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Incidence of osteoradionecrosis following oral and maxillofacial surgery in irradiated head and neck cancer patients

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Abstract

Aim: The aim of this study was to investigate the incidence of osteoradionecrosis following various surgical procedures, including tooth extraction, periodontal surgery, pre-prosthetic surgery, removal of bone spicules and removal of bone reconstruction/osteosynthesis plates.

Material and methods: The charts of 68 patients who had undergone post-radiotherapy surgical procedures were reviewed. The following information was obtained: gender, age, radiotherapy dose and field, type of surgical procedure and time between the end of radiotherapy and the surgical procedure.

Results: Osteoradionecrosis developed in 14 patients and did not statistically correlate with gender, radiotherapy dose and field or time between the end of radiotherapy and the surgical procedure. Removal of bone spicules was significantly associated with osteoradionecrosis ($P = 0.033$), compared with tooth extraction, pre-prosthetic surgery, removal of reconstruction/osteosynthesis plates and periodontal surgery.

Conclusions: Our findings show removal of bone spicules is a significant risk factor for the development of osteoradionecrosis, suggesting that careful evaluation and management of spicules in previously irradiated patients is particularly important in the prevention of osteoradionecrosis.

Clinical relevance

Scientific rationale for study: Although it is widely known that tooth extractions may lead to the development of osteoradionecrosis, few studies have addressed the impact of other oral and maxillofacial surgical procedures on the development of the condition.

Principal findings: The removal of bone spicules was significantly associated with the development of osteoradionecrosis.

Practical implications: Our findings indicate that clinicians must be especially vigilant when removing spicules in previously irradiated patients.

Introduction

Radiotherapy (RT) is largely employed as primary therapy, adjuvant to surgery, or in conjunction with chemotherapy for the treatment of head and neck cancer (HNC). Although RT can increase cure rates, it is unfortunately associated with several side effects[1]. Osteoradionecrosis (ORN), one of the most serious RT complications, is defined as the ischemic necrosis of the irradiated bone that becomes hypovascular, hypocellular and hypoxic[2–4].

Clinically, ORN may vary from small asymptomatic regions of exposed bone that remain stable over time to full-blown osteonecrosis that is characterised by

severe pain and suppuration[2]. Radiographic examination shows decreased bone density and, occasionally, fractures. ORN occurs most frequently on the mandible's posterior portion. The mandible is more affected than the maxilla, probably due to its smaller vascular component[5]. Management of ORN is still controversial, and the condition can be treated conservatively or surgically[6]. Importantly, it is estimated that more than half of all patients who develop the condition will require some form of surgical intervention[5,7].

Despite extensive research, controversy still exists regarding aetiology and mechanisms of ORN[8]. Several risk factors have been associated with the condition, including tumour size and stage, RT dose, poor oral hygiene and smoking/drinking habits[5]. Additional risk factors include bone biopsy, salvage surgery, trauma by prosthesis, periodontal disease and extractions performed after radiotherapy[9]. The latter may be the most important single risk factor in the development of ORN[10–12].

Although it is generally accepted that trauma, typically via post-RT tooth extraction, is an important risk factor in the development of ORN, the literature lacks studies that address the impact of other oral surgical procedures on its incidence. Identification of which procedures are more likely to cause ORN will improve our ability to prevent this complication. Thus, the aim of this study was to investigate the incidence of ORN following various surgical procedures in previously irradiated patients, namely: teeth extractions, pre-prosthetic surgery, removal of bone spicules, removal of bone reconstruction/osteosynthesis plates and periodontal surgery.

Material and methods

A retrospective, descriptive study was conducted. The charts of all patients seen between 2002 and 2007 at the Oral Oncology Service of the Universidade Federal de Minas Gerais were reviewed, and patients who had undergone oral and maxillofacial surgical procedures after completion of RT were included in the study. All subjects had biopsy-proven malignant neoplasms of the head and neck region, and received external beam RT at a minimum of 45 Gy. ORN was defined as chronically exposed bone, in the absence of recurrent cancer, for at least 3 months observed on clinical examination. All clinical examinations had been performed by specialists in oral surgery and/or oral medicine, with extensive experience in the management of patients undergoing radiotherapy.

