], DRONJ was more frequently observed in the mandible in our cohort.

Tooth extraction (45.5%) was the most common local factor associated with MRONJ development, consistent with previous reports[20,22]. This finding underscores the importance of avoiding tooth extraction whenever possible in patients receiving antiresorptive therapy. Other preceding events such as periodontitis, peri-implantitis, periapical inflammation, and dentoalveolar surgery, also appear to increase the risk of MRONJ, likely due to the potential for local infection. Preventive dental care prior to initiating antiresorptive therapy and ongoing oral hygiene management during treatment are therefore critical. Previous studies have shown that the implementation of routine preventive dental measures can reduce the incidence of ONJ[23,24].

Previous studies have reported surgical treatment success rates ranging from 68% to 91.5%, which is comparable to the results of this study, in which the combined proportion of complete and partial healing was 85%[9,10,12,18]. The initial reports of MRONJ had discouraged surgical intervention and suggesting that spontaneous healing might occur[7]. However, more recent studies have demonstrated favorable outcomes with surgical management. Hoefert et al.[10], reported complete healing in 80% of patients treated with major surgery. Pautke et al.[12], reported surgical success rate of 91.5% in DRONJ. Similarly, our study demonstrates that surgical treatment is effective in DRONJ, with a comparable success rate of approximately 80.9%.

The recurrence rate in this study (12.9%) was lower than that reported by Varoni et al.[19] (30.4%), and Mücke et al.[25] (28.7%), but higher than the 9% reported by Pautke et al.[12]. Direct comparison among studies remains challenging due to methodological heterogeneity, variations in follow-up duration, and the fact that recurrence may occur several months after treatment, which can bias the observed rates.

In a previous study by Pautke et al.[12], logistic regression analysis was conducted to determine whether factors such as time to MRONJ onset, sex, age, underlying disease, MRONJ stage, and precipitating events influenced treatment success; no significant association were identified. This finding is similar to the results of our study. However, in the present study, Dmab dosage was significantly associated with treatment success. It should be noted, however, that direct comparisons are complicated by differences in patient populations: patients receiving high-dose Dmab for cancer (e.g., breast or prostate cancer) may have poorer general health compared to those receiving low-dose Dmab for osteoporosis.

In this study, patients who switched from BP to low-dose Dmab developed ONJ after a significantly shorter period of Dmab treatment compared to other groups ($P<0.001$), suggesting that prior BP use may accelerate the onset of MRONJ. Interestingly, a previous study[12] reported a faster onset of MRONJ in the Dmab-only group (2.0 years) than in the BP to Dmab switch group (4.1 years). Other reports also indicated that switching from BPs to Dmab can increase the risk of MRONJ and may accelerate its onset[26-28]. Among cancer patients with bone metastases, the risk of MRONJ was significantly higher when switching from zoledronic acid to Dmab[29]. The mechanism underlying this increased risk may be explained by pharmacokinetics: Switching from BPs to

Dmab induces a rapid alteration in bone remodeling, which may contribute to increased susceptibility to MRONJ. Additionally, the cumulative duration of antiresorptive therapy, including both BP and Dmab administration, may further influence MRONJ risk[28]. In our BP to Dmab switching group, the mean duration of prior BP therapy was 56.7±46.4 months, which may explain the accelerated onset of DRONJ. However, a previous study by Hayashida et al.[11] reported that prior BP administration did not appear to affect MRONJ pathogenesis, clinical characteristics, or treatment outcomes. Further research with larger patient cohorts is needed to clarify these findings.

In the current study, apart from differences in the time to DRONJ onset, no significant differences were observed among the three groups regarding MRONJ stage, preceding event, lesion location, treatment modality (conservative vs. surgical), healing status, or recurrence. These results suggest that switching from BP to Dmab may influence the timing of DRONJ onset but does not appear to affect disease severity or prognosis.

This study provides valuable information on the clinical characteristics of DRONJ but has several limitations. As a retrospective study, some data—such as duration of medication, triggering factors, and the circumstances at the time of onset (for example, whether having drug holiday or not)—were obtained from patient history, which may be subject to recall bias. Furthermore, because the medical records were not specifically designed for this study, variations in surgical technique among oral and maxillofacial surgeons and a lack of standardized data collection may have affected the results. Future well-controlled prospective studies should further investigate the relationship between drug holiday periods, preceding events, and MRONJ onset.

V. Conclusion

Overall postoperative healing was favorable 3 months after DRONJ treatment. Tooth extraction was the most frequent preceding events associated with DRONJ development. Although the duration of Dmab administration differed significantly between the low-dose Dmab group and the BP to Dmab switching group, prior BP use appeared to accelerate the onset of DRONJ. This earlier onset in the BP to Dmab group may be attributable to the cumulative duration of antiresorptive therapy. However, prior BP exposure did not appear to influence disease severity or treatment outcomes. Dmab dosage was the primary factor affecting treatment success, whereas age, treatment duration, lesion location, and MRONJ stage were not significant predictors.

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Authors' Contributions

K.J.C. and M.X.J. collected and analyzed the patient data. S.Y.C. statistically analyzed the data. K.J.C., M.X.J., and S.Y.C. drafted the manuscript. S.Y.C. and T.G.K. critically revised the manuscript. All authors read and approved the final manuscript.

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Ethics Approval and Consent to Participate

This study was approved by the Institutional Review Board of Kyungpook National University Dental Hospital (KNUDH-2024-11-04-00). The requirement for informed consent was waived due to the retrospective nature of the study.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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