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Utility of quantitative standardized uptake value from pre-operative bone SPECT/CT for predicting post-surgical MRONJ healing response

Jung-Hyun Park[1,2†], Da-Mi Yoon[1,2†], Hai-Jeon Yoon[2,3*†] and Jin-Woo Kim[1,2*†]

Abstract

Background Medication-related osteonecrosis of the jaw (MRONJ) is a challenging condition often associated with long-term use of anti-resorptive medications. Accurate diagnosis is essential, but predicting the prognosis is particularly difficult due to the high likelihood of recurrence after surgery. This study assesses the utility of quantitative values from bone SPECT/CT as predictors of surgical outcomes in MRONJ patients.

Materials and methods We analyzed a cohort of 57 MRONJ patients who underwent surgical treatment. Preoperative bone SPECT/CT scans were used to obtain the maximal SUV (SUVmax) of MRONJ lesions and the ratio of the SUVmax to the mean SUV of a reference region (rSUVmax). Logistic regression analysis was performed to evaluate the relationship between preoperative SUVmax and rSUVmax and surgical outcomes, adjusting for confounders such as age, sex, diabetes, type of bone-modifying agent, MRONJ-affected sites, and stage.

Results Both SUVmax and rSUVmax values increased with the progression from MRONJ stage 1 to stage 3 and were higher in the No Resolution group compared to the Complete Resolution group. Multivariate logistic regression analysis revealed that higher rSUVmax values were significantly associated with poor surgical outcomes (OR, 1.51; 95% CI, 1.07–2.14), whereas SUVmax values were not significantly associated (OR, 1.05; 95% CI, 0.98–1.13). Preoperative MRONJ stages did not significantly predict MRONJ resolution.

Conclusion rSUVmax from bone SPECT/CT may serve as a valuable prognostic tool for assessing MRONJ severity and predicting surgical outcomes. Incorporating rSUVmax measurements into clinical practice could enhance decision-making and improve patient management.

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Clinical trial registration None.

Keywords Medication-related osteonecrosis of the jaw, MRONJ, Bone SPECT/CT, Surgical outcomes, Standardized uptake value

Introduction

Medication-related osteonecrosis of the jaw (MRONJ) is a severe and debilitating condition associated with the long-term use of bone-modifying agents such as bisphosphonates and other anti-resorptive medication [1]. This condition is characterized by the exposure of necrotic bone in the maxillofacial region, frequently accompanied by pain, infection, and impaired oral function [2]. The diagnosis and management of MRONJ present significant challenges due to the complexity involved in determining the severity of the disease and the extent of necessary surgical intervention [3]. Current staging criteria for MRONJ, which are based on bone exposure, inflammation, and anatomical involvement, remain controversial and often fail to provide clear clinical guidance [4]. This emphasizes the need for more precise and reliable diagnostic tools to aid in the management of MRONJ.

Bone single-photon emission computed tomography/computed tomography (SPECT/CT) has been proposed as a valuable imaging modality for MRONJ in several studies, offering potential insights into the extent and staging of the disease through standardized uptake value (SUV) measurements [5, 6]. These measurements have shown promise as quantitative markers for assessing the metabolic activity of jaw lesions [7]. Elevated SUVs in MRONJ lesions indicate increased metabolic activity, reflecting heightened osteoblastic activity and inflammation as the body attempts to heal or isolate necrotic bone. Thus, bone SPECT/CT could play a crucial role in assessing disease severity and treatment efficacy, enabling clinicians to monitor bone remodeling processes and guide surgical decisions more effectively.

Contrary to earlier MRONJ guidelines, such as the AAOMS 2014 [8], recent national MRONJ guidelines [9, 10] recommend surgical intervention over conservative therapy. However, factors contributing to recurrence following surgery or refractory courses with conservative therapy remain largely unexplored [11, 12]. Bone SPECT/CT, which can quantitatively monitor bone metabolism and inflammation in the jaw, could serve as a prognostic tool for MRONJ treatment outcomes, because the degree of bone metabolism and inflammation intensity at the time of diagnosis are significant predictors of surgical outcomes. Given these potential advantages, we hypothesized that quantitative values obtained from bone SPECT/CT could provide an accurate measure of MRONJ severity and predict patient prognosis more effectively than traditional staging criteria [13].

Relative maximal SUV (rSUVmax) is a metric used in medical imaging to provide a normalized measure of metabolic activity by comparing the maximal SUV (SUVmax) of a lesion to the mean SUV (SUVmean) of a reference region [14]. This ratio corrects for inter-individual variations in bone metabolism, reflecting the relative metabolic activity of the lesion compared to normal bone. Elevated rSUVmax values indicate increased metabolic activity in the lesion, making it a potentially more reliable indicator of disease severity and treatment outcomes. By accounting for individual metabolic differences, this normalization technique could deliver more consistent and reliable diagnostic information.

