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Review

Pre-Radiation dental considerations and management for head and neck cancer patients

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ABSTRACT

Treatment of head and neck cancer (HNC) is accompanied by a high rate of morbidity, and complications can have a lifelong, profound impact on both patients and caregivers. Radiation-related injury to the hard and soft tissue of the head and neck can significantly decrease patients' quality of life. The purpose of this study is to provide patent-specific guidelines for managing the oral health and related side effects of HNC patients treated with radiation therapy.

Based on reviewed articles retrieved on the PubMed database, guidelines for management of the oral health of this patient population were organized into three separate categories: cancer, patient, and dentition. The location, type, and staging of the cancer, along with the radiation used to treat the cancer significantly impact dental treatment. Several unique patient characteristics such as motivation, presence of support system, socioeconomic status, nutrition, and race have all been found to affect outcomes. Dental disease and available supportive dental management was found to significantly impact treatment and quality of life in this patient population.

By comprehensively assessing unique cancer, patient, and dental-related factors, this review provides individualized evidence-based guidelines on the proper management of this complex and vulnerable patient population.

Introduction

In 2016, there were over 48,000 new cases of head and neck cancer (HNC) resulting in over 9,500 deaths in the United States alone [1]. Approximately 90% of HNC are squamous cell carcinomas [2]. It is widely known that major risk factors such as smoking, alcohol, and use of smokeless tobacco products are associated with head and neck squamous cell carcinoma (HNSCC) [3,4]. HNSCC has been known to have a high incidence of lymph node metastasis, with over two-thirds of patients presenting with regional lymph node involvement, and 10% presenting with distant metastases [5,6]. Strong emphasis must be placed on early detection of these cancers, as the 5-year survival rate drops from 83% to 37% when the diagnosis is made at an advanced stage rather than at an early, localized stage [6].

Over 80% of HNC patients endure acute oral complications as a result of the effects of radiation [7,8]. Radiation-related injuries to the hard and soft tissues of the head and neck significantly decrease patients' quality of life. Treatment–related complications include xerostomia, oral mucositis, trismus, dental caries, periodontal disease, infection, odynophagia and osteoradionecrosis (ORN). These side effects

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can have dramatic implications on the ability to perform everyday functions such as talking, chewing, tasting, and swallowing, resulting in decreased caloric intake and difficulty in maintaining weight [8].

Few protocols have been developed for the dental management of head and neck cancer patients. The purpose of this article is to provide a novel approach to patient-specific, rather than standardized guidelines for dentally managing HNC patients prior to undergoing radiation therapy. In order to individualize the guidelines for each case, three separate factors must be considered: the cancer, the patient, and the dentition.

Methodology

A systematic literature search was conducted via PubMed online database for articles published between 1975 and 2017. The goals of this search were to identify articles that can be used to provide evidence to develop pre-radiation dental guidelines in HNC patients treated with radiation therapy (RT) alone or combined treatment modalities.

Results

Articles were reviewed as a result of the literature search. The cancer types evaluated included the following: lip cancer, oral cavity cancer, nasopharyngeal cancer, oropharyngeal cancer, hypopharyngeal cancer, laryngeal cancer, and salivary gland cancer. Relevant studies regarding patient- and tooth-related factors and their relation to radiation therapy of the head and neck, survival, or comorbidities were also evaluated. The findings of the literature review found to affect patient outcomes were divided into three major categories (cancer factors, patient factors, and dental factors) and evidence-based guidelines were developed and summarized below.

Cancer factors

Staging

Staging of HNC pertains to the analysis of tumor size (T), lymph node involvement (N) and presence of metastases (M). A specific TNM classification system exists for each HNC dependent on location. These three characteristics describing the cancer are collectively analyzed to provide a specific cancer stage [5,6]. Cancer staging is considered the most crucial aspect in determining disease prognosis as well as treatment options. Clear associations have been found between advanced stage cancer and poorer survival, independent of race, ethnicity, or financial status [6,9,10].

Staging per specific location has important implications in assembling an effective treatment plan that optimizes survival and minimizes complication rates. The National Comprehensive Cancer Network (NCCN) has assembled specific recommendations and algorithms regarding surgical treatment for HNC based on cancer site and stage. The presence of positive margins or new nodal involvement requires re-evaluation of cancer stage and alteration in treatment regimens [11]. All of this information is crucial to the dental provider in tailoring their individualized oral health treatment plan.

HPV p16/18 status

HPV (particularly the HPV-16/18 genotype) has emerged as a major risk factor in the development of oropharyngeal cancers, with some studies attributing over 60% of US cases to be HPV-associated [12,13]. HPV-positive HNC incidence has been on the rise and has been determined to be associated with a younger, white, male population with increased number of sexual partners [2]. Several studies have shown that HPV-positive HNC tends to have a more favorable prognosis than HPV-negative HNC. While the average 5-year survival rate for HNC has been reported to be 63%, studies have reported 5-year survival rates in HPV-positive HNC patients to be as high as 89% [14,15]. If there is clinical suspicion when evaluating or excising a lesion in a patient, then HPV staining is crucial. Careful communication must be made with the pathologist to ensure that appropriate HPV staining is done when sending the tissue for histology. Common stains include HPV 6/11, 16/18, and 31/33.