The following information was obtained from the charts: patients' gender and age; tumour site and Union for International Cancer Control stage; RT field, dose and number of sessions; type of surgical procedure; and time between the end of RT and the surgical procedure. To evaluate the influence of various surgical procedures on the development of ORN, procedures were divided as follows: extractions, pre-prosthetic surgery, removal of reconstruction/osteosynthesis plates, periodontal surgery and removal of bone spicules. Pre-prosthetic surgery consisted of bone re-contouring to facilitate the retention of dentures. Removal of reconstruction/osteosynthesis plates consisted of removing devices employed for the stabilisation of mandibulectomies. Removal of bone spicules consisted of removal of small bone fragments, remnants of a previous extraction. Spicules were present at the extraction site and were superficially located at the margins of the jaws. The fragments appeared vital upon clinical inspection, and the underlying bone showed normal aspect.

As part of our service protocol, all patients had been prescribed a single 600 mg clindamycin dose, 1 h prior to the surgical procedure. The drug was maintained for 7 days, in a 300 mg dose, four times a day.

For statistical analysis, the Mann–Whitney and Fisher tests were employed, using the SPSS software (SPSS Inc., Chicago, IL, USA). Significance was considered for $P < 0.05$.

Results

The charts of 240 patients were analysed. Of these, 68 had undergone post-RT surgical procedures (58 males, 10 females; mean age 55 years, range 23–88 years). ORN developed in 14/68 (20%) patients. Table 1 shows demographic, tumour and treatment characteristics of the 14 patients who developed ORN. No demographic

Table 1 Demographic, tumour and treatment characteristics of 14 patients that developed osteoradionecrosis

Variable	Category	*n* (%)
Age (years)	Mean	58.3
	Range	44–80
Gender	Male	10 (71)
	Female	4 (29)
Tumour site	Mouth	11 (78)
	Larynx	3 (22)
Clinical Stage (UICC)	I/II	3 (21)
	III/IV	11 (79)
Radiation dose (Gy)	Mean	59.7
	Range	50–71
Radiotherapy field	Included jaws	11 (78)
	Excluded jaws	3 (22)
Radiotherapy sessions	Mean	33
	Range	30–44

UICC, Union for International Cancer Control.

Table 2 Development of osteoradionecrosis according to the type of surgical procedure

Surgical procedure	Cases	Osteoradionecrosis (%)
Extraction	55	9 (16.3)
Pre-prosthetic surgery	3	1 (33.3)
Removal of bone spicule	6	4 (66.7)
Removal of reconstruction/ osteosynthesis plates	2	0 (0)
Periodontal surgery	2	0 (0)
Total	68	14 (20)

(age, gender), tumour (location, stage) and treatment (radiotherapy dose and sessions) differences were observed between patients with and without ORN. Ten patients with ORN were males (10/58 = 17.2%; P = 0.197), and four were females (4/10 = 40%; P = 0.114). No statistical correlation was found between gender and development of ORN. Time between the end of RT and the surgical procedure varied from 1 to 60 months. There was no correlation between the development of ORN and time (P = 0.381). Of the 68 post-radiotherapy surgeries, 48 had the jaws included in the radiation field. Of these, 11 (11/48 = 22.9%) developed ORN. In 20 cases, the jaws were outside radiation fields. Of these, 3 (3/20 = 15%) developed ORN. There was no significance between inclusion of jaws in the RT field and development of ORN (P = 0.532). ORN incidence increased with higher RT doses, but without statistical significance (P = 0.3).

When considering the different types of surgical procedures, the highest ORN incidence was seen in patients submitted to removal of bone spicules (66%) and lowest following teeth extractions (16.3%). ORN did not develop following removal of reconstruction/ osteosynthesis plates and periodontal surgery (Table 2). There was a significant association between removal of bone spicules and development of ORN (P = 0.033), compared with tooth extraction, pre-prosthetic surgery, removal of reconstruction/osteosynthesis plates and periodontal surgery. Thirteen cases of ORN were treated exclusively with surgery; one patient underwent hyperbaric oxygen therapy in addition to surgery. No follow-up data were available.