This study aims to address the unresolved aspects of MRONJ treatment, specifically focusing on recurrence and reoperation after surgery. Therefore, we investigated the association between the surgical outcome of MRONJ and preoperative bone SPECT/CT values, including rSUVmax, in MRONJ lesions and to explore their prognostic value.

Materials and methods

Patients

The Korean National Cohort for Osteonecrosis of the Jaw is a longitudinal cohort of patients diagnosed with MRONJ (http://onjcohort.org/). This multi-institutional cohort was established in 2018 to build a scientific foundation for MRONJ research, investigate the natural history of the disease, establish temporal relationships between risk factors and the disease, and evaluate the effectiveness of various treatment modalities [15]. All participants provided written informed consent. MRONJ was diagnosed and staged according to the diagnostic criteria set by the AAOMS [16]. Patients with any history of radiation therapy to the jaws, metastatic disease to the jaws, or hypercalcemic conditions were excluded. At cohort entry, comprehensive medical and dental examinations and histories were obtained. Demographic data and previous history of any related drugs were surveyed, including types of antiresorptive agents taken, duration, dose, administration route, and any previous medications that could affect bone metabolism. Medical images such as panoramic X-rays, computed tomography scans, and bone SPECT/CT were obtained for diagnosis and follow-up.

The subcohort for the present analysis was enrolled from the Project for the Korean National Cohort for Osteonecrosis of the Jaw. Patients diagnosed with MRONJ at the Department of Oral and Maxillofacial

Surgery, Ewha Womans University Mokdong Hospital, between January 1, 2018, and July 31, 2023, were included. Since the purpose of this study was to examine bone SPECT/CT and postoperative healing results of MRONJ, only patients with preoperative bone SPECT/CT who underwent surgery were included. Patients who could not be observed for more than 3 months after surgery were excluded. This study followed the Declaration of Helsinki on medical protocol and ethics and was approved by the Institutional Review Board of Ewha Medical Center, Seoul, Republic of Korea (IRB No. 2018-01-046).

The following patient information was collected: demographic and clinical variables such as age and sex, and MRONJ-affected sites, which were separately categorized into maxilla and mandible. Types of bone-modifying agents associated with MRONJ occurrence were divided into bisphosphonate, denosumab, and other drugs. Information on whether the reason for taking bone-modifying agents was osteoporosis or cancer was collected. The presence or absence of diabetes, which may affect the occurrence of MRONJ, was investigated, and the stage of MRONJ was determined based on the AAOMS standards. Staging of MRONJ lesions was performed according to the AAOMS position statement as follows [16]: stage 1, exposed and necrotic bone or a fistula that probes to bone in patients who are asymptomatic and have no evidence of infection; stage 2, exposed and necrotic bone or a fistula that probes to bone associated with infection as evidenced by pain and erythema in the region of exposed bone with or without purulent drainage; and stage 3, exposed and necrotic bone or a fistula that probes to bone extending beyond the region of alveolar bone in patients with pain, infection, and one or more of the following—pathologic fracture, extraoral fistula, oroantral or oronasal communication, or osteolysis extending to the inferior border of the mandible or sinus floor.

Imaging protocol of bone SPECT/CT

All SPECT/CT images were acquired using a SPECT/CT hybrid system (Symbia Intevo Bold, Siemens Healthineers) equipped with an integrated dual-head SPECT camera with a 16-slice helical CT scanner. Four hours after intravenous injection of Tc-99 m hydroxymethylene diphosphonate (HDP) 740 MBq (20 mCi), SPECT images were acquired under the following parameters: ± 7.5% energy window at 140 keV with a lower scatter window of 15%, low-energy high-resolution collimator, 256 × 256 matrix with 2.0-mm pixels, and rotation of 180°, 3° view angle, 10 s per projection.in a non-circular acquisition mode. Immediately following SPECT acquisition, CT images were acquired at 110 kV and 60 ref mA using adaptive dose modulation (CARE Dose 4D; Siemens Healthineers) with a 512 × 512 matrix, pitch 0.8, 0.6-s rotation, and 16 × 0.6-mm collimation. The CT data were reconstructed at a 5.0-mm slice thickness using a I50s attenuation filter (Siemens Healthineers). The SPECT data were reconstructed using xSPECT Bone Enhanced algorithm (Siemens Healthcare) with 60 iterations and 1 subset. Images were smoothed using a Gaussian filter (10 mm at full width half maximum).