Lip cancer

Initial treatment for early stage lip cancer (T1-2 primary tumors without nodal involvement) most commonly involves primary surgical resection. Stage I-II lip cancers can most often be treated surgically without need for adjuvant RT [16,17]. Primary radiotherapy with either brachytherapy or electron beam therapy is an alternative primary treatment approach for patients who refuse surgery or in those patients in whom functional or cosmetic outcomes after surgery are expected to be poor [11]. More advanced stage lip carcinomas (Stage III-IV) are generally managed with primary surgical resection and adjuvant RT ± chemotherapy.[11] In such cases, radiation doses to the maxillary or mandibular teeth can be substantial and dental evaluation is critical.

Oral cavity cancer

The group of oral cavity cancers includes the anterior tongue, buccal mucosa, floor of mouth, alveolar ridge, retromolar trigone, and hard palate. Patients with early stage oral cavity cancers are encouraged to have primary resection (with or without ipsilateral, or bilateral neck dissection). Some reports have demonstrated improved survival with elective neck dissection, however it remains debatable amongst HNC professionals [11,18–20]. Patients with advanced stage oral cavity cancer will also have primary resection, and then dose-dependent chemotherapy/RT based on the extent of nodal disease, perineural invasion, among other adverse pathologic features [11]. There are a substantial number of patients who are either medically or technically inoperable in this disease, or patients who may refuse surgical care due to morbidity. Those patients typically receive definitive chemoradiation and the gross disease is often treated to 70 Gy. These are the highest risk cases for oral/dental complications.

Cases more amenable to surgical resection may have adjuvant radiation levels closer to 44–66 Gy [11]. In cases with planned RT, the level of dental intervention should be based upon the patient's planned radiation dosage and affected sites. The affected sites can be coordinated with the radiation oncologist by reviewing the radiation simulation mapping.

Nasopharyngeal cancer

Nasopharyngeal cancers have the highest likelihood of metastasis among the HNCs, and most cases (83%) are diagnosed at a regional or distant stage [11]. Early stage nasopharyngeal cancer has similar survival rates as other HNCs detected at an early stage. However, a 5-year survival rate of 37% is observed for stage IV nasopharyngeal cancer [1]. They also pose a high risk for local recurrences, and locally advanced disease following definitive therapy. Early stage (T1, N0, M0) tumors can be treated with definitive RT alone of 66–70 Gy [11]. More advanced staging have treatment plans that vary with different regimens of RT and chemotherapy. The maxilla will be at higher exposure levels than the mandible, which from a dental standpoint is more favorable given that the maxilla has a decreased comparable incidence of ORN. Depending on the severity, palliative dental care may be more prudent.

Oropharyngeal cancer

Cancer of the oropharynx includes the base of tongue, tonsils, soft palate, and posterior pharyngeal wall. This area is also rich in

lymphatic drainage and the nodal involvement at initial presentation of patients in this group can range from 15 to 75% [11]. As previously mentioned, cancers of the oropharynx must have HPV testing. Currently, HPV testing is utilized for prognostic indications only. HPV-positive oropharyngeal cancers have been shown to have better response to treatment and improved survival [21]. Early stage (T1-2, N0-1) oropharyngeal cancers may be treated with primary surgery (± neck dissection) or definitive RT alone [22]. There are significant variations of cancer management and prognoses that exist within the oropharyngeal cancer subgroup with various combinations of surgery, chemotherapy and radiation therapy being utilized. Patients treated with RT alone typically receive near 70 Gy [11]. Dental management of patients with oropharyngeal cancers requires close communication with the HNC team as RT use and dose vary widely.

Hypopharyngeal and laryngeal cancer

The hypopharynx region extends from the superior border of the hyoid bone to the lower border of the cricoid cartilage, between the oropharynx to the cervical esophagus. Early stage cancers may be amenable to larynx preserving surgery; with more advanced staged cancers (T1,N+; T2-T4 any N) likely to have pharyngectomy with laryngectomy. RT levels in these patients are 66–70 Gy, with possible range of 44–50 Gy for low risk sites [11].

Salivary gland cancer

Salivary gland tumors can be found within major (parotid, submandibular, sublingual) or minor glands around the oral cavity. Clinically benign, or early stage carcinoma can be treated with surgical resection alone, and with any adverse features, the addition of RT may be necessary [11,23,24]. All N1 + salivary gland tumors require lymph node dissection with the addition of select N0 parotid gland tumors. When definitive or post-operative RT is needed in these cancers, the range varies from 44 to 70 Gy [11].

