Considerations for Dental Management of Post-Radiation Head and Neck Cancer Patients: A Literature-Based Critical Review

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ABSTRACT

Treatment-related side effects are common amongst head and neck cancer (HNC) survivors post radiation therapy (RT). These side effects have been linked to decreased quality of life scores and necessitate frequent follow-up with complex management, particularly regarding patients' oral health. The location of the HNC, associated type, and portal of RT have significant implications on post treatment dental care. The purpose of this review is to offer dental providers guidance for treating patients who have underwent RT for HNC. The PubMed online database was used to source articles for forming the review recommendations. These recommendations were organized into three separate categories: cancer, patient, and dental factors. Dental providers must consider a myriad of factors related to the cancer, patient, and dentition when formulating a comprehensive care plan for the treatment of the post-RT HNC survivor.

INTRODUCTION

Head and neck cancer (HNC) afflict over 50,000 new Americans each year.[1] Despite advancements in the treatment of HNC, acute and long term complications from disease and/or treatment frequently result in a decreased quality of life for survivors.[2,3] Radiation therapy, which is commonly used to treat HNC, has a myriad of side effects including trismus, dysphagia, odynophagia, radiation caries, xerostomia, speech difficulties, and osteoradionecrosis (ORN).

Dentists are significant stakeholders in this realm because oral health has a major impact on quality of life after treatment of HNC.[4] Since many large cancer institutions do not offer long term dental care, most patients return to their local general dentists.[5,6] However, some evidence suggests that many dentists may not be prepared to handle HNC patients; a 2012 survey of Michigan dentists found that 55% of respondents did not feel "adequately trained in dental school" to treat HNC cancer patients who have received radiation therapy.[7] If patients cannot find a dental home, their oral health can quickly deteriorate. Treatable dental diseases like caries and periodontitis can fester into destructive conditions, such as orofacial abscesses, and elevate the risk for osteonecrosis of the jaw. These adverse outcomes undo the quality of life gains achieved by successful cancer treatment and improvements in orofacial and maxillofacial prostheses. The challenge of providing comprehensive dental care to HNC survivors is a valuable opportunity for dentists to meaningfully improve the quality of life of some of our most vulnerable patients.

Unlike the recent efforts to bolster dentists' role in oral cancer screenings, there have been a paucity of discourse surrounding ensuring access to comprehensive dental care after patients defeat cancer.[8] While there have been some recent publications intended to guide dentists on the best clinical practices to manage oral and oropharyngeal cancer patients, these alone may not be sufficient to meet the demand.[4,9,10] In short, post-radiation guidelines for dental management of HNC patients is limited. As such, this article aims to synthesize the existing scientific evidence to provide a thorough discussion of best practices and considerations for dentists managing post-radiation treatment HNC patients. This article synthesized the latest scientific evidence up to July 2019 to develop evidence-based recommendations for dental management of post-radiation HNC patients.

CANCER FACTORS

Radiation Therapy Modalities

HNC is frequently treated with RT alone, or in conjunction with surgery and/or chemotherapy. Understanding the RT modalities utilized allows the practitioner to better understand sequela and anticipate care needs.[11]

External Beam RT (EBRT) delivers ionizing radiation to the target region while attempting to minimize dose to adjacent normal tissues.[12] Adverse effects of EBRT may include: decreased salivary flow, dysphagia, trismus, oral mucositis, and ORN.[13-15] Intensity modulated radiotherapy (IMRT) is currently the most common RT technique used in the management of HNC through delivery of radiation dose in a highly conformal manner to a patient's cancer while minimizing normal tissue exposure.[12,15] Utilization of IMRT significantly reduces radiation exposure to the uninvolved major salivary glands, mandible, larynx, oral cavity, pharyngeal constrictor muscles, and the spinal cord. The use of modern RT techniques has significantly improved rates of xerostomia, ORN, long-term dysphagia and feeding tube dependence.[13,16,17] Proton beam radiation is another RT technique with the potential to reduce radiation dose to normal tissue by harnessing the distinct physical properties of a proton beam during RT delivery. Stereotactic radiation therapy employs precise image guidance, patient immobilization, and conformal RT dosimetry to deliver higher ablative doses of RT in five or fewer treatments. Finally, Brachytherapy (BT) uses a direct radioactive source inserted within or near the tumor to deliver highly focal radiation.[12]

Factors influencing the adverse effects of RT include radiation dose, volume of target tissue and inclusion of other concurrent therapies.[14] A recent systematic review found that dose-response models for predicting hypothyroidism, oral mucositis, and xerstomia are fairly consistent, while those for dysphagia and esophagitis are more variable.[18] Documentation of the type of radiation therapy, dose, and portal must be gathered to formulate a comprehensive dental treatment plan for the post RT patient. It is critical to evaluate and document prior radiation dose to the mandible and maxilla within the regions of concern.