Quantitative analysis of bone SPECT/CT

To ensure accurate SUV quantification in SPECT/CT, a cylindrical water-equivalent phantom (volume: 6800 ml) filled with a known concentration of Tc-99 m HDP was used for validation. The phantom study was performed to assess quantitative accuracy with Tc-99 m (5mCi) activity calibrated using a dose calibrator before injection. For accurate quantification, CT-based attenuation correction (CTAC) was applied using Broad Quantification (Siemens Healthineers), dual-energy window scatter correction was used, and recovery coefficients derived from phantom studies were applied for partial volume effect (PVE) correction. SUV was normalized to body weight (SUV_{bw}) for consistency in clinical interpretation.

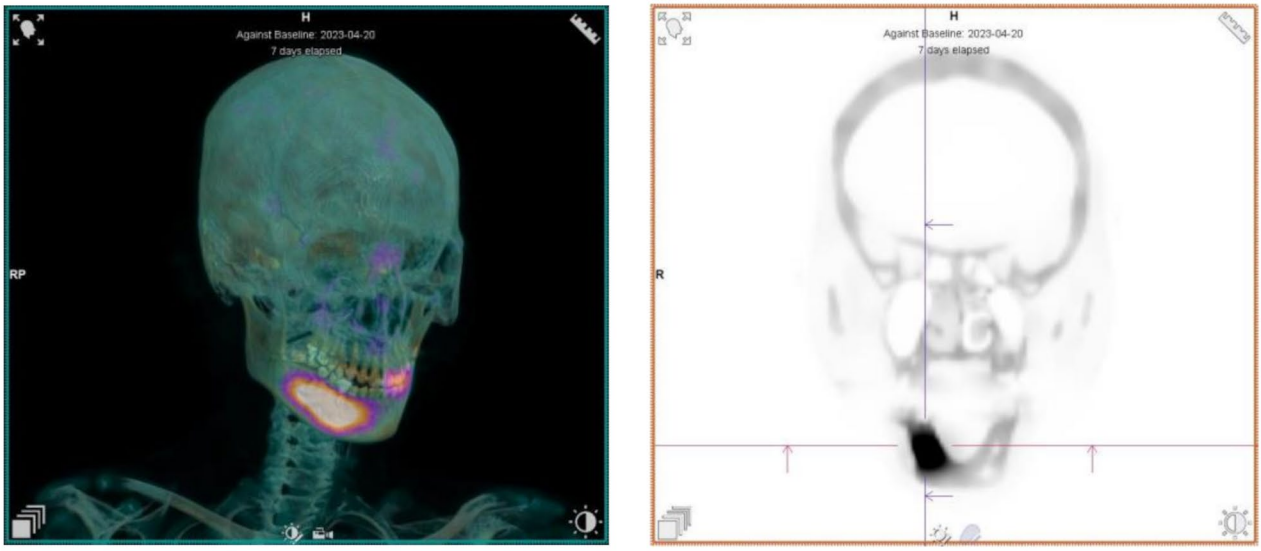
SPECT data were reviewed by a board-certified nuclear medicine physician. A dedicated software package (syngo.via VB60A, Siemens Healthineers) was used to measure SUV. The maximal SUV (SUV_{max}) of a MRONJ lesion was obtained by delineating a three-dimensional (3D) volume of interest (VOI) encompassing the lesion. Three spherical VOIs were drawn as a reference region over the normal parietal bone, and the mean SUV (SUV_{mean}) of the three VOIs were averaged into a single value. To correct for inter-individual variations in bone metabolism, the ratio of the maximum SUV of MRONJ lesion to the mean SUV of reference region was calculated and defined as the rSUVmax (relative SUVmax) (Fig. 1).

$$rSUVmax = SUVmax, lesion/SUVmean, reference$$

Operation and assessment of surgical outcomes

All participants received the same protocol of operation and were managed conservatively before surgery with daily irrigation with 0.12% chlorhexidine, professional dental prophylaxis, analgesics, and antibiotics if needed. The surgery was performed under intravenous sedation or general anesthesia, in addition to local anesthesia, depending on the extent of the lesions and the patient's general condition. Bony sequestra and granulation tissues were removed by surgical curettes until fresh bleeding from the bone was confirmed. Rotary instruments were used to smoothen out all sharp bony margins, followed by thorough irrigation with antibiotic solution to minimize further bacterial contamination and remove

(A)



(B)