Site specific survival rates

Survival rates and treatments vary critically depending on both the location and staging of the cancer. As of 2012, the overall 5-year survival rate for all sites of oral cavity and pharyngeal cancer was approximately 64%. Cancer of the hypopharynx has the lowest 5-year survival rate (32.2%), and cancer of the lip has the highest 5-year survival rate (90.2%) [25]. The poor prognosis of cancer of the hypopharynx has been linked to its high incidence of perineural and lymph invasion [26]. Additional site specific 5-year survival rates are as follows: salivary gland (72.7%), oropharynx/tonsil (66.8%), tongue (63.4%), gingiva (59.6%), and of the floor of the mouth (50.5) [25]. In certain cases with a grave prognosis, palliative dental therapy may be warranted. As the prognosis varies substantially per location and staging, the intensity of treatment follows in a parallel fashion, which would allow the oral health care provider to determine the appropriate extent of their dental treatment and prophylaxis.

Radiation therapy

Head and neck radiation therapy (HNRT) has been associated with a number of post-therapy comorbidities. Over 90% of these patients suffer damage to salivary glands resulting in xerostomia, and more than 50% of patients experience oral mucositis and post-therapy dental decay [27]. Additional complications that may accompany HNRT include increased risk of fungal infection, trismus, dysguesia and ORN [27].

The risk of complications such as ORN can be minimized with adequate knowledge of effective management of HNC patients. The risk of ORN after radiation therapy ranges from 5 to 15%, and is higher in patients who undergo an oral surgery procedure post-RT [28]. Protocols for pre-HNRT extraction of teeth have been developed to reduce the need for post-RT oral surgery [29–31]. These protocols typically take into account pre-existing dental disease including dental caries, pulpal and periapical disease, root resorption, periodontal disease with associated probing depths, furcation involvement, tooth mobility, and tooth impactions [29].

Over the past 20 years, intensity-modulation radiation therapy (IMRT) has become the most commonly used radiation technique for HNRT. IMRT allows for more selective targeting of the primary site and lymph node regions at risk while reducing radiation dose to normal tissues in the head and neck. IMRT has been associated with decreased risk for ORN and damage to other healthy tissue such as the parotid glands and pharyngeal constrictor muscles [32,33]. Several studies have shown an increased risk of ORN with mandibular radiation doses exceeding 50 Gy, and higher incidence of subsequent dental caries with parotid gland radiation doses exceeding 26 Gy. Both maxillary and mandibular teeth receiving radiation doses greater than 50 Gy are at increased risk of ORN [32,34]. IMRT can specifically distribute radiation dosage gradients across a target volume to adjust for high risk-ORN areas such as the posterior mandible [32,35,36]. Sparing of the posterior mandible was not possible with the use of three dimensional conformal radiation therapy (3DCRT). 3DCRT utilizes only the rough, “block” shape of the tumor itself with significantly less precision than IMRT. Knowing whether the radiation oncologist is utilizing 3DRT versus IMRT directly affects dental treatment planning. Ben-David et al. demonstrated in their study of 176 patients who underwent HNRT that strict dental evaluation and prophylactic treatment combined with IMRT can significantly minimize the incidence of ORN [29]. Several studies have also shown the use of parotid-sparing IMRT in preserving salivary flow rates and increasing oral health-related quality of life in HNC patients [37,38]. A dose of > 26 Gy to either parotid gland is predictive of future dental caries. A maximum and mean dose of radiation therapy to the mandible that was predictive of post-RT dental extractions was 70 Gy and 40 Gy, respectively [35]. Anticipation of future dental events, such as caries or extractions will depend on planned parotid or mandibular doses and affect dental planning accordingly.

For both 3DRT and IMRT, molars receive the highest mean amount of radiation doses with maxillary teeth receiving lower doses than mandibular teeth. Patients receiving IMRT for oral cavity or nasopharyngeal cancer receive significantly less radiation doses than 3DRT for all teeth [33]. In the case of oral cavity cancers, 3DRT doses reach a maximum of 66.8 Gy versus only 46.3 Gy for IMRT [33]. Patients with base of tongue, nasopharynx, and tonsil cancers will be subjected to the highest radiation doses in all of their teeth, with molars receiving the most irrespective of IMRT or 3DRT. It is important to consider laterality of the primary tumor, as contralateral teeth from the site of primary tumor have lower radiation doses.