Discussion

Despite extensive research, the pathogenesis of ORN is still unclear. Radiation-generated free radicals and damage to endothelial cells lead to hypovascularity, tissue hypoxia, destruction of bone-forming cells and marrow fibrosis[2]. In addition, bone turnover is likely suppressed and involved in the initiation of ORN[3]. Recently, it was shown that anaerobe bacteria might play a key role in pathophysiology of ORN, instead of being merely surface contaminants[4]. A fibro-atrophic theory, in which three successive clinical and histopathological phases (pre-fibrotic a specific inflammatory, constitutive fibrotic cellular and matrix densification/remodelling) may lead to terminal tissular necrosis, has also been proposed[13].

The incidence of ORN in HNC patients varies from 0.4% to 56%[5]. Such variation may be a result of differences in study populations and observation periods[14]. Importantly, the incidence of ORN has declined in recent decades. Before 1968, the incidence was 11.8%, and from 1968–1992, rates changed to 5.4%[15]. In 1997, incidence rates of approximately 3% were described[16]. Finally, a recent study found a 2% overall incidence rate[17]. Such decrease is presumably due to the advent of megavoltage RT and to the increased awareness of the importance of oral health care[3]. Indeed, ideally all required dental work and oral hygiene instructions should be accomplished before RT[16]. Also, there is growing consensus that multidisciplinary teams can reduce the irradiation sequelae[1]. In our study, the overall incidence was 20% (14 cases in 68 patients that underwent surgery). Our incidence after dental extractions was 16.3%, which is higher than the 7% incidence found in a recent meta-analysis[18]. Although new techniques of RT (such as IMRT) are available in Brazil, few patients have access to this treatment modality[19], thus explaining a higher incidence. Still, the incidence we found might have been even higher if not for the protocol we follow at our service, which emphasises pre-RT oral health care. Briefly, all patients are assessed prior to surgery and/or radiotherapy. A dental treatment plan is then developed, and oral hygiene instructions are given. Extractions of unrestorable teeth are performed whenever a minimum 21 days interval of healing time can be respected prior to initiation of RT. During RT, patients are seen on a weekly basis and receive comprehensive treatment in various dental specialties (oral medicine, oral surgery, operative dentistry, endodontics, periodontics, prosthodontics and radiology). In addition, patients are seen by nutritionists, psychologists and physiotherapists. Patients continue to be followed-up upon completion of RT to prevent, identify and manage late RT complications.

Several risk factors for the development of ORN have been identified but, despite the extensive literature, evidence of consistent and conclusive risk exists for only a fraction of factors examined[8]. Studies have shown that the incidence of ORN is approximately three-fold higher for men than for women. However, this is probably a reflection of the population profile of patients with HNC, which is more common in males[14].

In our study, most patients were males, but the incidence of ORN was higher in women (40%) than in men (17%). However, gender did not correlate significantly with development of the disease.

Though radiation dose undoubtedly contributes to the development of ORN, no consensus exists in the literature as to maximal safe dosing[8]. Thorn *et al*.[20] observed that in more than 90% of the ORN cases, RT doses employed were above 64 Gy. In our study, all patients were submitted to over 50 Gy of radiation. Although RT dose was not statistically related to the development of ORN, we verified that with increasing doses (60 Gy and 70 Gy), the incidence of ORN also increased. Field of RT has occasionally been shown to affect ORN risk, particularly when the jaws are included[5,21]. In our study, the incidence of ORN was higher in patients when the jaws were included in the field, although not reaching statistical significance. However, ORN developed even when the jaws were not included in the RT field. Similarly, Epstein *et al*.[10] observed 5.4% ORN rates after extractions in non-irradiated fields. Cases of ORN that develop outside the RT field are possibly a consequence of obliteration of the area's primary vascular supply and insufficient secondary blood supply[20].

