Osteonecrosis of the jaw and dental extractions: A single-center experience

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Objective. The aim of this study was to investigate the frequency of osteoradionecrosis/medication-related osteonecrosis of the jaw (ORN/MRONJ) after dental extraction with use of postextraction antibiotic coverage without prophylactic hyperbaric oxygen (HBO) in patients who received radiotherapy to head and neck (RT-HN) or antiresorptive medications and to determine possible associated factors.

Study Design. A retrospective study was conducted in patients who had a history of RT-HN or exposure to antiresorptives and who underwent dental extractions from 2003 to 2019. According to the clinical protocol, patients received amoxicillin 500 mg, 3 times daily (TID) for at least 14 days, and chlorhexidine 0.12% rinses, 2 times daily (BID), after extraction (or an alternative antibiotic if allergic to amoxicillin). HBO was not used for patients with RT-HN.

Results. Ninety patients underwent a total of 243 extractions. Fifty patients (55.5%) received a median of 54.1 Gray to the extraction site and 40 (44.4%) were on antiresorptives. None of the patients received both RT and antiresorptives. Of 40 patients, 3 (7.5%) developed MRONJ, and of 50 patients, 1 (2%) developed ORN. Among those at risk for MRONJ, male gender and concomitant immunosuppressant medications were associated with MRONJ development ($P < .05$).

Conclusions. In our patient cohort, the rate of postextraction ORN/MRONJ was lower and comparable with the rates reported in the literature. Larger prospective studies are required to validate the efficacy of postextraction antibiotics in reducing ONJ. (Oral Surg Oral Med Oral Pathol Oral Radiol 2020;130:515−521)

Osteonecrosis of the jaw (ONJ) may develop spontaneously or secondary to local trauma, such as dental extractions, most commonly after radiation therapy or antiresorptive therapy.[1,2] Although dental procedures involving direct osseous injury should be minimized in patients at risk of developing osteoradionecrosis (ORN) or medication-related osteonecrosis of the jaw (MRONJ), delays in extracting teeth harboring infection represent a potential risk for the development of ORN/MRONJ.[1,2] Therefore, it can become a necessity to perform extractions in patients traditionally considered at high-risk for ORN or MRONJ. Inflammation and bacterial infection have long been implicated in the pathogenesis of ONJ. A clinical study comparing the histomorphology of MRONJ with ORN showed the presence of bacteria, predominantly *Actinomyces* species, in all specimens of necrotic bone, indicating the involvement of bacterial infection in ONJ.[3] Preexisting severe periodontal disease and extensive caries with periapical disease are the main reasons for a hopeless prognosis, necessitating dental extractions. Hence, antibiotics have been used to control the infection of soft and hard tissues for the prevention and management of ONJ.[2,4]

The risk of MRONJ (in those exposed to intravenous [IV] bisphosphonates) and ORN (in patients who received radiotherapy to head and neck [RT-HN]) after dental extraction has been reported in the literature as 1.6% to 14.8% and 7%, respectively.[2,5] A review that included studies on ORN from 1986 to 2004 showed that the rate of postextraction ORN was approximately the same as the rate of ORN in those who did not receive prophylactic hyperbaric oxygen (HBO) or antibiotics[6]; however, the studies included in the review had insufficient details regarding antibiotic use (e.g., choice, timing, dosage); the definition of ORN was not consistent; and one of the studies included was a case report.[7-9] Although ORN/MRONJ is not considered primarily an infectious process, there is evidence that

Statement of Clinical Relevance

With an appropriate protocol for dental extractions, the risk of postextraction osteonecrosis of the jaw can be kept low. This small risk is outweighed by the potential sequelae of unaddressed odontogenic infections if the infected teeth with hopeless prognosis are left untreated.