Median dosage of radiation to the mandible and parotid

The dosing of RT used for each location of HNC, and the subsequent dose level received by the mandible and parotid gland varies greatly. Memorial Sloan Kettering Cancer Center reported radiation levels to the mandible per location are as follows: median max dose values 6,879 cGy for nasopharynx, 6,828 cGy for oral cavity, 6,480 cGy for larynx/hypopharynx, 6,537 cGy for sinus, and 7,199 cGy for oropharynx [35]. It is important to note that even though laryngeal and hypopharyngeal cancers may not have the focus of the radiation field on the mandible, when level II lymph nodes are irradiated, the mandible is in close proximity to the radiation field. The corresponding values for the maximum parotid dose were 2624 cGy, 2570 cGy, 2575 cGy, 2134 cGy, and 2873 cGy, respectively [35]. Complex treatment sequences are tailored to each individual patient and cancer location/stage to increase the probability of 100% tumor cell eradication while

attempting to reduce radiation doses to the mandible and parotid gland.

It is critical when working with the radiation oncologist, that the RT prescription is described so that oral health care providers can treat appropriately to the levels of expected RT in each separate site, irrespective of whether IMRT, or conventional RT is planned. The treating doctor should not complete any dental procedure without a full understanding of the planned radiation status of their patient.

Patient factors

Motivation

Compliance with an oral prophylaxis protocol is a crucial factor in the reduction of complications associated with HNRT. Despite significant decreases in salivary flow and salivary pH post-RT, patients with high compliance to prophylactic care develop less caries than those with low compliance [39]. Nonetheless, the importance of dental care compliance remains a major issue in HNC patients. Over 50% of irradiated HNC patients are lost to follow-up at a mean post-irradiation time of 7.5 months [40].

The level of motivation for obtaining oral care in this patient population should have a significant impact upon dental treatment planning. Given the low compliance rates, ample and persistent dental supervision is paramount in reducing oral side effects and low quality of life measures resulting from HNRT. Non-compliant patients may require an extraction-based pre-radiation dental treatment plan.

Socioeconomic status

Socioeconomic status has a considerable impact upon incidence, treatment outcomes, and survival rates of cancer patients, particularly in cancers with good prognoses [41]. A clear inverse relationship exists between the incidence of HNSCC and income [42,43] When compared to patients with private insurance, Medicaid and uninsured patients are significantly more likely to present with a more advanced HNSCC [44]. Lower socioeconomic status, poverty and lack of education are associated with worse overall survival rates [10,43,45,46]. Lack of insurance is associated with a more advanced stage at diagnosis, and results in poorer survival [47,48].

Lack of dental insurance and financial means places significant limitations on a HNC patient's ability to obtain pre-radiation dental treatment and to maintain a strict dental follow-up schedule necessary post-RT. The lack of funds to support the critical oral health care component of the treatment plan can lead to increased post-treatment complications, morbidity and decreased quality of life [8]. Pre-radiation therapy extraction-based dental treatment plan may be warranted for those patients with limited financial means to seek the required post-radiation dental care.

Psychiatric health and support system

The morbidity associated with the surgically-induced disfigurement, physical symptoms, and treatment complications associated with HNC can lead to negative mental and physical health outcomes. The prevalence of depression in HNC patients has been reported to be as high as 20%, with a higher likelihood of suicide attempt [49,50]. Other studies have found that 82% of HNC patients report high levels of distress without psychiatric intervention initiated [51]. A collaborative effort involving specific supportive care amongst the multidisciplinary healthcare team has proven to increase survival rates in HNC patients [52]. Personal support systems at home also have the potential to affect prognoses. Single, widowed, and divorced patients demonstrate significantly poorer disease course than those who are married [53]. Patients who are married are significantly more likely to receive definitive treatment and less likely to present with metastatic disease and ultimately die from HNC [54]. From an oral health care standpoint, patients with mental health stability and a strong support system are more likely to be compliant with strict dental follow-up and more likely to maintain the motivation necessary to avoid post-radiation complications.

Nutrition

A patient's dietary habits and nutritional quality are an important factor in HNC treatment outcomes [8,55,56]. A low pre-treatment body mass index ($< 22.8\ kg/m^2$) and a low serum albumin ($< 4.15\ g/dL$) are poor prognostic indicators [56]. Pre-treatment loss of appetite, difficulty chewing, and decreased dietary intake substantially impact symptom burden. A higher symptom burden is associated with weight loss and lower survival rates [57]. Difficulty eating is a complication in over 50% of 5-year HNC survivors [58]. Poor eating habits and a cariogenic diet can contribute to the progression of dental disease, necessitating surgical treatment and increasing risk of ORN. Thus, diet management is a crucial factor in the overall assessment of HNC patients pre-operatively, and effective nutrition counseling is essential in improving symptom burden and survival.

Race

There are racial disparities in stage at diagnosis, access to care, and overall survival rates for patients with HNC. Regardless of specific location of the cancer, black patients are more likely to present with a more advanced stage of disease [59]. Thus, black patients often have a very different course of treatment than white patients, with a higher rate of inoperable disease requiring a more robust regimen involving chemoradiation therapy [47]. Black patients are also less likely than white patients to have insurance to aid in treatment costs. There is a significant difference in the overall survival rate for white and black HNSCC patients, with 5-year survival rates of 67% and 45%, respectively [6].