The risk of ORN for post-RT teeth extractions ranges from 0 to 43%[21]. In our study, 16.3% (9/55) of the patients developed ORN following extractions without statistical significance. Many authors agree that post-RT extractions yield a higher rate of ORN[10–12] and thus advocate dental extractions should be delayed until at least 9 to 12 months after the end of RT[5]. In contrast, other studies claim ORN may develop even 10 years after RT due to a progressive and irreversible reduction in biologic activity, and thus risk may actually increase with time[22]. In our study, the time between the end of RT and the surgical procedure varied from 1 to 60 months and did not significantly increase the risk of ORN development. Finally, some studies have shown that post-RT extractions have a low risk of complications[23] and failed to show a particularly high incidence of ORN following extractions[16].

Any surgical procedure performed within an irradiated field increases the risk of developing ORN[9]. However, few studies have addressed the effects of other surgical procedures, other than extractions, on the development of the condition. Thus, in our study, we aimed to verify the impact of not only dental extractions, but also types of surgical procedures, on the development of ORN. ORN did not develop following reconstructive/osteosynthesis plates and periodontal surgery. It developed in 1/3 (33%) patients who underwent pre-prosthetic surgery. Our most important finding was that the removal of bone spicules – a relatively simple procedure – was a significant risk factor for ORN development. Possibly, hypovascularity induced by RT was more pronounced in the bone surface where the spicules were located. Further, loss of periosteal blood supply may occur following a marginal resection[9] and could have contributed to hypovascularity in the bone surface. Consequently, the area was unable to heal properly, ultimately resulting in ORN. It should be noted that the bone spicules were likely derived from pre-RT extractions; in fact, spicules are frequent and a part of the bone remodelling process, and it may be virtually impossible to predict if they will arise following an extraction[24]. Considering that 50% of the patients seen in our service require at least one extraction before RT, and that we extract on average 11 teeth per patient[25], the number of patients requiring spicules removal may be considered low. Further, since all extracted teeth were decaying and non-restorable, not extracting those (with the purpose of avoiding later formation of bone spicules) would have led to serious consequences as well. To prevent the occurrence of spicules in patients that will undergo radiotherapy, atraumatic extraction (to preserve the integrity of the perisoteum) and alveoloplasty should always be performed[18].

The effectiveness of prophylactic antibiotics to prevent ORN is still controversial[16]. Nonetheless, antibiotic prophylaxis before the extraction procedure is the most common initiative to prevent ORN. Indeed, 86% of surveyed surgeons would recommend prophylactic antibiotics for extraction of a residual root in an irradiated mandible[26]. Marx *et al*.[27] recommended large doses of intravenous penicillin, yet 30% of the patients developed ORN. Tong *et al*.[28] observed delayed wounding and ORN following extractions under antibiotics in 6.3% and 9.3% of the patients, respectively. In contrast, Maxymiw *et al*.[29] prescribed prophylactic antibiotics to 72 irradiated patients submitted to 96 extractions and found no cases of ORN. Similarly, Carl *et al*.[30] reported uneventful healing in 47 irradiated patients that underwent extraction of 187 teeth under antibiotic therapy. Among antibiotics, clindamycin is commonly chosen because it is active against most strains of *Staphylococcus aureus*, several other gram-positive cocci and gram-negative anaerobic pathogens. Importantly, the drug provides good penetration into the bone and has been proven successful for the treatment of osteomyelitis[31]. Clindamycin has been previously for prevention of ORN with daily doses of 1200 mg, for 21 days, starting 3 days before surgery[32]. In our service, we employed the same drug, in a lower dosage and for a shorter period. ORN developed in 20%

of patients that underwent surgery, and in 16.3% of patients that underwent extractions. However, since the aim of our study was not to assess the efficacy of prophylactic antibiotic, our results regarding clindamycin should be interpreted with caution. Considering that antibiotics carry a risk of development of resistant strains, and given the conflicting data existent in the literature, it is clear that large, well-controlled, double-blind, randomised trials are warranted to determine their effectiveness in the prevention of ORN.

Similarly to antibiotics, the usefulness of HBO in the prevention of ORN is also still in debate. Recently, a systematic review found insufficient information to prove that HBO reduces the incidence of ORN in patients requiring tooth extractions[33]. In contrast, another study found a 4% incidence of ORN following extractions with HBO, compared to a 7% incidence when HBO was not employed. The authors concluded that, based on weak evidence, prophylactic HBO is effective in reducing ORN[18]. In our study, only one patient was submitted to hyperbaric oxygen therapy (HBO). Thus, we were unable to analyse the impact of this procedure on our findings.

