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ORIGINAL ARTICLE

Oral health status of 207 head and neck cancer patients before, during and after radiotherapy

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Abstract The aim of this retrospective study was to describe the oral health status of patients before, during, and after radiotherapy (RT) for the treatment of head and neck cancer (HNC). Before RT, the following data was collected: presence of unrecoverable teeth, residual roots, unerupted teeth, use of dentures, periodontal alterations, caries, candidiasis, and xerostomia. Mucositis, candidiasis, and xerostomia were evaluated during RT. Patients continued to be followed after RT for evaluation of mucositis, candidiasis, xerostomia, radiation caries, and osteoradionecrosis. For statistical analysis, 95% confidence intervals (CI) were determined using sample size, population, and percentages. Before RT, 120 (57.9%) patients presented with alterations in the oral cavity namely, 85 (41.0%) with periodontal disease, 44 (21.2%) with residual roots, 25 (12.0%) with caries, 15 (7.2%) with candidiasis, and 12 (5.8%) had an unerupted tooth present. Xerostomia was a complaint of 19 patients (9.1%). Restorations were indicated for 33 patients (15.9%), whereas extraction was indicated for 104 (50.2%) patients. During RT, mucositis was found in 80 (61.7%) patients, candidiasis in 60 (45.8%), and xerostomia was a complaint of 82 patients (62.6%). After RT, mucositis persisted in 21 patients (19.2%), candidiasis was identified in 23 patients (21.1%), and xerostomia was reported by 58 patients (53.2%). Radiation caries developed in 12 patients (11.0%), whereas six patients (5.5%) developed osteoradionecrosis. The demographic profile herein presented will be useful as baseline data to provide additional epidemiological information and to determine future measures for prevention and treatment of RT-induced complications and sequelae.

Keywords Dental care · Oral health status · Head and neck cancer · Radiotherapy

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Introduction

Each year, approximately 500,000 new cases of head and neck cancer (HNC) are diagnosed worldwide [26]. Treatment of choice consists of surgery, radiation, and combined surgery/radiation. Recently, chemotherapy (CT) has been used as a neoadjuvant treatment, as adjuvant treatment after definite surgery and/or radiation, or concurrent with both definite and adjuvant radiotherapy (RT) [1].

Although RT plays an important role in the management of patients with HNC, it is also associated with several undesired reactions. Frequently, the salivary glands, oral mucosa, and jaws will inevitably be included in the RT field. Changes induced by exposure to radiation may occur during and after completion of therapy, including mucositis, candidiasis, osteoradionecrosis, and radiation caries [20, 28]. However, the precise incidence and prevalence of RT-induced side effects and sequelae are still difficult to obtain, with rates ranging from 13 to 89% [18]. The aim of this study was to survey the oral health status of a cohort of HNC patients before, during, and after RT.

Materials and methods

A retrospective, descriptive study was conducted. The charts of all patients seen between 2003 and 2005 at the Oral Oncology Service of the Universidade Federal de Minas Gerais (UFMG) were reviewed. All patients had a biopsy-proven malignant neoplasm of the head and neck region and received external beam RT at a minimum of 45 Gy. Patients were referred to our service by head and neck surgeons and radiotherapists working at three different hospitals in Belo Horizonte, Brazil.

Before radiotherapy

To gather baseline information on the oral health status of patients at the moment of their first consultation, i.e., before RT, the following data was collected from their charts: age, gender, ethnicity, tumor site, tumor staging, tumor histology, presence of unrecoverable teeth, presence of residual roots, presence of unerupted teeth, use of dentures, periodontal alterations (crestal bone loss relative to the distance from the apex to a point 2 mm apical to the cemento-enamel junction, determined by radiographic examination), caries, candidiasis (defined as the clinical presence of removable white intraoral plaques or white lesions associated with erythematous lesions), and xerostomia (assessed in a "yes/no" manner).

Our service is based in the School of Dentistry of the UFMG, working in conjunction with three outside hospitals from Belo Horizonte, Brazil. The patients' dental treatment plan is developed upon referral by head and neck surgeons and radiotherapists before surgery or RT. Patients receive comprehensive treatment by a team composed of dentists with training in the following specialties: oral medicine, oral surgery, operative dentistry, endodontics, periodontics, prosthodontics, and radiology. In addition, the team is composed of dental students, dental hygienists, nutritionists, psychologists, and physiotherapists. Patients receive free care in all above mentioned specialties.