Cancer Specific Treatment Plans

Treatment recommendations for HNC may vary depending on tumor location, histology, and other patient related factors. For instance, the American Society for Radiation Oncology (ASTRO) recently released evidence-based clinical guidelines on radiation therapy for oropharyngeal squamous cell carcinoma.[19,20] Radiotherapy may be used as either adjuvant therapy or definitive treatment with or without concurrent chemotherapy. Radiation doses for locally advanced squamous cell carcinomas may range from 50-66Gy as adjuvant therapy or 66-70 Gy for definitive treatment of gross disease.[21] Selected regions of the head and neck may receive differential doses depending on the extent of disease and estimated risk of recurrence. The American Cancer Society has released a guideline on management of HNC survivors, regarding topics such as surveillance and screening for cancer recurrence, health promotion care coordination, and more.[22] RT dose and targeted area may significantly influence the risk of the long term oral heath complications. Review of prior RT treatment summary and collaboration with radiation oncologists will help dental providers anticipate treatment side effects and impact on future dental care.

Lip Cancer

Lip cancer (LC) is the most frequently occurring tumor of the oral and maxillofacial region, commonly appearing on the vermillion border of the lower lip.[23,24] LC has a favorable prognosis, with a mortality rate of 10-15% and a five-year survival rate of 80-90%.[25] The majority are treated with surgical resection alone.[26] If RT is used, several modifications to traditional RT exist to minimize side effects. Brachytherapy (BT) has been shown to be an effective means of local treatment.[27,28] Both high and low-dose BT are effective modes of treatment when evaluating efficacy and toxicity.[29] It should be noted since most LCs are treated with surgery alone, the use of RT is typically limited to patients presenting with more advanced disease.

Oral Cancer

Oral cavity cancers are primary treated with surgical resection, with possible adjuvant RT or chemoradiation therapy.[30] The implementation of post-operative RT has been shown to improve overall survival and prevent locoregional recurrence.[24,31,32] When treated with post-operative radiation, the local-regional control rate for oral cavity cancer is between 44-64%.[33] RT for oral cavity cancers frequently results in relatively high doses to the mandible and salivary glands, thereby increasing risks of long-term oral health complications.

Nasopharyngeal Cancer

Definitive RT is the main treatment for nasopharyngeal carcinoma (NPC), with the radiation field extending from the skull base to the lower neck.[34,35] The use of IMRT for NPC has reduced the severity of laryngeal dysfunction, xerostomia, and trismus.[36] Stage I and stage II disease have a high cure rate post-RT, though most are diagnosed at later-stages.[37-39]

Oropharyngeal Cancer

Early stage oropharyngeal cancers may be treated by primary surgery with adjuvant RT or chemoradiation reserved for unfavorable pathologic features, or definitive RT alone.[40] RT is the primary form of treatment for stage I and II oropharyngeal cancer (OPC). Advanced-stage OPC is most often treated with concurrent chemoradiation, although use of primary surgical management is increasing.[41] Patients treated with RT may receive high doses to the posterior mandible, particularly if the primary tumor is located within the palatine tonsil.[42,43]

Human papillomavirus-related (HPV) – associated OPC has a rising incidence but a more favorable prognosis. Current therapeutic clinical trials are investigating reduced intensity radiation therapy that may reduce side effects.[44-46]

Hypopharyngeal and Laryngeal Cancer

Early stage hypopharyngeal cancer (HPC) is often treated with definitive RT or surgical resection, with adjunctive RT added for surgical cases with adverse findings. Advanced stage disease may be treated with chemoradiation or surgical resection and adjuvant RT. Definitive RT alone ranges from 66Gy-70Gy for high risk sites, the primary tumor and nodes, while low risk sites with suspected subclinical disease receive 44-50Gy or 54-63Gy.[47] IMRT and 3D conformal RT are the preferred RT methods. Frequently, RT doses to the mandible and/or oral cavity may be minimal in these cases, reducing the risks of oral health complications directly related to RT.

