



Important Considerations for Dental Safety to Prevent Osteoradionecrosis of the Jaws

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SUMMARY

Patients undergoing radiotherapy for malignancies in the head-and-neck region are prone to experiencing a range of dental complications. Osteoradionecrosis of the jaw (ORNJ) is a noteworthy complication that occurs infrequently but carries substantial significance, as evidenced by reported occurrence rates ranging from 2% to 22%. ORNJ is distinguished by bone necrosis and the inability to heal properly for at least 3 months. In the majority of cases, ORNJ typically demonstrates a gradual progression characterized by the subsequent development of infections, intra- or extra-oral fistulas, and bone necrosis with or without pathological fractures. There exists a multitude of risk factors that have been postulated to be associated with ORNJ. The literature extensively documents the influence of dental interventions on the progression of ORNJ; however, it continues to be a topic of continuing multidisciplinary debate. Establishing multidisciplinary collaborations that organize data and develop guidelines will be valuable for healthcare professionals operating in this specialized and relatively unfamiliar field. Therefore, this review has identified eleven key facts about dental safety precautions to prevent ORNJ and is prepared to give a clear and concise message to reduce the current uncertainty to provide recommendations, explanations, and measures.

Keywords: Dental implant; osteoradionecrosis; radiotherapy; tooth extraction.

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INTRODUCTION

Head-and-neck cancers are characterized by their aggressive nature, and the current therapeutic options for their treatment include surgery, radiotherapy (RT), and concurrent chemo RT (C-CRT).[1] Although RT and C-CRT offer tumor control and survival benefits, it is critical to acknowledge that a subset of patients may experience significant acute and chronic adverse effects, such as osteoradionecrosis of the jaw (ORNJ). [2] ORNJ is a late complication that significantly affects patients' life quality, with an incidence ranging from

2% to 22%[3] Regrettably, ORNJ often leads to facial disfigurement, pain, bone fractures, devitalization of the affected jaw bone, cutaneous or mucosal fistulas, halitosis, dysesthesia or anesthesia, trismus, challenges in mastication, speech problems, and as well as localized or systemic infections.[4]

In addition to the RT doses received by the jaws, oral surgical procedures such as tooth extraction and dental implant applications before and after RT or C-CRT are widely recognized as the most prominent risk factors for the development of ORNJ.[5] The impact of these dental interventions and their most

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appropriate timing relative to the irradiation course on the occurrence rate of ORNJ remains a topic of ongoing debate. Therefore, there remains a lack of consensus among dental professionals regarding the establishment of a conclusive protocol for the planning and management of dental treatments. As a result, the primary objective of the current review is to provide evidence-based messages that may help reduce misconceptions concerning dental security measures in the prevention of ORNJ.

METHODS

The present review was prepared through a comprehensive analysis of systematic reviews, original articles, meta-analyses, cohort studies, case reports, and abstracts published in English from 1984 to 2023. A search was conducted on PubMed using the following keywords: “RT,” “osteoradionecrosis,” “ORNJ,” “tooth extraction,” “dental implant,” “implant placement,” “implant survival,” “osseointegration,” and “head and neck cancer,” to identify pertinent articles. The studies that included fewer than 30 patients were excluded from this literature review.

RESULTS

A PubMed search yielded a total of 78 articles. However, 42 of them were excluded from the review process due to being case reports (n=9), case series with fewer than 30 patients (n=19), or duplicate studies (n=14). Hence, a total of 36 original (retrospective or prospective) and review studies meeting the specified selection criteria were analyzed to formulate the recommendations presented in this study.

DISCUSSION

Before initiating any cancer-related treatment, particularly head-and-neck RT, it is crucial to have a qualified dentist evaluate the patient’s oral and dental health. It is of utmost importance to ascertain the necessary measures that must be implemented to mitigate the occurrence of any adverse effects during and after radiation therapy (RT) in individuals diagnosed with head and neck cancer. In addition, conducting a comprehensive clinical and radiographic assessment of the oral and dental regions before RT or C-CRT is crucial for providing patients and radiation oncologists with pertinent information. While

tooth extraction and dental surgery are widely recognized as significant risk factors for ORNJ, it is necessary to note that not all dental procedures entail this particular risk. Procedures such as dental tartar cleaning, dental filling, and soft tissue interventions that do not cause injury to the bone or periosteum can be safely conducted on head-and-neck cancer patients at any given time.[6,7]

