Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies ***NLM ID:*** *101716117*

Journal home page: www.jamdsr.comdoi: 10.21276/jamdsr Index Copernicus value = 85.10

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Original Research

Evaluation of risk factors of osteoradionecrosis of jaws in patients of head and neck cancer

Kaluram Khande[1], Abhishek Pathak[2]

[1]Associate professor, Department of Dentistry, G R Medical College, Gwalior M.P., India;
[2]Former Senior resident, Department of Dentistry, G R Medical College, Gwalior M.P., India

ABSTRACT

Background: Osteoradionecrosis of the jaw (ORNJ) is among the most serious late complications observed in patients with head and neck squamous cell carcinoma (HNSCC) treated with radiation therapy (RT). The present study was conducted to evaluate risk factors of osteoradionecrosis of jaws in patients of head and neck cancer. **Materials & Methods:** 42 patients who developed osteoradionecrosis of jaws following postoperative RT to the head and neck cancer of both jaws were included. Risk factors such as history of smoking or alcohol use, diabetes mellitus, pre-RT dental evaluation, pre- or post-RT tooth extraction, primary tumor site, T-stage, nodal status and treatment-related factors were recorded. **Results:** Out of 42 patients, males were 30 and females were 12. Common risk factors found to be diabetes in 30, alcoholism in 15, smoking in 35, oropharyngeal cancer in 24, oral cancer in 12, hypopharyngeal cancer in 4 and nasopharyngeal cancer in 2 cases. The difference was significant (P< 0.05). **Conclusion:** Common risk factors found to be diabetes, alcoholism, smoking, oropharyngeal cancer, oral cancer, hypopharyngeal cancer and nasopharyngeal cancer.

Key words: Alcoholism, Smoking, Osteoradionecrosis

Received: 15, January 2021 Accepted: 17 February, 2021

Corresponding Author: Dr. Abhishek Pathak, Former Senior resident, Department of Dentistry, G R Medical College, Gwalior M.P., India

This article may be cited as: Khande K, Pathak A. Evaluation of risk factors of osteoradionecrosis of jaws in patients of head and neck cancer. J Adv Med Dent Scie Res 2021;9(3):49-52.

INTRODUCTION

Osteoradionecrosis of the jaw (ORNJ) is among the most serious late complications observed in patients with head and neck squamous cell carcinoma (HNSCC) treated with radiation therapy (RT). The associated morbidity of this condition and its subsequent treatment, which can range from close observation to radical surgical resection, can be substantial.[1]

While ORNJ was first described in 1922, the definition, mechanism of pathogenesis, incidence, risk factors, and clinical staging, as well as treatment protocols associated with the disease require further investigation.[2] Despite the lack of a standard and unified definition, ORNJ is usually defined as an area of exposed irradiated bone that fails to heal over a period of 3–6 months in the absence of local tumor recurrence. Radiological evidence of bone necrosis within the target volume is also important for the diagnosis and classification of ORNJ severity. Several risk factors of ORNJ have been reported, including patient-related, tumor-related and treatment-related factors.[3]

The key event in the development of ORN is the activation and regulatory disturbance of fibroblast activity. The combination of dying osteoblasts without osteoblast replication and excessive proliferation of myofibroblasts results in a reduction of bone structure. The regulatory disturbance leads finally to vulnerable, atrophic-fibrous tissue in the irradiated area.[4] The irradiation dose to the bone is believed to be associated with the risk of ORN. However, the mandible seems to be especially susceptible to the development of ORN because the blood supply is limited to a single functional terminal artery. The facial artery does not seem to be able to produce enough collateral blood vessels to compensate for the loss of the blood supply to the mandible that occurs after fibrosis of the inferior alveolar artery.[5] The present study was conducted to evaluate risk factors of osteoradionecrosis of jaws in patients of head and neck cancer.

MATERIALS & METHODS

The present study was conducted among 42 patients who developed osteoradionecrosis of jaws following postoperative RT to the head and neck cancer of both jaws. All were informed regarding the study and their consent was obtained.

Data such as name, age, gender etc. was recorded. IMRT treatment included volumetric-modulated arc therapy using the simultaneous integrated boost (SIB-VMAT) technique. In general, 69.96 or 70 Gy (delivered in 2.12 Gy or 2 Gy per fraction) was prescribed for definitive RT, 50–60 Gy (delivered in 2 Gy per fraction) was prescribed for postoperative RT in cases with minor risk features, and 66 Gy (delivered in 2 Gy per fraction) was prescribed for postoperative RT in patients with high risk features. Risk factors such as history of smoking or alcohol use, diabetes mellitus, pre-RT dental evaluation, pre- or post-RT tooth extraction, primary tumor site, T-stage, nodal status and treatment-related factors were recorded. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of subjects