Our results need to be interpreted in light of its limitations. The major drawback of our study was that the information was collected retrospectively, thus being subject to inherent inaccuracies, including the inability to control bias and confounders. Small sample size (particularly after stratification by different surgical procedures) and the imbalance between the numbers of cases between the subgroups, coupled with the low incidence rate of ORN, were also additional limitations. Finally, it should be noted that it is possible that the bone spicules observed in this study represented in reality early osteoradionecrotic lesions and that the act of removing the bone spicules might actually have been a minor sequestrectomy procedure itself. However, as stated previously, the bone spicules removed in this study were neither necrotic nor exposed upon clinical inspection, and the underlying bone was also clinically normal. Considering these facts, and the definition of ORN (area of exposed devitalised irradiated bone that fails to heal over a period of 3–6 months), we believe we were in fact dealing with spicules, rather than early osteoradionecrotic lesions.

In conclusion, removal of bone spicules in previously irradiated patients was a significant risk factor for ORN, even under antibiotic therapy. This is particularly important since HNC patients commonly undergo several extractions prior to RT initiation and are thus prone to the development of spicules. Additional studies with larger samples are warranted to confirm our findings.

References

1. Koga DH, Salvajoli JV, Alves FA. Dental extractions and radiotherapy in head and neck oncology: review of the literature. Oral Dis 2008;14:40–4.
2. Sciubba JJ, Goldenberg D. Oral complications of radiotherapy. Lancet Oncol 2006;7:175–83.
3. Teng MS, Futran ND. Osteoradionecrosis of the mandible. Curr Opin Otolaryngol Head Neck Surg 2005;13: 217–21.
4. Store G, Eribe ERK, Olsen I. DNA-DNA hybridization demonstrates multiple bacteria in osteoradionecrosis. Int J Oral Maxillofac Surg 2005;34:193–6.
5. Jereczek-Fossa BA, Orecchia R. Radiotherapy-induced mandibular bone complications. Cancer Treat Rev 2002;28:65–74.
6. Hunter SE, Scher RL. Clinical implications of radionecrosis to the head and neck surgeon. Curr Opin Otolaryngol Head Neck Surg 2003;11:103–6.
7. Wong JK, Wood RE, McLean M. Conservative management of osteoradionecrosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1997;84:16–21.
8. Goldwaser BR, Chuang SK, Kaban LB, August M. Risk factor assessment for the development of osteoradionecrosis. J Oral Maxillofac Surg 2007;65:2311–6.
9. Chrcanovic BR, Reher P, Sousa AA, Harris M. Osteoradionecrosis of the jaws – a current overview – part 1: physiopathology and risk and predisposing factors. Oral Maxillofac Surg 2010;14:3–16.
10. Epstein J, Wong F, Stevenson-Moore P. Osteoradionecrosis: clinical experience and a proposal for classification. J Oral Maxillofac Surg 1987;45:104–11.
11. Beumer J, Harrison R, Sanders B, Kurrasch M. Osteoradionecrosis: predisposing factors and outcomes of therapy. Head Neck Surg 1984;6:819–27.
12. Murray CG, Herson J, Daly TE, Zimmerman S. Radiation necrosis of the mandible: a 10-year study. Part II. Dental factors; onset, duration, and management of necrosis. Int J Radiat Oncol Biol Phys 1980;6:549–2.
13. Delanian S, Lefaix JL. The radiation-induced fibroatrophic process: therapeutic perspective via the antioxidant pathway. Radiother Oncol 2004;73:119–31.
14. Reuther T, Schuster T, Mende U, Kübler A. Osteoradionecrosis of the jaws as a side effect of radiotherapy of head and neck tumour patients – a report of a thirty year retrospective review. Int J Oral Maxillofac Surg 2003;32:289–95.
15. Clayman L. Management of dental extractions in irradiated jaws: a protocol without hyperbaric oxygen therapy. J Oral Maxillofac Surg 1997;55:275–81.
16. Wahl MJ. Osteoradionecrosis prevention myths. Int J Radiat Oncol Biol Phys 2006;64:661–9.
17. Nabil S, Samman N. Risk factors for osteoradionecrosis after head and neck radiation: a systematic review.

Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113: 54–69.
18. Nabil S, Samman N. Incidence and prevention of osteoradionecrosis after dental extraction in irradiated patients: a systematic review. Int J Oral Maxillofac Surg 2011;40:229–43.
19. Bonan PR, Lopes MA, Pires FR, Almeida OP. Dental management of low socioeconomic level patients before radiotherapy of the head and neck with special emphasis on the prevention of osteoradionecrosis. Braz Dent J 2006;17:336–42.
20. Thorn JJ, Hansen HS, Specht L, Bastholt L. Osteoradionecrosis of the jaws: clinical characteristics and relation to the field of irradiation. J Oral Maxillofac Surg 2000;58:1088–93.
21. Sulaiman F, Huryn JM, Zlotolow IM. Dental extractions in the irradiated head and neck patient: a retrospective analysis of Memorial Sloan-Kettering Cancer Center protocols, criteria, and end results. J Oral Maxillofac Surg 2003;61:1123–31.
22. Notani K, Yamazaki Y, Kitada H, Sakakibara N, Fukuda H, Omori K *et al*. Management of mandibular osteoradionecrosis corresponding to the severity of osteoradionecrosis and the method of radiotherapy. Head Neck 2003;25:181–6.
23. Lye KW, Wee J, Gao F, Neo PS, Soong YL, Poon CY. The effect of prior radiation therapy for treatment of nasopharyngeal cancer on wound healing following extractions: incidence of complications and risk factors. Int J Oral Maxillofac Surg 2007;36:315–20.
24. Tran Van P, Vignery A, Baron R. An electron-microscopic study of the bone-remodeling sequence in the rat. Cell Tissue Res 1982;225:283–92.
25. Jham BC, Reis PM, Miranda EL, Lopes RC, Carvalho AL, Scheper MA *et al*. Oral health status of 207 head and neck cancer patients before, during and after radiotherapy. Clin Oral Investig 2008;12:19–24.
26. Kanatas AN, Rogers SN, Martin MV. A survey of antibiotic prescribing by maxillofacial consultants for dental extractions following radiotherapy to the oral cavity. Br Dent J 2002;192:157–60.
27. Marx RE, Johnson RP, Kline SN. Prevention of osteoradionecrosis: a randomized prospective clinical trial of hyperbaric oxygen versus penicillin. J Am Dent Assoc 1985;111:49–54.
28. Tong AC, Leung AC, Cheng JC, Sham J. Incidence of complicated healing and osteoradionecrosis following tooth extraction in patients receiving radiotherapy for treatment of nasopharyngeal carcinoma. Aust Dent J 1999;44:187–94.
29. Maxymiw WG, Wood RE, Liu FF. Postradiation dental extractions without hyperbaric oxygen. Oral Surg Oral Med Oral Pathol 1991;72:270–4.
30. Carl W, Schaaf NG, Sako K. Oral surgery and the patient who has had radiation therapy for head and neck cancer. Oral Surg Oral Med Oral Pathol 1973;36: 651–9.
31. Naal FD, Salzmann GM, von Knoch F, Tuebel J, Diehl P, Gradinger R *et al*. The effects of clindamycin on human osteoblasts in vitro. Arch Orthop Trauma Surg 2008; 128:317–23.
32. Németh Z, Somogyi A, Takácsi-Nagy Z, Barabás J, Németh G, Szabó G. Possibilities of preventing osteoradionecrosis during complex therapy of tumors of the oral cavity. Pathol Oncol Res 2000;6:53–8.
33. Fritz GW, Gunsolley JC, Abubaker O, Laskin DM. Efficacy of pre- and postirradiation hyperbaric oxygen therapy in the prevention of postextraction osteoradionecrosis: a systematic review. J Oral Maxillofac Surg 2010;68:2653–60.