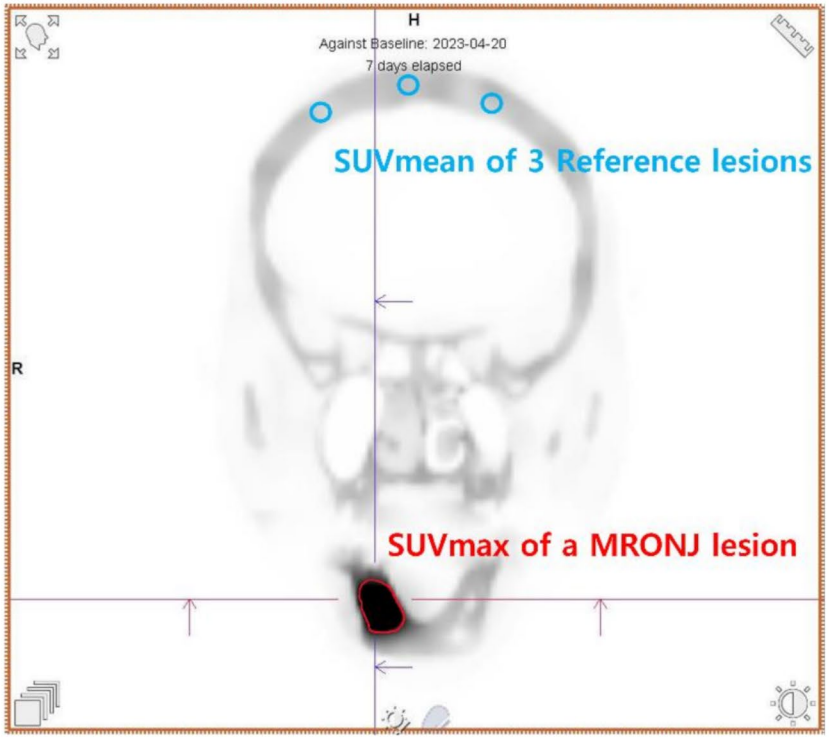


Fig. 1 (**A**) Bone SPECT/CT images. (**B**) Diagram depicting the measurement of SUVmax and SUVmean, and the calculation of rSUVmax values

debris and foreign bodies. Primary closure of the mucoperiosteal flap was achieved.

After the operation, patients were followed once every week or two for the first month. Surgical sites were clinically and radiographically evaluated at 4 and 12 weeks postoperatively for outcome assessment. Complete resolution was defined as full mucosal coverage with the absence of clinical or radiographic evidence of MRONJ at 12 weeks (3 months) postoperatively. No resolution was defined as the persistence of clinical signs and symptoms or radiographic progression of MRONJ with exposed bone or bone that could be probed through a fistula at 12 weeks postoperatively.

Statistical analysis

Continuous data were presented as means with standard deviations, and categorical data as frequencies and percentages. Differences between groups were assessed using the independent t-test for continuous variables and χ^2 test for categorical variables. For the comparison among more than three groups, ANOVA test was used and followed by post-hoc pair-wise comparisons. Logistic regression analysis was performed to assess the relationship between preoperative SUVmax and rSUVmax and surgical outcomes. Both models were adjusted for age, sex, MRONJ-affected sites, diabetes, type of bone modifying agent, reason for the bone modifying agent, and MRONJ stage: Model 1 included the SUVmax as a predictor variable to evaluate its association with surgical outcomes. Model 2 included the rSUVmax as a predictor variable to evaluate its association with surgical outcomes. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each variable. Values were considered statistically significant at $P<0.05$. Statistical analyses were performed using SPSS software (version 28.0; SPSS, Chicago, IL).

Table 1 Baseline characteristics of patients

	Compete resolution ($n=41$)	No resolution ($n=16$)	*P* value
Age	72.2 (9.45)	70.0 (10.55)	0.461
Sex			0.534
Female	38	14	
Male	3	2	
MRONJ-affected sites			**0.004**
Mandible	22	15	
Maxilla	19	1	
Diabetes	15	3	0.193
Type of Bone Modifying Agent			0.096
Bisphosphonate	10	9	
Denosumab	11	3	
Both*	3	4	
Reason for the bone modifying agent			0.062
Osteoporosis	18	8	
Cancer	6	8	
MRONJ Stage			0.965
1	7	3	
2	13	9	
3	4	4	

Shown as mean (standard deviation); Bold indicates $P<0.05$

* 'Both' indicates denosumab user after bisphosphonates administration

Results

A total of 57 patients were included in this study. The average age of the patients was 71.6 ± 9.7 years, with lesions occurring in the maxilla and mandible in 20 and 37 cases, respectively. Among the patients, the reason for the bone modifying agent was cancer in 18 cases and osteoporosis in 39 cases. The lesions were classified into two groups based on surgical outcomes: 41 lesions in the Complete Resolution group and 16 lesions in the No Resolution group. Regarding the initial stage of MRONJ, there were 12 lesions classified as Stage 1, 31 lesions classified as Stage 2, and 14 lesions classified as Stage 3. The demographic and clinical characteristics of these groups are presented in Table 1.