Total- 42		
Gender	**Males**	**Females**
Number	30	12

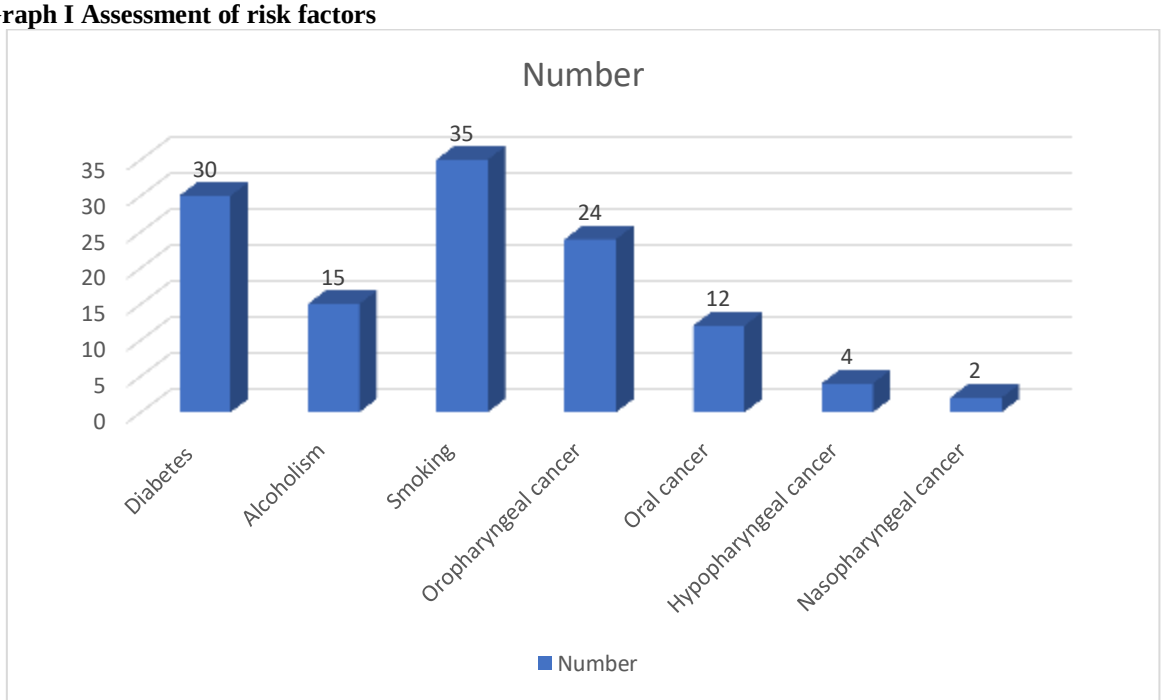
Table I shows that out of 42 patients, males were 30 and females were 12.

Table II Assessment of risk factors

Risk factors	Number	P value
Diabetes	30	0.021
Alcoholism	15	
Smoking	35	
Oropharyngeal cancer	24	
Oral cancer	12	
Hypopharyngeal cancer	4	
Nasopharyngeal cancer	2	

Table II, graph I shows that common risk factors found to be diabetes in 30, alcoholism in 15, smoking in 35, oropharyngeal cancer in 24, oral cancer in 12, hypopharyngeal cancer in 4 and nasopharyngeal cancer in 2 cases. The difference was significant (P< 0.05).

Graph I Assessment of risk factors



DISCUSSION

During the last decade, there have been several technical advancements in radiation therapy (RT) that reduce acute and chronic therapy-related side effects, especially in patients undergoing RT for head and neck cancer.[6] The introduction of three-dimensional conformal RT (3D-CRT) and intensity modulated RT (IMRT) allows for greater protection of the major salivary glands thus preserving the salivary flow rate and allowing better recovery of the salivary glands. Consequently, patients' quality of life has been improved, and the risk of radiation-induced damage to dentition has decreased.[7]

Currently, osteoradionecrosis (ORN) of the jaw is one of the most severe chronic side effects of RT to the head and neck region.[8] The associated morbidity of this condition and its subsequent treatment, which can range from close observation to radical surgical resection, can

be substantia. Concomitant chemotherapy may also be a potential risk factor for ORN development.[9] Cisplatin derivatives are the most commonly used chemotherapeutic drugs; the function of these derivatives is based on the intracellular generation of an increased number of free oxygen radicals, so-called as reactive oxygen species, which inhibit the DNA repair capacity of the bone cells in the normal tissues.[10] The present study was conducted to evaluate risk factors of osteoradionecrosis of jaws in patients of head and neck cancer.

In present study, out of 42 patients, males were 30 and females were 12. Kuhnt et al[11] included 776 patients who underwent 3D-CRT or IMRT for head and neck cancer. Sex, dental status prior to radiotherapy, tumor site, bone surgery during tumor resection, concomitant chemotherapy, and the development of advanced ORN were documented for each patient. ORN was classified as grade 3, 4, or 5 according to the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer classification or grade 3 or 4 according to the late effects in normal tissues/subjective, objective, management, and analytic scale. The cumulative incidence of ORN was estimated. Fifty-one patients developed advanced ORN (relative frequency 6.6 %, cumulative incidence 12.4 %). The highest risk was found in patients who had undergone primary bone surgery during tumor resection and in patients with tumors located in the oral cavity. Sex, dentition (dentulous vs. edentulous), and chemotherapy had no clinically relevant influence.