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exposed bone is covered with a biofilm of microbes, and microbial infection can stress the healing process.[2] Because the healing capacity of irradiated bone/bone exposed to antiresorptive medications is compromised, the rationale for using postextraction antibiotics is providing an environment where microbial infection does not interfere with the healing process in the extraction socket. The antibiotic of choice should be one that is capable of penetrating bone; penicillin, amoxicillin (with or without clavulanic acid), and clindamycin are the commonly used agents.[10] However, to date, there is no clear consensus on the standard of care for performing extractions to prevent ONJ in patients at risk for ORN/MRONJ .[4]

The objective of this retrospective study was to investigate (1) the frequency of ORN/MRONJ in patients who received RT-HN with postextraction antibiotic coverage, but without prophylactic HBO or antiresorptive medications; and (2) to identify the factors associated with the development of ORN/MRONJ.

MATERIALS AND METHODS

Patient characteristics and study design

Electronic medical records were reviewed to identify patients who were "at risk" for the development of ORN/MRONJ and who received dental extractions in the Oral Medicine and Dentistry Clinic at Brigham and Women's Hospital (BWH) between January 2003 to October 2019. This study was approved by the Partners Healthcare Institutional Review Board.

The study included patients with a history of (1) RT-HN, (2) parenteral antiresorptive therapy (bisphosphonates/RANKL inhibitors); or a history of therapy with antiangiogenic agents (for multiple myeloma, metastatic bone disease from solid tumors or osteoporosis); or dental extraction and received postextraction antibiotics for 14 days. For most patients with RT-HN, computed tomography (CT) of the graphic plan was used to estimate the radiation dose to the alveolar bone of the extracted tooth/teeth from treatment planning software (TPS). If the plan was not available in TPS, doses were estimated from a paper chart. Of patients with RT-HN, only those that received RT to the alveolar bone of the extracted teeth were included.

Exclusion criteria were (1) treatment with oral bisphosphonates only, (2) no postextraction antibiotics for 14 days, and (3) loss to follow-up after extraction (s) (n = 18). Electronic medical records were reviewed, and the study variables collected included demographic data (age and gender); pertinent medical history (underlying diagnosis, comorbidities, immunosuppressive medications, antiresorptive/antiangiogenic medications); and duration of antiresorptive therapy. Other information recorded included social history (tobacco use and alcohol consumption); the number and site of dental extractions; and postextraction sequelae.

Primary outcome

The primary outcome was the development of ORN/MRONJ at the extraction site after dental extraction. MRONJ was defined as exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region, persisting for longer than 8 weeks, [2] and ORN was defined as exposed devitalized irradiated bone that failed to heal over 3 months.[1] ORN and MRONJ were classified according to the American Association of Oral and Maxillofacial Surgeons (AAOMS) classification of MRONJ.[2]

Clinical protocol

Our clinical protocol for dental extractions in patients at risk for ORN/MRONJ included (1) performing atraumatic dental extraction, gentle curettage of the socket, saline irrigation, and achieving primary closure when possible; (2) postextraction prescription of amoxicillin 500 mg TID for at least 14 days (or an alternative broad-spectrum antibiotic for patients allergic to amoxicillin) and chlorhexidine 0.12% rinses 2 times daily until complete healing of the extraction site. Additional 2-week systemic antibiotic coverage with the same antibiotic was considered if signs of infection were noted at the follow-up visit. HBO was not used for any of the patients with a history of RT because HBO is not routinely recommended at our institution for prevention or management of ORN.[11]

Postoperative follow-up

A 2-week postoperative follow-up was carried out to ensure adequate healing, with additional follow-up visits scheduled, as needed. Patients were evaluated for signs of re-epithelialization/closure of the gingiva, indicating healing; presence of infection (erythema, swelling, or any purulent discharge); presence of exposed necrotic bone; and reports of pain.

Statistical analysis

Descriptive statistics, such as median and range, were used for continuous variables, and frequency (%) was used for categorical variables. Differences between patients who developed ONJ versus those who did not were calculated by using the Pearson's and Wilcoxon's tests. P values were considered statistically significant at $P < .05$. Statistical analyses were performed by using JMP Pro-14 (SAS Institute, Cary, NC).