Salivary Gland Cancer

Surgery remains the definitive treatment for salivary gland cancers without evidence of distant metastases, though RT is the primary modality for patients with unresectable

disease.[48-50] High risk salivary gland tumors receive radiation dosages of 66-70 Gy and low to intermediate risk tumors of 44-50 Gy to 54-83 Gy. Post-operative RT is indicated in advanced-stage disease with high-grade tumors, nodal metastases, and additional risk factors remaining after resection.

PATIENT FACTORS

Maintenance and Motivation

The success of dental treatment post RT requires effective, continual post-radiation follow-up and maintenance care, which is contingent on patient motivation to seek and comply with recommendations. Patient motivation can be influenced by psychological factors during the survivorship period. While anxiety decreases in HNC patients upon completion of RT, depression increases substantially, likely due to symptoms related to the cancer and treatment.[51] Elevated pre-radiation therapy depression levels and disruptions in eating and social habits confer the highest risk for elevated post RT depression levels.[52] Acknowledgement of the psychiatric duress HNC patients experience in the post-RT period and its potential impact on follow-up care is essential.

Nutrition

The adverse impact of RT on HNC patients, including poor nutritional status, progressive weight loss, and malnourishment, is well documented.[53-56] The repercussions of RT extend well beyond the treatment window, with over 50% of patients demonstrating >10% weight loss six to eight weeks after RT.[53] Due to the large correlation between alcohol and tobacco use with malnutrition and HNC, nearly half of patients are considered malnourished at the time of diagnosis.[56] As treatment commences, 80% experience unintentional weight loss.[56] It is recommended HNC patients receive weekly dietary counseling to make modifications as needed. As the effects of RT last long after its conclusion, this monitoring should occur for at least one year after the final treatment.[56] New studies recommend nutritional supplements as a prophylactic measure to mitigate weight loss, increase quality of life, and improve tolerance of cancer treatments.[57]

As dysgeusia, dysphagia, mucositis, and xerostomia increase, the tolerated diet often consists of high calorie, liquid cariogenic meal substitutes.[57] Dental providers should provide nutritional counseling aimed at maintaining oral health while adhering to dietary nutritional standards. Recommendations include using water, salvia substitutes, and sugar-free gum to alleviate xerostomia, substituting artificial sweeteners for simple sugars, and eliminating added sugar to foods like coffee and tea.[58] Vigilant oral hygiene routines should be reinforced.[58]

Socioeconomic Status

Socioeconomic status (SES) defined by the surrogate markers such as insurance status and type, household annual income, and education level completed, is recognized as a significant influencer of overall survival for HNC patients.[59,60] Many variables contribute to a poorer outcome for lower SES patients; these patients often have a delayed diagnosis, poorer nutrition, and higher prevalence of medical comorbidities.[59] Patients with non-government issued insurances and higher income levels were diagnosed sooner and showed improved overall survival.[59] Nearly 94% of high income HNC patients received the standard treatment regimen, as compared to only 87% of low income patients.[61]

For dental management, low SES patients presenting post-RT demonstrated a poorer compliance with fluoride use and displayed more caries development post therapy.[62] Low SES patients may be unable to adhere to a

strict maintenance schedule or compliance with recommended oral care post RT. Decreased health literacy rates and access to resources among low SES patients means providers should take additional steps to ensure proper follow-up for dental health. Although, patients from low SES neighborhoods do not seem more at risk for recurrence, they do demonstrate higher rates of secondary primary malignancy and poorer overall survival, and thus even patients without dentition require routine oral cancer screenings.[60,63]

Race

Race and ethnicity are recognized as influential patient factors in HNC. African American (AA) HNC patients have a shorter median survival time, 19 months for men and 26 months for women, as compared to 39 and 43 months for Caucasian men and women respectively.[64] Hispanic HNC patients have a greater median survival time than both non-Hispanic white and non-Hispanic black HNC patients.[63] Differences are also appreciated in the progression of treatment, with black patients having delays in treatment 61% of the time *vs*. 49% for non-blacks.[65] Black race also confers a decreased local region control of cancer three years out when compared to white, Asian, and other races. AA and white patients additionally receive surgical interventions, chemotherapy, and radiation therapy at different rates.[64,66] Whites underwent surgical intervention 13% more often than AA patients.[64] There is a complex interplay between many societal and social factors, and not biological differences, that account for disparities in diagnosis, treatment, and prognosis.[67]