Tooth factors

Perhaps the most critical factor when evaluating patients for pre-radiation dental treatment is the current health status of the teeth. Likely due to the complexity and individual subjectivity in determining tooth prognoses, few reports have been published regarding objective guidelines for proper pre-radiation dental treatment [30,60]. Some practitioners have adopted a more aggressive pre-radiation approach in performing dental extractions for teeth with questionable prognoses. The primary goal of this approach is to avoid the need for post-radiation dental extractions when the risk of ORN is relatively higher than pre-radiation rates. Studies have demonstrated that clinicians are more concerned with preventing this complication rather than maintaining post-radiation dental functionality [61]. This is likely in response to established higher rates of ORN associated with tooth extraction performed post-HNRT [62,63].

The timing between tooth extraction and initiation of radiotherapy is very important, with most guidelines suggesting a minimum of two weeks [11,35,63,64].

The goal of a dental treatment plan in HNC patients is to treat active disease while minimizing risks and complications associated with HNRT. It is necessary to comprehensively evaluate pre-existing dental disease including dental caries, pulpal and periapical disease, root resorption, periodontal disease with associated probing depths, furcation involvement, tooth mobility, and tooth impactions [29].

Tooth prognosis

Defining an absolute prognosis for individual teeth is a difficult task. In addition to the multiple dental-related factors that influence tooth prognosis, the variability in patient motivation, quality of treatment

rendered, and material longevity also complicate the assignment of prognosis [65–67]. Thus far, studies reporting an accurate determination of absolute tooth prognosis based on both restorative or periodontal factors are lacking [65]. Several dental characteristics often evaluated in terms of their relationship to tooth prognosis are briefly described below.

Periodontal disease

Many studies have been done to predict prognoses of teeth with active periodontal disease. There are significant differences in the range of tooth loss independent of disease severity and treatment rendered [67,68]. A clear association exists between certain periodontal disease parameters (i.e. percent bone loss, tooth mobility, furcation involvement, lack of periodontal maintenance) and increased risk of tooth loss [67,69–71]. McGuire et al's prediction of tooth prognoses based on these clinical parameters were fairly accurate for single-rooted teeth in initially good condition, but accuracy decreased considerably for multi-rooted teeth with less than good prognosis [67,72]. HNC patients with periodontitis are at an increased risk (19%) for ORN, and those patients with periodontitis who did not have aggressive therapy (poor or hopeless teeth extracted) had an even greater incidence of ORN (33%) [73].

Mobility/crown-to-root ratio

Tooth mobility has been shown to negatively affect prognoses. Teeth with increased mobility continued to demonstrate increased attachment loss despite ongoing maintenance [71,74]. Teeth with greater mobility and unsatisfactory crown-to-root ratios were more likely to be lost [67].

Furcation involvement

Teeth with periodontal disease involving the furcation have diminished prognosis compared to teeth without furcation involvement [66,71]. Continued attachment loss has been noted in teeth with furcation involvement regardless of treatment intervention [75]. Other studies have demonstrated eventual loss of one-third to over one-half of teeth initially described as having furcation involvement [68,76].

Periapical pathology

Periapical pathology when identified on pre-assessment evaluation must be addressed [11,77].

Depending on the nature of the patient's immune system at time of screening, endodontic therapy or extraction is recommended. In HNC patients, pre-existing asymptomatic periapical pathosis can become problematic during oncologic therapy, or new pathology can develop warranting treatment [11,73].

Dental prognostic guidelines

While there is no accurate method of assigning an absolute prognosis to individual teeth, a comprehensive evaluation must be provided for each individual tooth prior to RT. To aid in treatment planning, a comprehensive rating system that accounts for the periodontal condition, restorability, endodontic status, and tooth position can be utilized [65].

A relative prognosis of individual teeth can be assigned using the Samet and Jotkowitz (S/J) classification system [65]. This classification system offers a means of evaluating individual teeth based on four main criteria: alveolar bone support, restorability, endodontic condition, and occlusal plane/tooth position. Based on this system, each tooth is placed into one of five classes: A, B, C, D, or X (Fig. 1). The tooth class assigned for a particular tooth is the most severe class assigned of the four main criteria. Patient-related factors can increase or decrease the prognosis for the dentition. The decision to not treat favorable teeth (Class A, B) and treat non-salvageable teeth (Class X) should be straightforward for the clinician. Class X teeth should be extracted and include teeth with < 30% periodontal support, loss of coronal structure deep into the root dentin and canals, vertical root fractures, severe malpositioning within the occlusal plane, and teeth refractory to multiple endodontic treatments. Additional teeth that can be unequivocally removed are exposed root tips, mobile, symptomatic teeth with furcation involvement, and symptomatic impacted or partially erupted teeth. The subjective nature and required individualized treatment plans are mostly for more questionable (Class C) and compromised (Class D) teeth. The prognoses of these teeth are more equivocal and have < 50% of periodontal support remaining, < 50% of coronal structure remaining that compromises future restorations and crown/root ratios, active endodontic issues, and tooth alignment challenges for the patient [65]. As previously stated, it is pertinent that the dental treatment plan (particularly for these Class C and D teeth) be made in the context of individual patient factors and cancer factors.