Preoperative bone SPECT/CT values according to MRONJ stages and surgical outcomes

Figure 2 shows the preoperative bone SPECT/CT values according to MRONJ stages and surgical outcomes. It was observed that the SUVmax and rSUVmax values increased from the stage 1 group to the stage 3 group. SUVmax values increase across stages with values of 19.92 ± 4.69 for Stage 1, 20.89 ± 8.08 for stage 2, and 30.44 ± 11.61 for stage 3. ($P<0.05$); rSUVmax also increased with values of 6.28 ± 4.69 for stage 1, 7.18 ± 2.88 for stage 2, and 10.52 ± 5.18 for stage 3. ($P<0.05$) A post-hoc pairwise comparison showed that both SUVmax and rSUVmax values of Stage 3 were significantly higher than those of Stage 1 or Stage 2. However, there was no significant difference between both SUVmax and rSUVmax values of Stage 1 and Stage 2. (Table 2)

In terms of surgical outcomes, both preoperative SUVmax and rSUVmax values at diagnosis were higher in the No Resolution group compared to the Complete Resolution group. The SUVmax was higher in the No Resolution group (29.37 ± 14.06) compared to Complete resolution group (20.56 ± 8.94), indicating greater metabolic activity in the non-resolving lesions. ($P<0.05$) The rSUVmax values were significantly higher in the No Resolution group (11.26 ± 5.10) compared to the Complete Resolution group (6.47 ± 2.47), highlighting a strong association between higher rSUVmax values and recurrence. ($P<0.001$) Representative cases are shown in Fig. 3.

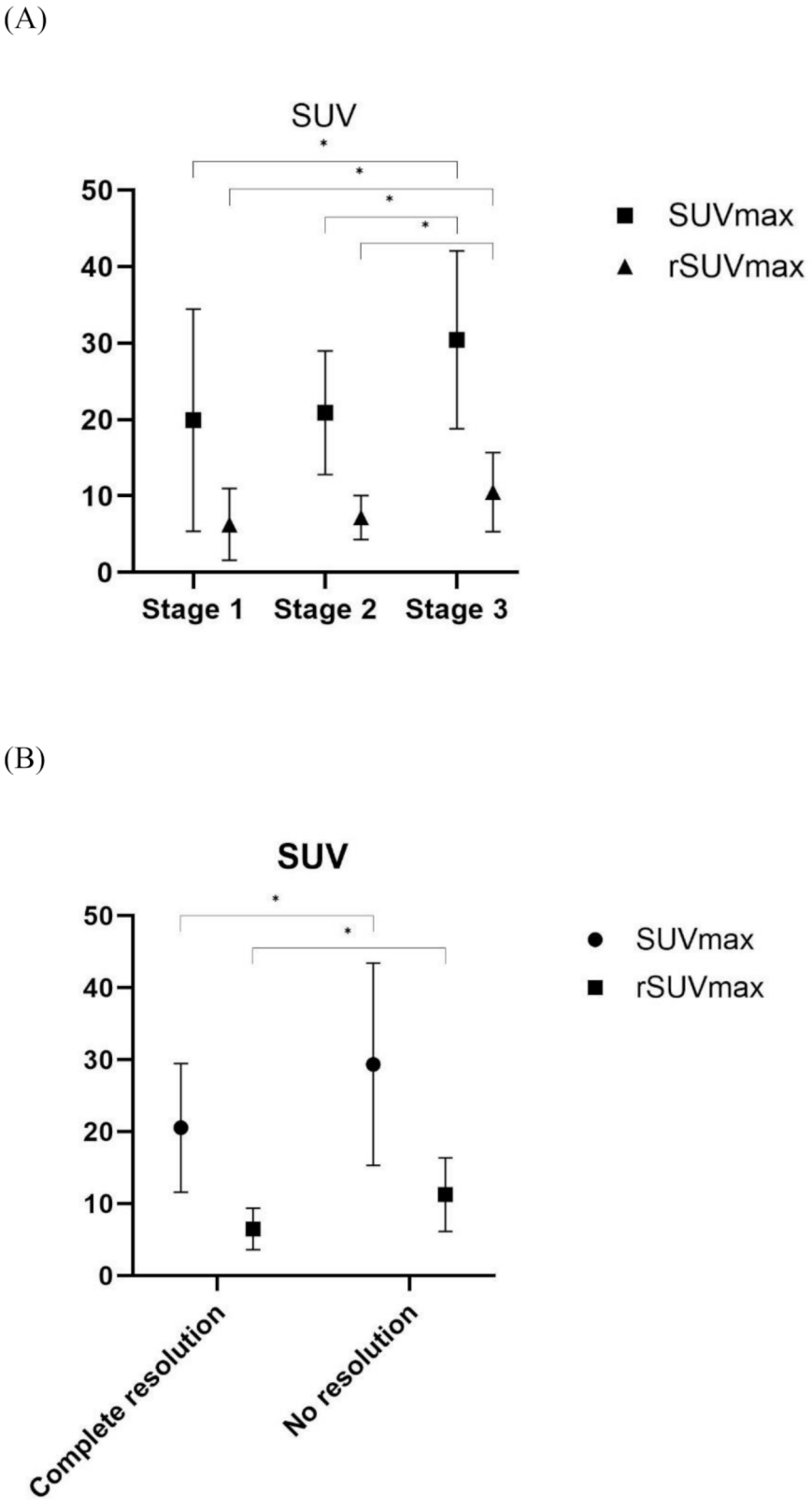


Fig. 2 (**A**) SUVmax and rSUVmax according to the MRONJ stages. (**B**) SUVmax and rSUVmax according to surgical outcomes. * indicates $P < 0.05$