RESULTS

Patient characteristics

A total of 90 patients (36.6% females; median age 63 years; range 29−90 years) were included in this analysis (see Appendix I). Fifty patients (55.5%) received a median of 64 Gray (Gy) (range 44−71 Gy) of RT-HN to the primary tumor site, and 40 (44.4%) were on antiresorptive medications and underwent a total of 243 extractions (median 1; range 1−16). None of the patients had both HN-RT and antiresorptive therapy. All the patients received 14 days of postextraction antibiotics, but 7 of these (4 in the MRONJ risk group and 3 in the ORN risk group) received an additional 14-day course with the same antibiotic because of signs of infection at the 2-week follow-up visit.

Patients with a history of RT

Among patients who received RT (n = 50), 56% had a history of oropharyngeal squamous cell carcinoma (SCC); 6% had oral SCC; and 10% had salivary gland adenoid cystic carcinoma (2 involving the parotid and 3 involving submandibular gland). The majority (94%) received intensity-modulated radiation therapy, and 3 patients (6%) underwent 3- dimensional conformal radiation therapy. Dosimetric analysis was carried out to quantify the dose to the extraction site. The median radiation dose to the extraction site was estimated to be 51.4 Gy (range 22.4−72 Gy). The median number of extractions performed was 1.5 (range 1−16). Most patients (58%) received mandibular dental extractions, 32% had maxillary extractions, and the remaining 10% received extraction of both maxillary and mandibular teeth (Table I). After dental extractions, 32 patients were prescribed amoxicillin 500 mg TID; 10 were prescribed amoxicillin−clavulanic acid 875 mg−125 mg (Augmentin) BID; 7 received clindamycin 300 mg TID; and 1 received IV ampicillin−sulbactam with transition to Augmentin upon discharge for 14 days. The decision to prescribe Augmentin or IV antibiotics may represent a deviation from the clinical protocol, but it was made at the discretion of the treating dental clinician.

One of the 50 patients (2%) developed ORN subsequent to dental extraction, 18 months after completion of RT. The medical history of this patient was significant for SCC of the right posterior mandible, status post segmental mandibulectomy, and adjuvant chemoradiation therapy. This patient had received a maximum radiation dose of 54.1 Gy to the extraction site. Delayed healing was observed at the 2- and 6-week follow-up after extraction of 2 grossly carious maxillary molars, and the patient presented with asymptomatic exposed bone at the 12-week follow-up. The ORN sites exhibited complete resolution 9 months after dental extractions.

Table I. Primary outcome: development of osteoradionecrosis (ORN) among "at risk" patients

Variable n (%)	*ORN Yes (n = 1)*	*ORN No (n = 49)*	*P value*
Age (years)			
Median (range)	59 (59)	61 (29−90)	.96
Gender			
Male	1 (2)	36 (72)	.51
Female	0 (0)	13 (26)	
Immunosuppressive medications			
No	1 (2)	48 (960)	.97
Yes	0 (0)	1 (2)	
Diabetes Mellitus type II			
Yes	0 (0)	7 (14)	.68
No	1 (2)	42 (84)	
Smoking Status			
Never	0 (0)	21 (42)	.63
Former	1 (2)	25 (50)	
Current	0 (0)	3 (6)	
Radiation dose to primary tumor site (Gy)			
Median (range)	60 (60)	64 (44−71)	.49
Radiation dose to extraction site (Gy)			
Median (range)	54.1 (54.1)	50.4 (22−72)	.71
Months between completion of radiation therapy and extraction			
Median (range)	18 (18)	36 (3−264)	.56
No. of extractions			
Single extraction	0 (0)	24 (48)	.79
Multiple extractions*	1 (2)	25 (50)	
Site of extraction			
Maxillary posterior	1 (2)	12 (24)	.68
Maxillary anterior	0 (0)	3 (6)	
Mandibular posterior	0 (0)	23 (46)	
Mandibular anterior	0 (0)	6 (12)	
Maxillary and mandibular posterior	0 (0)	5 (10)	

*Multiple extractions were considered when 2 or more teeth were extracted.