Additionally, considerations related to oral health must be taken into account when developing a comprehensive treatment plan. Samet et al. organized these considerations into three types of risk factors: biologic, environmental/behavioral, and financial. These include but are not limited to increased age, smoking, decreased salivary flow, high bacterial load, cariogenic diet, low fluoride exposure, certain systemic disease and even family history and genetics [65]. Many caries risk [78,79] and periodontal disease risk assessment [80,81] tools have been developed to aid providers in determining a patient's risk of disease development and appropriate management strategies.

Dental-related factors cannot be assessed without taking into account systemic and treatment-related factors. The overall cancer-specific survival rate is important in fabricating an effective dental treatment plan.

Supportive therapies and management

Fluoride therapy

Patients who undergo HNRT are at increased risk for developing dental caries. All carious lesions should be restored prior to radiation therapy to decrease risk of disease progression. In addition to inducing a shift toward cariogenic oral microflora, HNRT may result in decreased salivary flow [27,82]. All patients who have received HNRT should be placed on a strict, high-fluoride regimen to help prevent demineralization [82,83]. Given that damage to salivary glands results in permanent hyposalivation, fluoride therapy must be continued indefinitely to avoid the development of dental caries [60,84]. Multiple recommendations exist for a wide variety of regimens including daily 2.2% or 3% NaF rinse [30,83,85], application of 1% NaF gel every second day via custom trays [60,85,86], daily 0.4% stannous fluoride application [87], and twice daily 1.1% NaF toothpaste [30]. While all methods are effective, the fluoride gel with custom trays have shown to be the most reliable in its ability to prevent post-radiation dental caries [86,88]. The benefits of maintaining patients on strict fluoride protocols have been well described. Sulaiman et al. reported that on their fluoride protocol (1.1% NaF toothpaste or 2.2% NaF rinse), 84% of patients who received RT did not require extraction therapy [30].

Dry mouth

Dry mouth is the most common complication in patients who have received HNRT. Due to radiation-induced damage to salivary glands, over 90% of patients who undergo HNRT experience xerostomia [27]. Parotid-sparing IMRT techniques improve post-radiation salivary flow [37,38]. An attempt to restore salivary flow in these patients can be made with several pharmacotherapies. Muscarinic-cholinergic agonists stimulate salivary flow and relieve symptoms without major side effects [89,90]. If stimulation of the salivary glands fails, saliva-replacement