Table 2 SUV indices according to stage and healing

		Mean	Standard deviation	*P* value
SUVmax	Stage 1	19.92*	14.51	**0.014**
	Stage 2	20.89*	8.08	
	Stage 3	30.44	11.61	
	Compete resolution	20.56	8.94	**0.007**
	No resolution	29.37	14.06	
rSUVmax	Stage 1	6.28*	4.69	**0.014**
	Stage 2	7.18*	2.88	
	Stage 3	10.53	5.18	
	Compete resolution	6.47	2.87	**< 0.001**
	No resolution	11.26	5.10	

Bold indicates $P < 0.05$

* indicates post-hoc comparison with Stage 3

Multivariate logistic regression analysis was conducted to assess the relationship between preoperative bone SPECT values (SUVmax and rSUVmax) and surgical outcomes, adjusting for potential confounders (Table 3). Model 1 included SUVmax as a predictor variable. The analysis showed that SUVmax values were not significantly associated with surgical outcomes (OR, 1.09; 95% CI, 0.99–1.19). Model 2 included rSUVmax as a predictor variable. The analysis revealed that higher rSUVmax values were significantly associated with poorer surgical outcomes (OR, 1.51; 95% CI, 1.07–2.14). For every one-unit increase in rSUVmax, the likelihood of the non-resolution after surgery increased by 51%. Other variables such as age, sex, MRONJ-affected sites (maxilla or mandible), diabetes, type of bone modifying agent, reason for the bone modifying agent (osteoporosis or cancer) were not significantly associated with surgical outcomes in either model. The results suggests that rSUVmax may be a more reliable indicator of MRONJ resolution compared to SUVmax alone. Elevated rSUVmax values indicate increased metabolic activity relative to normal bone, which is associated with a higher likelihood of non-resolution post-surgery. Notably, preoperative MRONJ stages also did not significantly predict MRONJ resolution.

Discussion

This study investigated the association between the surgical outcome of MRONJ and SUV values in bone SPECT/CT images. Our results indicate that an increase