First and foremost, there are certain criteria that dentists ought to consider when deciding whether to perform tooth extractions before RT. Before RT, periodontally weak teeth in the RT field, teeth with fractures and loss of substance that cannot be restored, teeth with any acute or chronic infection at the root tip, semi-impacted teeth at risk for pericoronitis, and teeth that are elongated on the opposing edentulous alveolar crest must be extracted. However, impacted teeth that have not been exposed to the oral environment and are wholly bone-covered may be left in place.[7]

The timing of tooth extraction remains an unresolved issue for patients diagnosed with head and neck cancer. While pre-RT tooth extraction is generally regarded as a safer option when compared to extractions conducted during or after RT, recent studies have indicated that pre-RT tooth extraction can also lead to the development of ORNJ.[8] It is prudent to allow an adequate wait time between the tooth extraction procedure and the onset of the RT for the wound to undergo satisfactory healing. It is recommended that this period not be shorter than 14 days[9] to facilitate the healing process of soft tissues and reduce the risk of potential complications, including ORNJ development. It is recommended not to perform tooth extractions after RT to minimize the occurrence of ORNJ, but if mandated, post-RT tooth extractions should be carried out within the first 5–6 months after the completion of RT. This timing takes into account the expected progression of tissue fibrosis and vascular deterioration resulting from RT.[10,11]

Some authors have argued that pre-RT extractions may be associated with a lesser risk of ORNJ development.[12–14] The studies conducted by Kojima et al.[13] and Moon et al.[14] were unable to identify any statistically significant correlation between tooth extraction before RT and the occurrence of ORNJ. However, conversely, some other authors have pleaded that pre-RT extractions may also be linked to a heightened risk of ORNJ, similar to post-RT extractions.[11,12] Owosho et al.[12] conducted a retrospective cohort study that included 1023 patients diagnosed with oral cavity or oropharyngeal

cancers. The study found that only 18% of cases of ORNJ had tooth extractions before RT, suggesting a limited but significant connection between pre-RT extractions and an increased likelihood of developing ORNJ. Similarly, in a critical review by Wahl, the authors emphasized that the incidence of ORNJ after pre-RT tooth extraction (3.2% vs. 3.5%; $p>0.05$) was approximately identical to the ORNJ incidence in patients with post-RT post-extractions.[11] As a result, the extraction of teeth before RT should be regarded as a substantial risk factor for ORNJ. That is why dental and radiation oncologists should engage in comprehensive discussions regarding the pre-RT tooth extraction decision. When the decision is to perform tooth extraction, it is imperative for the responsible physician to ensure that the patient is adequately informed and their consent is obtained.

It is widely advised that individuals scheduled for RT undergo comprehensive radiographic and clinical dental assessments. These evaluations are typically conducted to identify any required interventions and administer them approximately 2–3 weeks before the initiation of RT.[15] Nevertheless, in certain instances, such as traumatic events or situations where RT results in unanticipated and intensified adverse responses, such as tooth fractures, tooth extraction may become mandatory during the RT course. It is crucial to bear in mind that the likelihood of developing ORNJ increases when tooth extractions or mandibular surgery becomes necessary during RT. Therefore, it is advisable to prioritize minimally invasive interventions, whenever feasible, to mitigate the associated risk.[15]

Limited research has been conducted regarding the potential hazards associated with surgical interventions performed on patients during RT. The existing literature primarily consists of recommendations for precautionary measures before or during surgery. [15,16] Indeed, the hypoxia resulting from vascular occlusion and the development of fibrosis due to hypoxic activity play a significant role in the pathogenesis of ORNJ. This biological activity sets off a detrimental cycle, exacerbated by the active involvement of inflammatory mediators. Consequently, the destructive effects of ORNJ on the bone structure become irreversible in the later stages, making them imperceptible during the initial application of RT. As a result, the principal objective of surgical procedures, such as tooth extraction, performed during RT should be to minimize any further damage to the affected tissue and mitigate the risks of infection and ORNJ.

An additional inquiry that arises in the context of dental interventions for patients undergoing or having undergone RT pertains to the efficacy of administering antibiotics to patients before or following a tooth extraction, intending to reduce the likelihood of developing ORNJ. Several authors have suggested the administration of clindamycin as a prophylactic measure for 10 days, with the initial dose given 3 days before surgical procedures and tooth extractions.[17] However, the efficacy of this application remains inconclusive due to a lack of definitive evidence. While it is not often required, the administration of antibiotics in instances of acute infection may have a beneficial impact on the process of wound healing following a surgical procedure.