Patients with a history of antiresorptive or antiangiogenic medications

There was a total of 40 patients in the "at risk" MRONJ population, of which 55% had multiple myeloma; 37.5% had metastatic bone disease from solid tumors (prostate cancer, colorectal cancer, breast cancer and other); and 7.5% had osteoporosis. Among patients with cancer, 57.5% had received zoledronate, 10% had received denosumab, and another 10% had a history of exposure to both medications. The median duration of antiresorptive medication therapy was 24 months (range 3−72 months). The duration of antiresorptive treatment and the development of MRONJ did not reach a statistically significant association (P = .17). The median number of extractions performed in this group was 1 tooth (range 1−9), and most extractions were of posterior mandibular teeth (Table II).

Table II. Primary outcome: development of medication-related osteonecrosis of the jaw (MRONJ) after dental extraction(s)

Variable n (%)	*MRONJ Yes (n = 3)*	*MRONJ No (n = 37)*	*P value*
Age (years)			
Median (range)	65 (61−75)	66 (41−78)	.55
Gender			
Male	3 (7.5)	17 (42.5)	< .05
Female	0 (0)	20 (50)	
Smoking status			
Never	1 (2.5)	19 (47.5)	.34
Former	2 (5)	11 (27.5)	
Current	0 (0)	7 (17.5)	
Diabetes mellitus type II			
Yes	1 (2.5)	4 (10)	.36
No	2 (5)	33 (82.5)	
Concomitant corticosteroids			
No	0 (0)	22 (55)	< .05
Yes	3 (7.5)	15 (37.5)	
Diagnosis			
Multiple myeloma	1 (2.5)	21 (52.5)	.52
Metastatic cancer	2 (5)	13 (32.5)	
Osteoporosis	0 (0)	3 (7.5)	
AR/AA medications			
Zoledronic acid (Zometa)*	2 (5)	21 (52.5)	.95
Zoledronic acid (Reclast)†	0 (0)	2 (5)	
Pamidronate	0 (0)	4 (10)	
Pamidronate/Zometa	0 (00)	1 (2.5)	
Denosumab (Xgeva)‡	1 (2.5)	3 (7.5)	
Denosumab (Prolia)§	0 (0)	1 (2.5)	
Bevacizumab	0 (0)	1 (2.5)	
Zometa/Xgeva	0 (0)	4 (10)	
Duration of AR/AA (months)			
3−12	1 (2.5)	13 (32.5)	.17
12−48	2 (5)	17 (42.5)	
48−72	0 (0)	7 (17.5)	
No. of doses of AR/ AA before extractions, median (range)			
Zoledronic acid	20 (16−24)	24 (3−72)	.82
Pamidronate	0 (0)	8 (4−13)	
Denosumab	5 (5)	12 (3−72)	
Bevacizumab	0 (0)	24 (24)	
No. of extractions			
Single extraction	2 (5)	24 (60)	.92
Multiple extractions‖	1 (2.5)	13 (32.5)	
Site of extraction			
Maxillary posterior	0 (0)	14 (35)	.06
Maxillary anterior	0 (0)	2 (5)	
Mandibular posterior	2 (5)	17 (42.5)	
Mandibular anterior	0 (0)	1 (2.5)	
Maxillary and mandibular posterior	1 (2.5)	3 (7.5)	

AR/AA, Antiresorptive/antiangiogenic.
*Zometa: 4 mg infusion every 4, 6, 8, or 12 weeks for bone metastasis or multiple myeloma (as decided by the oncology team).
†Reclast: 5 mg infusion once yearly for osteoporosis.
‡Xgeva: 120 mg subcutaneous administration once monthly for bone metastasis or multiple myeloma.
§Prolia: 60 mg subcutaneous administration once every 6 months for osteoporosis.
‖Multiple extractions were considered when 2 or more teeth were extracted.