We found that common risk factors found to be diabetes in 30, alcoholism in 15, smoking in 35, oropharyngeal cancer in 24, oral cancer in 12, hypopharyngeal cancer in 4 and nasopharyngeal cancer in 2 cases. Kutoba et al[12] retrospectively reviewed the medical records of 616 patients with HNSCC treated with curative-intent or postoperative radiation therapy (RT) during 2008–2018. Patient-related (age, sex, history of smoking or alcohol use, diabetes mellitus, performance status, pre-RT dental evaluation, pre- or post-RT tooth extraction), tumor-related (primary tumor site, T-stage, nodal status), and treatment-related (pre-RT surgery, pre-RT mandible surgery, induction or concurrent chemotherapy, RT technique) variables and DVH parameters (relative volumes of the jaw exposed to doses of 10 Gy–70 Gy [V10–70]) were investigated and compared between patients with and without ORNJ. Forty-six patients (7.5%) developed ORNJ. The median follow-up duration was 40 (range 3–145) months. The median time to ORNJ development was 27 (range 2–127) months. DVH analysis revealed that V30–V70 values were significantly higher in patients with than in those without ORNJ. In univariate analyses, primary tumor site, pre- RT mandible surgery, post-RT tooth extraction, and V60 > 14% were identified as important factors. In multivariate analyses, V60 > 14% ($p = 0.0065$) and primary tumor site ($p = 0.0059$) remained significant. The 3-year cumulative ORNJ incidence rates were 2.5% and 8.6% in patients with V60 ≤ 14% and > 14%, respectively ($p < 0.0001$), and 9.3% and 1.4% in patients with oropharyngeal or oral cancer and other cancers, respectively ($p < 0.0001$).

CONCLUSION

Authors found that common risk factors found to be diabetes, alcoholism, smoking, oropharyngeal cancer, oral cancer, hypopharyngeal cancer and nasopharyngeal cancer.

REFERENCES

1. He Y, Liu Z, Tian Z, Dai T, Qiu W, Zhang Z. Retrospective analysis of osteoradionecrosis of the mandible: proposing a novel clinical classification and staging system. Int J Oral Maxillofac Surg. 2015;44:1547–57.
2. Reuther T, Schuster T, Mende U, Kubler 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.
3. 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.
4. Goldwaser BR, Chuang SK, Kaban LB, August M. Risk factor assessment for the development of osteoradionecrosis. J Oral Maxillofac Surg. 2007;65:2311–6.
5. Hoff AO, Toth B, Hu M, Hortobagyi GN, Gagel RF. Epidemiology and risk factors for osteonecrosis of the jaw in cancer patients. Ann N Y Acad Sci. 2011;1218:47–54.
6. Chen JA, Wang CC, Wong YK, Wang CP, Jiang RS, Lin JC, et al. Osteoradionecrosis of mandible bone in patients with oral cancer—associated factors and treatment outcomes. Head Neck. 2016;38:762–8.
7. Monnier Y, Broome M, Betz M, Bouferrache K, Ozsahin M, Jaques B. Mandibular osteoradionecrosis in squamous cell carcinoma of the oral cavity and oropharynx: incidence and risk factors. Otolaryngol Head Neck Surg. 2011;144:726–32.

8. Sathasivam HP, Davies GR, Boyd NM. Predictive factors for osteoradionecrosis of the jaws: a retrospective study. Head Neck. 2018;40:46–54.
9. Moon DH, Moon SH, Wang K, Weissler MC, Hackman TG, Zanation AM, et al. Incidence of, and risk factors for, mandibular osteoradionecrosis in patients with oral cavity and oropharynx cancers. Oral Oncol. 2017;72:98–103.
10. Owosho AA, Tsai CJ, Lee RS, Freymiller H, Kadempour A, Varthis S, et al. The prevalence and risk factors associated with osteoradionecrosis of the jaw in oral and oropharyngeal cancer patients treated with intensity modulated radiation therapy (IMRT): the Memorial Sloan Kettering Cancer Center experience. Oral Oncol. 2017;64:44–51.
11. Kuhnt T, Stang A, Wienke A, Vordermark D, Schweyen R, Hey J. Potential risk factors for jaw osteoradionecrosis after radiotherapy for head and neck cancer. Radiation Oncology. 2016 Dec;11(1):1-7.
12. Kubota H, Miyawaki D, Mukumoto N, Ishihara T, Matsumura M, Hasegawa T, Akashi M, Kiyota N, Shinomiya H, Teshima M, Nibu KI. Risk factors for osteoradionecrosis of the jaw in patients with head and neck squamous cell carcinoma. Radiation Oncology. 2021 Dec;16(1):1-1.