Studies fail to address the genetic heterogeneity in self-reported racial categories, specifically AA and black. These categories may not accurately represent the ancestral composition of a cohort due to admixture within a population. When genetic composition is accounted for there was no linkage between diagnosis and prognosis outcomes in patients with HNSCC, but self-identified racial category was correlated with stage.[67]

In the post treatment stages, providers must be cognizant of the influence of healthcare disparities amongst patients from racial backgrounds and the influence on outcomes. Understanding the complex social determinants of health involved in caring for heterogeneous populations is critical to delivering equitable care and decreasing disparities in the post RT period.

Social Support

RT for HNC can lead to substantial morbidities with eating, drinking, and speaking, as well as, severe changes in appearance leading to a decreased QoL.[68] Having robust social support can provide emotional strength, companionship, and financial aid both during and after treatment. Patients with HNC with a live-in significant other reported a better QoL with regards to social wellbeing post diagnosis.[69] Married patients were diagnosed sooner, more compliant with treatment, and pursued more aggressive treatment modalities.[70,71] For HNCs of the oral cavity and larynx, being married decreases the chances of having metastasis on initial diagnosis.[72] Marriage increases the likelihood of definitive treatment regardless of the site of HNC.[72] An indirect benefit of being married is that patients may have access to insurance and financial stability, which can lead to better outcomes.[71]

When evaluating HNC patients post-RT, it is important to understand the complex interactions between the patient's social infrastructure and its impact on their ability to comply with post RT recommendations. Patients without these social structures and financial support may be less likely to

maintain oral maintenance during the post RT period and should receive guidance from dental providers.

Smoking Status

Smoking is a well-defined risk factor for HNC. Continued smoking post diagnosis reduces the five-year local control rate from 80% for former smokers to 67% for active smokers, along with a decrease in the overall survival rate.[73] Former and actively smoking HNC patients also reported more severe symptoms such as need for pain medication, cough, feeling unwell, problems with eating, talking, social interactions, sense of taste and smell, and weight loss.[74] Actively smoking HNC patients reported decreased QoL scores in physical function, general health, vitality, social functioning, and emotional health.[75] Smokers also saw a greater occurrence of secondary primary malignancy.[73] As such, HNC patients need extensive tobacco cessation counseling as part of their overall dental management. Dental providers are an arm of the HNC team uniquely qualified to provide smoking cessation counseling including recommending over the counter products like gum, lozenges, and patches, as well as prescription products, such as bupropion or varenicline, to help patients quit.[76]

Comorbidities

HNC patients often present with other medical comorbidities that negatively impact their overall survival, as well as disease-specific survival.[64,77-79] Cardiovascular, respiratory, and substance abuse comorbidities were found to negatively influence overall survival rate, while cardiovascular, respiratory, diabetes, and gastrointestinal comorbidities were associated with increased short-term mortalities.[79] Comorbidities also have a negative impact on the QoL for patients after they receive their diagnosis, particularly how they rate their physical QoL.[80]

Many comorbidities, such as diabetes and substance abuse, have a sizable impact on oral health and disease. Monitoring these medical conditions in close communication with the patient's primary care physician is critical to delivering comprehensive oral care.

DENTAL FACTORS

Recall Appointments

Routine dental visits and care are key to reducing radiation caries, assessing post RT oral sequela, and promptly addressing oral disease processes. Patients with high adherence to routine dental visits were found to have increased compliance with recommended home oral hygiene (84%) and dietary modifications (85%).[62]

Acute and chronic oral repercussions of RT are well-documented and a vigilant course of oral maintenance is necessary. Patients should be placed on a three-month dental recall schedule with the potential to transition to every six months once the oral environment is stabilized.[58,81,82] The oral health provider should individualize the recall schedule based on the patient's oral condition. During recalls, thorough review of oral hygiene, dietary counseling, scaling and prophylaxis, intraoral examination, HNC screening, and fluoride treatments should be completed.[81] Bitewing and periapical radiographs should be updated at six to 12 month intervals for life.[58] Regular and thorough recall appointments allow for surveillance of cancer recurrence and early detection of lesions.[82] Recall visits for post-RT HNC patients are pivotal to help identify sequela and monitoring overall oral health.