Three male patients (7.5%) developed MRONJ (2 patients: stage 1 MRONJ; 1 patient: stage 2 MRONJ). Two patients had metastatic castration-resistant prostate cancer (mCRPC), and the third one had multiple myeloma. All the 3 patients were on systemic corticosteroids as part of the treatment of their malignancy (dexamethasone 4 mg QD [on prescription], prednisone 10 mg QD, and dexamethasone 8 mg QD, respectively). Male gender ($P < .05$; odds ratio [OR] 1.7; 95% confidence interval [CI] 0.5−3.0) and concomitant use of immunosuppressant medications ($P < .05$; OR 1.6; 95% CI 0.4−2.8) were significantly associated with development of MRONJ. No antibiotic-related side effects were reported after the 14-day regimen of antibiotics in any of the patients.

DISCUSSION

Dental extractions in patients who have undergone RT-HN or those who have received antiresorptive/antiangiogenic medications carry the risk of ONJ. The risk of development of ORN in the literature has been reported to be in the range of 2% to 6.8% among irradiated patients with HN cancer.[12] This risk increases to 7% after dental extraction.[5] In our study cohort, the one patient who developed stage 1 ORN had received adjuvant radiation therapy for SCC of the right posterior mandible. Poor dental health has been implicated as a risk factor in the development of ORN.[13] The patient mentioned above had undergone extraction of 2 grossly carious right maxillary molars after RT, with one of them harboring periapical infection.

Diabetes mellitus, active smoking, and excessive alcohol consumption have also been identified as risk factors for ORN.[14] This study did not find such an association. However, this may be attributed to the small number of events. In this cohort, stage 2 or stage 3 ORN did not develop in any patient after dental extractions. Eighteen patients (10 from the ORN risk group and 8 the MRONJ risk group) were lost to follow-up. These patients did not present for the 2-week postextraction follow-up, and as a result, some cases of ONJ may have been missed. In our clinical experience, the usual pattern among patients who experience discomfort, including adverse events secondary to antibiotic use, and those with nonhealing extraction sockets is to contact their dental clinicians. Thus, it is likely that these patients had uneventful healing of the extraction sites.

Bisphosphonate use is associated with MRONJ in patients receiving cancer therapy (risk of 1%−7%) and those with osteoporosis (risk of 0.02%).[2] In patients exposed to denosumab for cancer treatment, the risk of MRONJ ranges from 0.7% to 1.9%.[2,15] After tooth extraction, the risk of MRONJ after IV bisphosphonate was found to be in the range of 1.6% to 14.8%.[2] The risk and incidence of MRONJ, associated with exposure

to zoledronate or denosumab for cancer, rise with increased duration of medication therapy (0.6% at 1 year, 0.9%−1.1% at 2 years, and 1.3% at 3 years).[16] A 10-year retrospective study conducted at Memorial Sloan Kettering Cancer Center revealed that MRONJ developed in patients on denosumab earlier in comparison with those on bisphosphonates.[17] Our study, however, did not find an association between the duration, dose, or type of antiresorptive medication therapy and the development of MRONJ, and this could be attributed to the small sample size in our study.

Stage 1 MRONJ developed in 2 (5%) of the 40 patients and stage 2 MRONJ 1 patient (2.5%) after dental extractions. Stage 3 MRONJ did not develop in any of the patients. Discontinuation of any antiresorptive therapy before dental extraction was not recommended by the dental team, and if implemented, this was solely at the decision of the oncologist. In only 1 of the patients with MRONJ, the zoledronic acid infusion had been discontinued for 4 months before extraction.

The 3 patients (2 with mCRPC and 1 with multiple myeloma) with MRONJ had been on daily oral systemic corticosteroids. Dexamethasone is given as part of the RVD (Revlimid [lenalidomide] + Velcade [bortezomib] + dexamethasone) chemotherapy for multiple myeloma,[18] and daily oral corticosteroids have been frequently used in conjunction with chemotherapy in prostate cancer for its anti-inflammatory and palliative benefits, such as decrease in prostate-specific antigen.[19] Interestingly, in early animal models, MRONJ could not be induced unless bisphosphonate was combined with steroids in a tooth extraction socket,[20] indicating concomitant administration of steroids as a risk factor. Systemic immunosuppressant medications were found to be significant for MRONJ development ($P < .05$).