Table 2	An evaluation of pathology and the scale of severity
Class A	A tooth in this category is one that is considered to have a **good** prognosis. Such a tooth is assumed to have minimal risk of being lost in the foreseen future.
Periodontal health and alveolar support	80% to 100% bone support. Can be easily maintained.
Remaining tooth structure	80% to 100% remaining sound coronal tooth structure. Can be easily restored.
Endodontic condition	A tooth that can receive a straightforward primary endodontic treatment, or already has good endodontic therapy.
Occlusal plane and tooth position	A tooth that is in the correct occlusal plane and/or position, or one that is slightly deviated from ideal and may require minimal enameloplasty.
Class B	A tooth in this category does not belong to Class A but has a **fair** prognosis such that treatment outcome is considered predictable. Such a tooth poses a low risk of being lost in the foreseen future.
Periodontal health and alveolar support	50% to 80% bone support, which can be well maintained with rigorous periodontal and maintenance therapy. Vertical defects or furcations that can be periodontally treated to become easily cleansable or treated predictably with regenerative therapy.[62] Molars are at higher risk than single-rooted teeth.[8,63]
Remaining tooth structure	50% to 80% remaining sound coronal tooth structure. Involved restorative procedures result in no infringement of biologic width, adequate ferrule,[26,27,34] or good crown-root ratio and would minimally affect adjacent structures (if at all).
Endodontic condition	A failing endodontic treatment with obvious causes of failure and that can be predictably retreated, Or a tooth that requires a difficult primary endodontic treatment.
Occlusal plane and tooth position	A tooth that is out of the occlusal plane and can be adjusted so that it functions within the correct occlusal plane. Such a tooth may require additional treatment to seal exposed dentin.
Class C	A tooth in this category is one that has one or more problems and can be treated and maintained, but its prognosis remains **questionable**. Such a tooth has a medium risk of being lost.
Periodontal health and alveolar support	30% to 50% remaining bone support. No ongoing acute outbreaks, but maintaining cleansability is difficult. Periodontal therapy and a thorough maintenance program will enable the tooth to be maintained for an acceptable period of time.[64]
Remaining tooth structure	30% to 50% remaining sound coronal tooth structure. Or a tooth with so little tooth structure that achieving adequate ferrule would result in compromising the crown-root ratio to some extent, and/or may affect adjacent structures.
Endodontic condition	An acute/chronic failing endodontic treatment that presents difficulty to predictably retreat.
Occlusal plane and tooth position	A tooth that is out of the occlusal plane and requires multiple procedures to function within the occlusal plane.
Class D	This category is for a **compromised** tooth that has a high risk of being lost. This includes those teeth that have no active pathologic conditions requiring immediate extraction, but it may not be in the patient's best interest to invest in such a tooth. Since there is no obvious indication for extraction, external factors influencing the overall case and patient factors will play a major role in determining how to approach such a tooth.
Periodontal health and alveolar support	A tooth with < 30% bone support, and/or one that cannot be cleansed or maintained well and has evidence of active periodontal disease.
Remaining tooth structure	A tooth with < 30% sound tooth structure, or one in which the extent of the lost tooth structure does not enable a good ferrule to be achieved without totally compromising the support of the adjacent tooth structures or crown-root ratio.
Endodontic condition	A tooth with a failing endodontic treatment that cannot predictably be retreated.
Occlusal plane and tooth position	A tooth so severely out of the occlusal plane or severely tilted that after extensive treatment will exhibit reduced crown-root ratio, which will prevent it from serving as a long-term unit in the arch. Or a tooth whose position impacts the health of the adjacent structures.
Class X	A tooth in this category is **nonsalvageable** and is indicated for extraction. Such teeth cannot be restored or present pathologies that currently dentistry does not have a solution for. These include teeth that may pose risk to the patient's health.
Periodontal health and alveolar support	A tooth with < 30% bone support and cannot be cleansed or maintained without acute outbreaks of periodontal infection.
Remaining tooth structure	No remaining supragingival sound coronal tooth structure.[65,66] Loss of tooth structure deep into the root dentin/canals.[30,67]
Endodontic condition	A vertical root fracture,[3,68] or a tooth that has been retreated several times endodontically and/or surgically without resolution.
Occlusal plane and tooth position	A tooth so far super-erupted or tilted out of the occlusal plane that it cannot be restored into correct function, or would interfere with the restoration of that arch or the restoration of the opposing arch.

Fig. 1. Tooth prognosis assignment in relation to dental disease severity [65]. *From Samet et al. Quintessence Int 2009; 40(5): 377–87. Used with permission from Quintessence International Editorial Office.

Table 1
WHO Oral Mucositis Classification adapted from Maria et al. [96].

	Symptoms
Grade 0	No mucositis symptoms
Grade 1	Oral soreness, erythema
Grade 2	Oral erythema, ulcers, tolerates solid diet
Grade 3	Oral ulcers, tolerates liquid diet
Grade 4	Oral alimentation impossible

therapy can be initiated. Sialogogues such as salivary replacement rinses, carboxymethylcellulose, carmellose and mucin sprays, polyacrylic acid, and sugarless gum improve symptoms [91–93].

Oral mucositis

Oral mucositis (OM) is a major source of significant radiation and/or chemotherapy related pain and discomfort for HNC patients. OM can also potentially lead to functional deficits, nutritional deficiencies, interrupt or alter radiation therapy, increase medical costs, and negatively impact overall quality of life [94–97]. OM manifests as painful mucosal erythema with or without ulceration within the first two to three weeks of radiation therapy, predominantly affecting non-keratinized tissue [60,95]. OM can be classified by the World Health Organization (WHO) mucositis scale, which classifies signs and symptoms on a 0–4 scale (Table 1) [96,98].

A number of methods have been developed to help prevent mucositis-inducing damage to oral issue. Pre-existing oral bacterial colonization is associated with OM, and thus maintaining good oral hygiene remains the major preventive method [96,99]. Patients should follow an oral care protocol including soft brushing with fluoride toothpaste, maintenance of a soft, non-cariogenic diet, minimizing denture use, saline rinse, and avoidance of smoking [96,100].

In addition to improved radiation dosages due to IMRT techniques [29,101], oral devices attenuate radiation dosage of adjacent tissues [30,102,103]. The use of a 3 mm protective synthetic stent worn as a mouthguard during radiation exposure effectively decrease radiation overdose to surrounding tissue [102,103]. Radiation mouthguards reduce symptoms, weight loss and inpatient hospitalizations related to nutritional support [103].

Human keratinocyte growth factor agents (i.e. palifermin) are FDA-approved for OM prevention in patients treated with chemotherapy or RT for hematologic malignancies. Photobiomodulation (low-level laser therapy) prior to RT reduces OM specifically in HNC patients [96,104]. Cryotherapy and amifostine have been used to prevent radiation-induced OM, but there is limited and conflicting evidence [96,100].