Fluoride

Post-RT trismus and xerostomia create many barriers to maintaining a disease-free oral cavity. Fluoride is a cost-effective method for remineralizing dentition and preventing demineralization. Topical fluoride application is correlated with a 14% reduction in moderate and severe tooth decay for each additional fluoride use per week.[83] High caries risk post-RT HNC patients must adhere to a strict fluoride regimen,[84] and should brush twice daily with high potency fluoridated toothpastes (i.e. Duraphat 5,000ppm or OraNurse 1,450ppm) supplemented with 0.5% or 3% sodium fluoride mouth rinse and interdental cleansing. Patients with radiation caries may also benefit from Chlorhexidine rinses daily for the first two weeks followed by a twice weekly regimen.[58,81-83]

Additional fluoride application via daily insertion of custom trays or soft splints lined with topical fluoride, such as Duraphat 5000ppm or 1% sodium fluoride gel, for approximately five to 30 minutes once a day is recommended.[82,85-87] Patients who applied 1% fluoride gel in a mouth tray for five minutes daily had a 3% caries rate compared to 11% for those using only fluoridated toothpaste twice a day.[86,88] Trismic patients may choose between varnishes, lacquers, lozenges, and pastes for supplemental fluoride application. Fluoride medicaments should contain 5000ppm fluoride and applied to a dry mouth.[84,85,89]

Calcium and phosphate are necessary to remineralize dentition and to supplement traditional fluoride regimens. Products include Caphosol®, Clinpro Tooth Crème®, Colgate Sensitive Pro-Relief Toothpaste®, Minimal intervention (MI) paste®, and Enamelon®.[85,87] Dental providers should encourage patients to explore the varied products to achieve optimum fluoride use.

Xerostomia

Post-RT salivary gland dysfunction is one of the most recognized side effects, with nearly 90% of patients reporting a decrease in saliva production. Greater than 50% of patients report difficulties with mastication, swallowing, sleeping, and speaking, and greater than 30% of these patients characterizing them as moderate to severe.[90] Clinicians in the post-RT setting should assess salivary gland capacity in these patients. Multiple evaluation methods have been attempted, including histological assessment, sialometry, ultrasound, scintigraphy, MRI, CT, and patient surveys. No method has been determined to provide sufficient information regarding both quantity and quality of saliva output for HNC patients. However, combinations of these diagnostic techniques can provide detailed information.[91] Clinicians should also employ patient-based questionnaires to monitor subjective information regarding xerostomia and its impact.

Clinicians can recommend neutral pH or fluoride-containing saliva substitution or stimulation products.[92] Sugar free gum or lozenges are only effective if there is remaining endogenous salivary gland function.[92] Medications with cholinergic activity, such as pilocarpine, bethanecol, and cevimeline, may be prescribed to patients with residual gland function.[85] Patients using these prescriptions have noted differences after use for six to eight weeks.[93] Due to the downstream effects of xerostomia, follow-up and management from dental providers must be consistent and frequent to limit adverse oral events and improvement in QoL.

Trismus

Trismus can impact 4-77.3% of HNC patients treated with RT, preventing effective oral hygiene and adequate professional dental care.[94] Post-RT fibrosis of the muscles of

mastication leads to decreased opening. 47.1% of post RT patients treated for squamous cell carcinoma developed trismus three months to three years after therapy.[95] A systematic review suggests trismus affects 25.4% of those treated with conventional RT and 5% treated with IMRT.[93-96]

Patients can develop radiation induced trismus in the period following radiation treatment.[94,95,97] Providers should note higher radiation dosage, MIO <40mm prior to treatment, greater length of time since RT, low BMI, depression, and chemoradiation therapy are risk factors for developing trismus post-RT.[95] Trismus effects mastication and talking, as well as receiving adequate dental care or screening for disease recurrence.[95,97] Trismic patients cite decreased QoL in the context of social interactions, intimate interactions, mouth quality and opening, ability to maintain nutrition, and weight loss.[95]