Concomitant inflammatory disease, such as periapical disease, is a known risk factor contributing to ONJ.[21] Among our study cohort, all 3 patients with ONJ had grossly carious teeth with periapical disease contributing to local infection. One of the patients with mCRPC had generalized poor oral hygiene and was an active smoker, who continued to smoke after dental extraction despite counseling. Although smoking status was not statistically significantly associated with ONJ, smoking may have delayed the healing process.

Several theories have been proposed in the literature to explain the pathogenesis of ORN, including the most popular hypoxic−hypocellular−hypovascular tissue theory[1] and the radiation-induced fibroatrophy theory.[22] The role of microorganisms in the pathogenesis of ORN has been implicated since 1970, when it was proposed that ORN development results from a combination of 3 factors—radiation exposure, tissue injury, and infection.[23] Marx could not identify bacteria in ORN lesions with use of histologic staining methods[1]; however, Støre et al. demonstrated bacteria occupying marrow spaces in bone in ORN by using electron microscopic and molecular DNA-DNA hybridization studies.[24] The bacteria identified were rods, spirochetes, and cocci, with anaerobic rods constituting the predominant species.[20] In MRONJ as well, infection and inflammation have been considered to play a possible role in its pathogenesis, in addition to altered bone remodeling as a result of inhibition of osteoclastic bone resorption and inhibition of angiogenesis.[2,25] Hansen et al. demonstrated the presence of *Actinomyces* in both ORN and MRONJ biopsy samples.[3] On the basis of these studies, the possibility of an infectious etiology cannot be ruled out for these 2 histologically and pathogenically different, yet clinically similar, lesions.

As a result, in an attempt to prevent or reduce the risk of development of ONJ, antibiotics have been recommended for patients at risk for ONJ and who need to undergo exodontia. Although widely used, it is unclear if antibiotics are successful in preventing osteonecrosis, and to date, there is no clear consensus on the ONJ prevention protocols for performing extractions in patients at risk of ORN/MRONJ.[4,26] A survey conducted to analyze the antibiotic prescribing trends for exodontia in patients with a history of RT-HN found that 86% of British maxillofacial surgeons recommended preoperative prophylaxis and 89% postoperative antibiotics (duration range 3−28 days) for extraction of a mandibular molar in the radiotherapy field.[4] A study including 72 patients who underwent postradiation dental extractions without HBO reported no incidence of ORN under prophylactic antibiotic coverage with 2 g oral penicillin V 1 hour before extraction, followed by 600 mg 4 times a day after the procedure for 1 week.[27] In those at risk for MRONJ, a prospective case series of patients on IV bisphosphonates showed that the extraction protocol, including initiation of systemic antibiotics (1 g of amoxicillin TID), 3 days before extraction and continued for 17 days subsequently, was effective in reducing the risk of ONJ.[28] Nicolatou-Galitis et al. recommended the use of antimicrobial mouth wash and systemic antibiotics before and/or after the extraction to minimize the risk of MRONJ.[29] The clinical protocol at BWH for dental extractions in at-risk patients favors postextraction antibiotics starting on the day of the extraction(s) for at least 14 days, instead of prophylactic antibiotics, to effectively reduce microbial load, preventing subsequent infection during healing of the extraction(s) site.[11] The systemic antibiotics were continued for an additional 2 weeks if the patient presented with signs of infection at the follow-up visit. There is also a recommendation of chlorhexidine 0.12% rinse BID, to be used until the surgical site has completed healed. None of the patients in this study reported any antibiotic-associated adverse event.