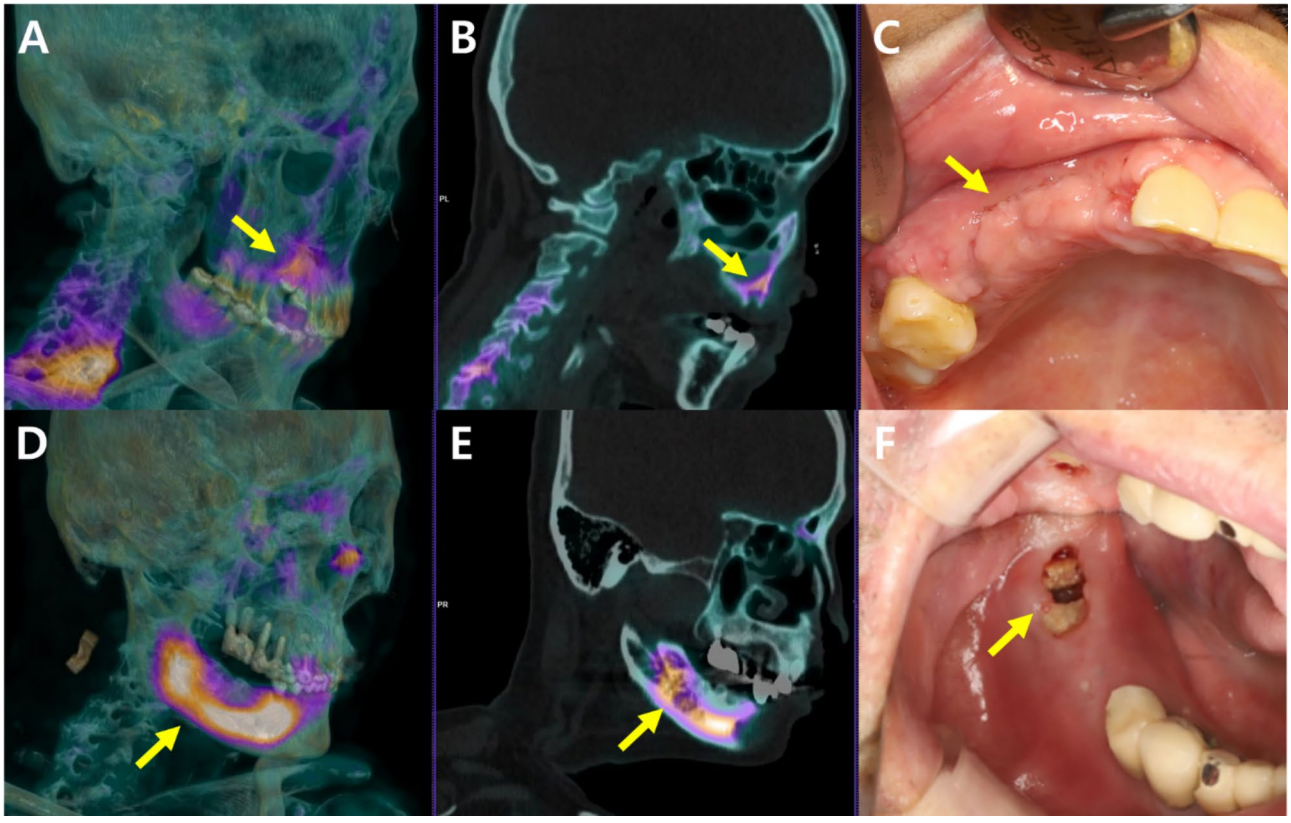


Fig. 3 Representative cases of (**A**-**C**) complete resolution and (**D**-**F**) no resolution. (**A**-**C**) A 75-year-old female with MRONJ stage 2 underwent bone SPECT/CT for preoperative evaluation. The 3-dimensional maximum intensity projection (MIP) image (**A**) and trans-sagittal fused image (**B**) show mild to moderate uptake in the right side of maxilla (arrows, SUVmax = 11.07, rSUVmax = 4.23). The gross image (**C**), taken 12 weeks post-surgery, demonstrates normal healing and is classified as complete resolution. (**D**-**F**) A 77-year-old male with MRONJ stage 2 underwent bone SPECT/CT for preoperative evaluation. The 3-dimensional MIP image (**D**) and trans-sagittal fused image (**E**) show intense uptake in the right side of mandible (arrows, SUVmax = 20.98, rSUVmax = 13.45). The gross image (**F**), taken 12 weeks post-surgery, shows a lack of healing and signs of recurrence, classified as no resolution

Table 3 Association between clinical factors and Non-resolution after MRONJ surgery

Variables	Model 1			Model 2		
	Odds ratio	95% CI	*P* value	Odds ratio	95% CI	*P* value
Age	1.05	0.93–1.18	0.412	1.02	0.89–1.16	0.793
Sex						
Female	Reference			Reference		
Male	0.01	0.00-1.42	0.070	0.01	0.00-1.80	0.082
MRONJ-affected sites						
Mandible	Reference			Reference		
Maxilla	0.04	0.00-0.74	**0.031**	0.04	0.00-0.96	**0.047**
Type of Bone Modifying Agent			0.080			0.130
Bisphosphonate	Reference			Reference		
Denosumab	0.78	0.07–8.92	0.838	1.85	0.10-33.63	0.677
Both*	0.02	0.00-0.82	**0.039**	0.06	0.00-2.44	0.137
Reason for the bone modifying agent						
Osteoporosis	Reference			Reference		
Cancer	205.13	3.45-12195.50	**0.011**	79.67z	1.03-6177.87	**0.049**
Diabetes	0.08	0.00-1.84	0.113	0.16	0.01–5.15	0.299
MRONJ Stage			0.528			0.663
1	Reference			Reference		
2	0.19	0.01–5.58	0.338	1.18	0.02–88.93	0.941
3	1.00	0.09–11.04	0.998	2.96	0.16–56.33	0.470
SUVmax	1.09	0.99–1.19	0.083			
rSUVmax				1.51	1.07–2.14	**0.021**

Model 1: Adjusted odds ratios including SUVmax

Model 2: Adjusted odds ratios including rSUVmax

Bold indicates $P < 0.05$

* 'Both' indicates denosumab user after bisphosphonates administration

'Reference' indicates the baseline category in the logistic regression model, against which all other categories were compared

in rSUVmax is significantly associated with a poor surgical prognosis, whereas SUVmax values and MRONJ stages do not show a significant association with surgical outcomes. These findings suggest that rSUVmax may serve as a more reliable predictor of surgical prognosis in MRONJ patients compared to traditional staging criteria.

The strength of this study lies in the use of rSUVmax to normalize individual differences in bone metabolism [14], addressing the variability in radiotracer accumulation even in non-MRONJ regions. The calculation of rSUVmax by dividing the MRONJ lesion's SUVmax by the mean SUV of three frontal bone locations ensures a more accurate assessment, reinforcing the utility of bone SPECT/CT in assessing metabolic activity and anatomical changes. Although previous studies have noted significant changes in SUVmax before and after treatment [6], our research adds value by specifically analyzing rSUVmax and its connection to prognosis.