Dental providers should counsel these patients on the utilization of professional physical therapy and at-home therapy with tongue blades, corkscrews, TheraBite® appliances and Dynasplints®.[93,94] At-home regimens for acute onset trismus would be 7-7-7, or seven repetitions seven times per day for holding open for seven seconds. Another regiment is 5-5-30, five repetitions five times per day for 30 seconds, for patients with existing histories of trismus, pain, and TMJ arthralgia as well as new radiation trismus.[92] Patients who fail conservative therapy can be referred to an oral and maxillofacial surgeon for evaluation of temporalis myotomy and coronoidectomy.[98,99] Dental clinicians must identify the patients most at risk for developing trismus, counsel all patients in prevention, and adequately provide treatment regimens if symptoms develop.

Root Canal Therapy with Coronectomy in Non-restorable Dentition

Root canal therapy (RCT) with coronectomy for the post-RT HNC patient is the most conservative therapy for treating non-restorable dentition. Posts and crowns should only be placed in patients with meticulous home hygiene and follow-up to minimize the risks of complications.[100] Along with the elimination of infection and preservation of alveolar bone, RCT with coronectomy can improve cleansability for patients and decrease periodontal disease.[100] Post-RT patients undergoing RCT demonstrate an 85-95% likelihood of retaining the roots with no reports of ORN.[100,101] However, patients should be cautioned that resolution of radiographic periapical radiolucency is decreased due to lower rates of bone healing following irradiation.[100]

Case selection for RCT with coronectomy should place emphasis on early diagnosis of lesions and treatment within six months or less of irradiation for the best opportunity of apical healing due to intact vascularity of the surrounding bone.[100] Endodontic therapy in post-RT HNC patients is complicated by the prevalence of radiation trismus. Rubber-dam techniques must be followed to the extent patient opening will permit.[100] Clinicians may be able to bend instruments or use hemostats to access canals in trismic patients.[100] Coronectomy prior to RCT or prudent use of facial access may also aid instrumentation and obturation in patients with limited opening.[100]

Despite the decreased rate of ORN associated with RCT, there are limitations associated with cost and availability. Not all teeth are candidates for endodontic therapy due to anatomy, extent of disease, or previously failed treatments, nor can all patients afford the fees. Though these limitations exist,

endodontic therapy is an acceptable choice for RT patients who have non-restorable teeth with a high risk for ORN. Dental clinicians may present RCT with coronectomies as a more conservative treatment option available to patients.

Extraction of Non-Restorable Dentition

While endodontic therapy for nonrestorable teeth is the preferable treatment for HNC patients during and following RT, RCT may not be financially feasible or ameliorate infection entirely. In these situations, patients often elect for extraction. Extractions in post-RT HNC patients carry the risk of developing ORN of the jaw. For post-RT patients, the total incidence of ORN following extraction is 7%, with the mandible having a higher incidence compared to the maxilla.[102] After initiation or conclusion of RT, it is key that any necessary extractions be completed during RT or less than six months after concluding RT, as the irradiated tissue progressively fibroses.[103]

Risk of ORN following extractions is influenced by a constellation of factors. Patients who receive >60Gy of RT with subsequent extractions in the irradiated area have a greater chance of developing ORN.[102,103] However, extractions performed outside the field of radiation do not pose additional risk for ORN.[104] When patients are uncertain about the field of radiation, the radiation oncologist who developed the radiation plan should be consulted. Location of the extracted dentition is a significant factor as well, with posterior mandibular extractions conferring higher risk for ORN.[92,103] The quantity of teeth extracted is additionally important to assess, since removing more than five teeth puts the patient at an even greater risk for ORN.[103] Given the potential severity of ORN, all risk factors must be assessed and discussed with the patient prior to ensure a comprehensive understanding of risks.

Extractions must be performed using atraumatic technique, defined a limited soft tissue disturbance, careful flap design, alveoloplasty and tension-free primary closure.[104,105] However, absence of alveoloplasty and inability to achieve primary closure does not substantially increase ORN risk.[105] Providers must consider the patient's HNC prognosis and QoL when considering extraction based treatment plans. For patients with advanced and terminal disease states, extractions of asymptomatic teeth are not indicated.[104] It is essential to consider all patient factors impacting risk of ORN with each tooth, the goal of extractions, and prognosis.