The survival rate of head-and-neck cancer patients has improved significantly in the past two decades thanks to advancements in treatment methods and standard care. As a result, patients now have a longer life expectancy. However, this also means that the side effects of RT, both short-term and long-term, have become more significant for these patients.[18,19] Individuals who receive RT targeting the head-and-neck region face an elevated susceptibility to dental caries. This heightened risk arises from the permanent reduction of saliva, increased consumption of sugar, and the development of a cariogenic flora.[7] During the follow-up period, a significant proportion of patients in this group experienced the loss of multiple teeth. This fact can be attributed to various factors, including the extensive and rapidly progressing tooth decay process caused by reduced saliva production, degradation of salivary components, and complications arising from RT, such as mucositis, which has a detrimental impact on oral hygiene.[20,21] In turn, it is imperative for patients to undergo dental rehabilitation to enhance their physiological abilities, specifically in terms of mastication, deglutition, and oral occlusion, thereby ensuring the fulfillment of their nutritional requirements in their daily lives.[22]

It is not advisable to utilize removable prostheses in head-and-neck cancer patients who are currently undergoing or are scheduled to undergo RT unless there is a compelling medical need. This recommendation is based on the potential risk of ORNJ resulting from the degradation of salivary content caused by RT and the compression of the prosthesis.[15] Due to anatomical changes in the orofacial region and jaws, such as dry mouth, traditional removable dentures may not provide an appropriate and comfortable fit following RT and or surgery.

Consequently, dental implants are often preferred. [23,24] The rationale behind this decision is commonly rooted in the notion that dental implants have the potential to offer superior oral rehabilitation outcomes concerning chewing ability, aesthetic appearance, and speech function among individuals within this specific patient demographic. [25] As a result, implant-supported fixed or semi-fixed dental prostheses should be favored over conventional ones if prostheses are medically needed.

Given that the dental implant placement procedure is an invasive surgical intervention, it is imperative to subject it to a comprehensive evaluation using criteria analogous to those employed for tooth extraction. [7,26] While it is generally advised to wait 6–12 months after RT for safer implant placement, there is currently a lack of substantial scientific evidence regarding the optimal timing. [27,28] Nevertheless, it is necessary to assume that if the dental implant is placed more than 6–8 months after RT, there is a possibility that the resulting scar may undergo fibrosis formation. This process occurs due to the obstruction of blood vessels and insufficient blood flow to the affected bone. Consequently, this may result in bone resorption due to inadequate healing and potentially ORNJ. [29] Hence, it is reasonable to suggest that the most appropriate time frame would be approximately 5–6 months following RT or 3–4 months preceding RT, as this coincides with the ideal duration for the process of dental implant osseointegration. [30]

ORNJ appears to occur more frequently in patients with complete dentition. However, the absence of some teeth or an edentulous state does not necessarily eliminate the risk of developing ORNJ totally, which contradicts prevailing beliefs. The prevalence of spontaneous occurrences of ORNJ among all ORNJs is estimated to be approximately 10.8%. [31] It is also reasonable to expect the formation of the ORNJ as a result of trauma caused by removable dental prostheses in patients with extensive tooth loss. [32] Therefore, it is advisable to modify or substitute current dental prostheses.

Regular dental check-ups are essential for patients with head and neck cancer undergoing RT or C-CRT to prevent ORNJ and to ensure timely diagnosis and treatment if it does occur. As a result, patients who have undergone RT should be evaluated clinically and radiologically with a frequency of 3–6 months, depending on their susceptibility to these complications. This is because RT has a deleterious effect on the salivary glands, which causes dental caries formation, xerosto-

mia, and indirectly periodontal disease by affecting saliva flow and lubrication and disrupting the anti-caries effect. [33] It is advisable to administer oral hygiene education to this cohort of patients during each follow-up visit, accompanied by a comprehensive explanation of the potential signs, symptoms, and complications associated with RT.