Table 2
Patient, cancer, and dental related factors affecting treatment outcomes in irradiated HNC patients.

Patient	Cancer	Dental
Motivation	Location	Dental caries/remaining tooth structure
Socioeconomic status	Staging	Periodontal disease
Race	Cancer type	Parafunctional habit
Support system	Radiation type	Prosthodontic considerations
Nutrition	Radiation dosage	Oral hygiene risk factors
Smoking		Biologic risk factors

The management of radiation induced OM is challenging. There are currently no FDA-approved treatments for symptomatic radiation induced OM [96,97]. Topical local anesthetics (i.e. topical lidocaine, dyclonine hydrochloride, benzocaine lozenges, “magic mouthwash”) have shown to be effective in several studies, however there is a paucity of well-designed clinical trials to develop formal guidelines [105–108]. Currently, the Multinational Association of Supportive Care in Cancer (MASCC)/International Society of Oral Oncology (ISOO) recommends use of 2% morphine mouthwash in alleviating mucositis-related pain [100,109,110]. Other commonly utilized agents such as Gelclair [111], chlorhexidine [112,113], corticosteroid rinses [100,114], sucralfate [115], pentoxyfylline, granulocyte-macrophage-colony-stimulating-factor, and anticholinergic agents have limited evidence supporting use [100]. Benzydamine hydrochloride has sufficient evidence of benefit with radiation dosages < 50 Gy, but there is insufficient and conflicting evidence for its use in patients with > 50 Gy [112,113,116].

Management of dentures

Especially in the setting of xerostomia, dentures are considered a source of soft tissue trauma [117]. Patients should be instructed to refrain from wearing ill-fitting dentures to prevent worsening mucositis or development of ORN [118,119]. It is recommended that patients delay insertion of a well-fitting denture or the initiation of the denture fabrication process for 1–3 months post-radiation therapy [117,119].

Box 1
Approach to Initial Pre-Assessment of the HNC Patient.

1. **Cancer Diagnosis**
2. **Dental History**
   a. Prior dental work completed or *not* completed (i.e., compliance, motivation)
   b. Assess currrent motivation and oral hygiene
3. **Social History**
   a. Support system - Marital status? Life partner? Family?
   b. Living environment - alone?
   c. Finances
4. **Comprehensive Clinical and Radiographic Examination**
   a. Comprehensive Oral Evaluation
   b. Radiographic Evaluation
5. **Develop Prognosis of Dentition**
6. **Communicate Directly with Radiation Oncologist**
   a. Type of RT to be used
   b. Median and maximum planned dose to maxilla, mandible, parotids
   c. Start date
7. **Develop Comprehensive Treatment Plan**
8. **Patient Education**
   a. Importance of oral health complications associated with HNC RT, CRT

Box 2
Summary of High-Risk Factors with Poor Oral Heath Prognosis.

CANCER FACTORS.
Advanced Stage Cancer Requiring RT[^].
Nasopharyngeal and Oropharyngeal Tumors.
Tongue Cancer.
RADIATION FACTORS.
> 26 Gy to Parotid Glands[$].
> 50 Gy to Mandible[*].
> 40 Gy (mean); > 70 Gy (max.) to Mandible[++].
3DRT or Conventional RT.
PATIENT FACTORS.
Poor History of Dental Compliance.
Oral Hygiene Status.
Low Socioeconomic Status (Without Insurance).
Without Home Support-Network.
TOOTH FACTORS.
Endodontic Disease.
Periodontal Disease.
Periapical Pathosis.
Prosthetic Factors.
[^]Important to take into account for advanced stage disease the prognosis and expected 5 year survival of the patient versus the patient's future risk for oral complications from conservative treatment.
[$]Denotes increased risk for future dental caries.
[*]Denotes increased risk for osteoradionecrosis to the jaws.
[++]Denotes increased risk for future dental extractions.

Extension of the waiting period to 6 months is advisable for patients who underwent dental extractions prior to radiation therapy [119].

Follow-Up

The importance of continued and frequent professional dental follow-up care must be stressed to every HNC patient. Long term and frequent follow up provides the best means for the dental provider to consistently monitor the status of the patients' oral health, provide timely interventions, and prevent surgical therapy. Given the risk of caries development just months post-radiation, standard 3-month follow-up visits are recommended for these patients [92,120]. Patients should also receive thorough nutritional counseling in order to emphasize the importance of a non-cariogenic diet as well as the importance of maintaining adequate nutrition and body weight [119].

Conclusion

Management of HNC is often accompanied by a high rate of morbidity. Treatment complications can have a lifelong impact on quality of life. Dentists have the potential to play a major role in preventing and minimizing these complications (Box 1). The cancer, the patient, and the dentition should be analyzed (Table 2, Box 2) thoroughly to assemble an effective pre-radiation dental treatment plan.

Conflict of interest

The authors declare no financial or personal conflicts of interest.

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