Adjuvant Therapies for Extractions: Antibiotics, Hyperbaric Oxygen Therapy, and Pentoxifylline and Tocopherol

For unavoidable extractions, several adjuvant therapies have been proposed to decrease complications and reduce the risk for ORN. Two commonly implemented adjuvants are systemic antibiotic therapy and hyperbaric oxygen therapy (HBO). A lesser known and novel adjuvant is the use of pentoxifylline and tocopherol therapy.

Antibiotics, primarily amoxicillin and clindamycin, are used to prevent superimposition of infections on irradiated tissue post-extraction due to stunted healing capacity. However, they have not been shown to prevent ORN[102] – the incidence of ORN while on antibiotic therapy is still 6%.[102] Thus, the rationale for prescribing antibiotics should be to reduce the risk of infection due to compromised health status or oral condition, rather than to prevent ORN.

Historically, the most well-known adjuvant therapy in irradiated patients was the use of pre-and post-extraction HBO therapy, consisting of 20 pre-extraction and 10 post-

extraction 90-minute sessions of 100% O_2.[102,106,107] However, recent data utilizing modern RT techniques has demonstrated a low incidence of ORN, ~5%, post extractions or implants in the irradiated mandible of high-risk patients regardless of HBO therapy, and therefore suggests HBO therapy is not necessary prior to dental surgery.[108]

Prophylactic pentoxifylline and tocopherol (vitamin E) is a novel therapy employed in post-RT patients requiring extractions. Prophylaxis begins one month prior, with 400mg twice daily of pentoxifylline and 1000IU daily of tocopherol. The regimen continues post operatively until the socket is healed. Small scale studies have demonstrated lower incidences of ORN in extraction patients having received the regimen, though larger randomized control trials are still needed.[109,110] Pentoxifylline and tocopherol should be considered in post-RT HNC patients requiring dental extractions.

Restoration of Missing Dentition

Restoring dentition lost during HNC treatment to restore function and esthetics is paramount for post-treatment quality of life. This can be done via removable or implant-secured maxillofacial prostheses.

For removable prostheses, post-insertion complications are often minimal if the oral tissues are given appropriate healing time post-RT and patients maintain follow-up. Complications were more often noted in patients with radiation treatments >50Gy, bilateral radiation fields, and pre-insertion complications.[111] Opinions vary on the appropriate window of time between end of RT and prosthesis completion; however, one year is generally cited as a reasonable time with consideration for individual patient readiness.[111] Considerations when fabricating prostheses include eliminating use of metallic oxide, evaluating MIO, decreasing VDO, and scheduling post insertion follow-ups to monitor for soft tissue irritation.[112]

Dental implants offer an alternative method of restoring oral function and esthetics. Despite decreased vascularity and impaired healing post RT, greater than 70% of implants placed in irradiated patients were successful, with greater survival being noted in the mandible.[113-117] Success rates have been even higher, greater than 95%, for implants with altered surfaces such as those with chemically-modified and traditionally-sandblasted surfaces.[118] For patients irradiated with doses above 55Gys, there is a statistically significant decrease in implant survival compared to those who received less. Specifically, tissues receiving less than 50Gys saw an implant survival rate of 84% while those with a greater radiation experience had only a 71% survival rate.[117] This has led some clinicians to advocate for HBO therapy prior to placement, although recent data indicates it is not necessary prior to dental surgery in the mandible. [108, 113, 114, 119, 120]

There is no consensus on the most appropriate time to place implants post-RT, though placing implants an average of 30 months after conclusion of RT confers a greater overall implant survival.[115, 117, 119] HNC patients may also have had reconstruction of resection sites with grafting and flaps, which pose their own unique challenges for implants. Vascularized flaps, such as fibula free flaps, have better outcomes and implant survival than non-vascularized grafts, such as iliac crest bone grafts. Irradiated grafts are even less viable for implant placement than irradiated native bone.[119] Careful case selection and management may enable implant rehabilitation to provide a significant emotional, social, and functional improvement to HNC patients during the survivorship phase.

CONCLUSION

The post-RT period for HNC patients and their dental providers can be a challenging period owing to the physical and psychological sequelae these patients endure. Dental providers can serve an integral role in helping navigate the survivorship phase. Providing comprehensive and thoughtful care requires the dental clinician to consider factors related to the cancer, patient, and oral cavity while formulating the care plan with the patient.

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