Atraumatic extraction is another essential aspect of our clinical protocol. It can be described as exodontia, with limited disruption of the mucoperiosteum and the least possible osseous injury.[25] The rationale that supports the role of atraumatic extraction in the prevention of ONJ is the preservation of periosteal integrity, with the periodontium being a vital source of vascular supply, especially in impaired tissues.[30] In this study cohort, all the 243 extractions were simple extractions, performed without elevating a mucoperiosteal flap or gross manipulation of supporting bone.

HBO therapy is not routinely recommended at our institution because evidence for its role in the prevention and management of ORN is inconclusive in the literature.[11] HBO therapy is based on the use of high oxygen tension to potentially facilitate wound healing. However, in light of the limited evidence regarding benefit, increased associated cost, and potential side effects, including pneumothorax, arterial air embolism, and middle ear barotrauma, using HBO monotherapy or adjuvant therapy is not a part of our clinical protocol for dental extractions in irradiated patients.[11]

Our study has several limitations. One limitation is the absence of a control group for comparison of the ONJ risk in those with a history of RT-HN/antiresorptive exposure undergoing extractions with no antibiotic coverage because it is our clinical protocol to provide antimicrobial coverage during the postoperative period. Although patient outcomes were mostly favorable with use of postoperative antibiotics, it does not necessarily show cause and effect because there was no control group. Second, our small sample size limited our ability to evaluate more risk factors for the development of ONJ in patients with RT-HN and/or patients with a history of antiresorptive/antiangiogenic medications. Additionally, because of the retrospective nature of the study, details in the medical records about the extent and severity of the periodontal disease, which may be a risk factor or predictor of the development of ONJ, were insufficient. Although ORN and MRONJ are 2 different conditions with differing pathophysiology, treatment options are often similar, and as such, we decided to combine the 2 conditions in this study; but because no patient was exposed to both RT and antiresorptive therapy, we believe that it does not confound the results.

CONCLUSIONS

Atraumatic dental extractions with antibiotic coverage, comprising postoperative oral antibiotics for at least 14 days and antimicrobial mouthwash BID, is a safe approach in patients who require a dental extraction and are at risk for ONJ. HBO was not used for any of the patients with RT-HN. In our patient cohort, the frequency of postextraction ORN was lower, and the rate of MRONJ was comparable with that reported in the literature. Further larger prospective studies are required to validate the efficacy of postextraction antibiotics in reducing the incidence of ONJ.

APPENDIX I. PATIENTS' CHARACTERISTICS

Baseline characteristics n (%)	*Total patients N= 90*
Age (years)	
Median (range)	63 (29-90)
Gender	
Male	57 (63.3)
Female	33 (36.6)
Smoking status	
Never	41 (45.5)
Former	39 (43.3)
Current	10 (11.1)
Alcohol usage	
Never	15 (16.6)
Former	41 (45.5)
Current	34 (37.7)
Patients with co-morbidities	
Diabetes Mellitus type II	12 (13.3)
Hypertension	44 (48.8)
Diagnosis[1]	
SCC tongue	4 (4.4)
SCC floor of mouth	2 (2.2)
SCC mandible	1 (1.1)
SCC oropharynx	28 (31.1)
SCC nasopharynx	5 (5.5)
SCC hypopharynx	2 (2.2)
ACC salivary gland	5 (5.5)
SCC cutaneous HN	3 (3.3)
Multiple myeloma	22 (24.4)
Metastatic cancer	15 (16.6)
Osteoporosis	3 (3.3)
Teeth extracted, n (%)	
0-1	50 (55.5)
2-3	21 (23.3)
4+	19 (21.1)
Median (range)	1 (1 - 16)
Site of extraction	
Maxillary posterior	26 (28.8)
Maxillary anterior	5 (5.5)
Mandibular posterior	43 (47.7)
Mandibular anterior	7 (7.7)
Maxillary & mandibular posterior	9 (10.0)

1SCC: Squamous cell carcinoma; ACC: Adenoid cystic carcinoma; HN: Head & neck

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