Finally, another factor contributing to the increased rate of ORNJ is the administration of chemotherapeutic agents, particularly bone-acting ones, as part of the treatment. [32] While RT is a significant triggering factor for oral complications, co-administration of bone-acting and antiangiogenic medications may render patients more vulnerable to ORNJ. [34] The accurate distinction of whether the necrosis observed in patients taking bone-influencing medications is ORNJ or medication-related osteonecrosis is a separate but critical problem that must be resolved. In this setting, Zadik et al. emphasized the importance of considering the diagnosis of ORNJ only in cases where there has been exposure to radiation exceeding 40 Gy. This is crucial for avoiding misdiagnosis and ensuring appropriate treatment, especially in patients using bone-acting medications. In addition, the authors suggested that medication-related osteonecrosis should be considered a highly probable diagnosis in cases where the radiation exposure is <40 Gy. [35,36] Therefore, using bone-acting medications in a rational and limited manner can be a preventive measure for jaw osteonecrosis. This approach can also help avoid the unknown contributing effects of these medications on the development of ORNJ and the diagnostic challenges associated with their use. Hence, it is imperative to implement comprehensive preventive measures and administer more aggressive dental interventions and follow-up procedures for this particular cohort of patients (Table 1).

CONCLUSION

The collaborative efforts of various health-care professionals, including dentists, dental oncologists, oral and maxillofacial surgeons, periodontologists, prosthodontists, otorhinolaryngologists, radiologists, and radiation oncologists, play a crucial role in dental assessment as well as the prevention and management of ORNJ in patients undergoing or scheduled to undergo RT or C-CRT. Such an approach in routine practice holds significance in establishing dental plans for patients before RT, which is vital to accurately an-

Table 1 The recommendations, explanations, and precautions for avoiding osteoradionecrosis of the jaw [6,7,9,10,11,15,30,33,35,36]**Key facts for dental safety to avoid osteoradionecrosis**

Recommendation	Explanations and precautions
Assess oral and dental health prior to radiotherapy to reduce the risk of osteoradionecrosis	A comprehensive clinical and radiological examination is conducted to ascertain the current oral condition and necessary dental treatment
Dental cleaning, filling, and gingival interventions are deemed safe to be performed at any given time	Non-invasive dental procedures are generally regarded as having a relatively low risk of osteoradionecrosis
It is necessary to extract teeth that cannot be restored before undergoing radiotherapy, if possible. It is recommended to allow a minimum of 2 weeks for healing before starting the radiotherapy	It is imperative to ensure that the interval between tooth extraction and the initiation of radiotherapy is no shorter than 14 days to facilitate optimal wound healing
When tooth extraction is necessary during radiotherapy, it can be performed by taking the necessary precautions	It is important to consider that the likelihood of developing osteoradionecrosis escalates with the passage of time following radiotherapy
If tooth extraction is deemed necessary after radiotherapy, it is recommended to undertake the extraction procedure within the initial 5–6 months following the completion of radiotherapy	The formation of fibrous tissue 6–8 months after radiotherapy is a result of vascular obliteration and insufficient blood supply to the affected bone, which poses a significant risk for osteoradionecrosis
The administration of prophylactic antibiotics before tooth extraction is not obligatory to prevent osteoradionecrosis	The effectiveness of antibiotic administration, except for acute infections, lacks definitive evidence
The assessment of dental implants ought to be conducted using comparable criteria as those employed for tooth extractions after radiotherapy	While there is a dearth of conclusive evidence, it is advisable to consider scheduling dental implant procedures within the first 5–6 months following radiotherapy or 3–4 months before the initiation of radiotherapy
Having edentulism or fewer teeth does not completely eliminate the risk of osteoradionecrosis	Similar care should be provided to dentate patients
It is advised to schedule regular clinical and radiological dental assessments every 3–6 months following radiotherapy	Regular dental check-ups are advised to prevent complications resulting from the exacerbating impact of radiotherapy on dental caries and periodontal diseases
It is advisable to adopt a proactive approach when undergoing bone-active systemic treatment in conjunction with radiotherapy	The use of bone-acting agents increases the incidence of osteoradionecrosis and makes its accurate diagnosis difficult. Medication-related osteonecrosis should be taken into consideration as a potential differential diagnosis when jaw doses are below 40 Gy
It is essential that your dental procedures are meticulously planned by a team of qualified experts	It is recommended to involve a multidisciplinary team consisting of at least a dentist, an oral and maxillofacial surgeon, a periodontologist, a prosthodontist, an otolaryngologist, a radiologist, and a radiation oncologist in the decision-making process

anticipate potential complications, including the ORNJ, implement preventative and treatment measures, and enhance the overall quality of life during the remission phase. Hence, it is imperative to document treatment requirements, procedures, and potential complications by creating a Dental Treatment Chart before RT. Furthermore, the implementation of multidisciplinary collaboration within this particular field, the organization of the data acquired through this collective effort, and the development of guidelines will serve as valuable resources for healthcare professionals.

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