Our findings highlight the limitations of current MRONJ staging criteria in predicting surgical outcomes. While traditional staging based on clinical and radiographic features provides some insight into disease severity, it does not adequately forecast surgical prognosis. This discrepancy underscores the need for more precise and reliable biomarkers in MRONJ management. In MRONJ lesion, the significance of SUV measurements in bone SPECT/CT imaging has been increasingly recognized, linking high SUV values with more severe bone involvement [17]. This aligns with our findings, showing a significant relationship between rSUVmax and surgical outcomes, confirming its prognostic utility. Although we did not establish a specific threshold, our results suggest that rSUVmax serves as a continuous predictor, with progressively higher values correlating with an increased risk of non-resolution. However, further studies are needed to establish consistent thresholds for clinical decisions.

A potential explanation for the association between high rSUVmax and poor surgical outcomes is the increased bone metabolic activity and inflammatory burden in MRONJ lesions with higher rSUVmax values. Prior studies have reported that increased SUV values in bone SPECT/CT correlate with active bone remodeling and inflammation, which could explain why higher rSUVmax values predict non-resolution in MRONJ patients [6]. This imbalance may contribute to prolonged inflammation, delayed bone healing, and a greater risk of persistent necrotic bone after surgery due to impaired vascularization and chronic inflammatory responses.

Based on prior research that underscores the importance of a multidisciplinary approach, our study

emphasizes the need for a comprehensive strategy for MRONJ prevention and management, which includes regular examinations and imaging [18]. This approach acknowledges the complex and varied etiology of MRONJ, highlighting the important role of diagnostic imaging in the diagnosis, treatment planning, and therapeutic monitoring of this condition. Specifically, bone SPECT/CT imaging, with its ability to provide both functional and anatomical insights, may be useful for the quantitative evaluation of MRONJ activity and extent. The deployment of such imaging technology could be beneficial for early diagnosis, determining the appropriate direction for treatment, and assessing the response to treatment, ultimately enhancing patient outcomes.

This study has several limitations. The relatively small sample size may limit the generalizability of the results, and larger cohorts are essential to validate these observations. The lack of standardized protocols for rSUVmax measurement across different institutions could affect the consistency of results. Future studies should aim to develop and validate standardized protocols for rSUVmax measurement and explore its potential role in guiding therapeutic interventions. Additionally, while our findings demonstrated that higher rSUVmax values were consistently associated with an increased likelihood of non-resolution, we did not define specific cutoff values or risk stratification intervals. Establishing clinically relevant rSUVmax stratifications or cutoff values is necessary to enhance its applicability in MRONJ prognosis, and future research should focus on identifying optimal thresholds for clinical decision-making.

Conclusion

In conclusion, our study demonstrates the importance of incorporating quantitative imaging biomarkers, such as rSUVmax, into the diagnostic and prognostic framework of MRONJ. Unlike conventional MRONJ stages, rSUVmax shows a significant association with poor surgical prognosis, making it a valuable tool in clinical assessment and treatment planning. Integrating rSUVmax measurements into routine evaluations can lead to more informed decision-making and potentially improve patient outcomes. Further studies with larger cohorts are needed to validate the prognostic value of rSUVmax and develop standardized measurement protocols for widespread clinical adoption.

Abbreviations

AAOMS	American Association of Oral and Maxillofacial Surgeons
CI	Confidence Interval
CT	Computed Tomography
IRB	Institutional Review Board
MRONJ	Medication-Related Osteonecrosis of the Jaw
OR	Odds Ratio
rSUVmax	Relative Standardized Uptake Value Maximum
SPECT	Single-Photon Emission Computed Tomography
SUV	Standardized Uptake Value
SUVmax	Maximum Standardized Uptake Value
SUVmean	Mean Standardized Uptake Value
VOI	Volume of Interest

Acknowledgements

None.

Author contributions

JHP and DMY contributed to conception, design, and interpretation and drafted the manuscript. JHP and DMY contributed to data acquisition and analysis and critically revised the manuscript. HJY and JWK contributed to conception, design, data acquisition, and interpretation and critically revised the manuscript. All authors gave final approval and agreed to be accountable for all aspects of the work.

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Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Declarations

Ethical approval

This study was approved by the Institutional Review Board of Ewha Medical Center, Seoul, Republic of Korea (IRB No. 2018-01-046). All methods were carried out in accordance with relevant guidelines and regulations that is Declaration of Helsinki.

Consent to participate

All participants provided written informed consent.

Consent to publish

The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1 A, 1B, 1 C, 3 A, 3B, 3 C, 3D, 3E and 3 F.

Competing interests

The authors declare no potential conflicts of interest with respect to authorship and/or publication of this article.

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