All patients enrolled in the service had been submitted to a standardized set of procedures namely, (1) upon the first visit, patients were interviewed, clinically examined, and a complete set of oral radiographs was taken, (2) patients received oral care instructions by dental hygienists, whereas those who did not have teeth were instructed on how to clean their mouth with gauze soaked in 0.9% NaCl solution, (3) patients who wore prostheses were advised to place them overnight in a glass of water, (4) extractions and periodontal surgical procedures were performed before RT, whenever a minimum interval of 15 days could be respected before initiation of RT, (5) patients were prescribed sucralfate mouthwash at 10% (four times a day/duration of 10 min; used concomitant with irradiation), and sodium fluoride at 1% was prescribed to dentate patients (nightly mouthwash/duration of 1 min; used concomitant with irradiation), (6) patients underwent weekly oral examinations and prophylaxis during RT. Nontraumatic therapy, such as restorative dentistry and endodontics, was performed during RT. Prosthodontic therapy was postponed until the end of RT.

During radiotherapy

In this stage of the study, information on mucositis, candidiasis, and xerostomia was gathered from the patients' charts. Mucositis was scored weekly using the World Health Organization method, as follows: grade 1 (soreness and erythema), grade 2 (erythema or ulcers but can eat solid foods), grade 3 (ulcers, requires liquid only), and grade 4 (no possible alimentation) [19]. The frequency, initial development, and presentation (localized/generalized) of mucositis and candidiasis, and the frequency and initial development of xerostomia was collected from the charts.

After radiotherapy

Patients continued to be followed up after the end of RT, with the minimum post-RT period for inclusion into this stage of the study being 3 months. The frequency of follow-up visits after RT varied from patient to patient, according to oral health status upon completion of RT. Mucositis, candidiasis, xerostomia, radiation caries, and osteoradionecrosis information was gathered from the charts.

Statistical analysis

For statistical analysis, 95% confidence intervals (CI) were determined using sample size, population, and percentages. CI values are presented after each point estimate, inside parenthesis.

Results

Before radiotherapy

Table 1 shows demographic, clinical, histological, and RT characteristics of the study patients. Before RT, the charts of 207 patients were analyzed. Regarding dental status, 135 (65.2%, CI 58.7–71.7) patients still had teeth, whereas 72 (34.8%, CI 28.2–41.2) were totally edentulous. Of the latter, only 20 (27.8%, CI 17.4–38.1) wore dentures. A total of 120 (57.9%, CI 51.2–64.7) patients presented with alterations in the oral cavity, as follows: 85 (41.0%, CI 34.3–47.7) with periodontal disease, 44 (21.2%, CI 15.6–26.8) with residual roots, 25 (12.0%, CI 7.6–16.5) with caries, 15 with

Table 1 Clinical, demographic and radiotherapy characteristics of the 109 patients who were included in all three stages of the study

Variable	Category	Number (%)
Age (years)	Mean	57.8
	Range	14–87
Gender	Male	86 (79.0)
	Female	23 (21.0)
Race	White	57 (52.0)
	Others	52 (48.0)
Tumor site	Oral cavity	57 (52.0)
	Larynx	28 (26.0)
	Others	24 (22.0)
Clinical Stage (UICC)	I/II	43 (41.0)
	III/IV	64 (59.0)
Histology	Squamous cell carcinoma	91 (84.0)
	Others	18 (16.0)
Treatment plan	Radiotherapy	12 (10.8)
	Radiotherapy+surgery	83 (76.4)
	Radiotherapy+chemotherapy	9 (7.9)
	Radiotherapy+chemotherapy+surgery	5 (4.9)
Radiotherapy equipment	Cobalt	51 (47.0)
	Linear accelerator	58 (53.0)
Radiation dose (Gy)	Mean	58.9
	Range	50–72
Radiation field	Cervicofacial	94 (86.0)
	Cervical	15 (14.0)
Radiotherapy sessions	Mean	34
	Range	25–47

candidiasis (7.2%, CI 3.7–10.7), and 12 (5.8%, CI 2.6–8.9) had an unerupted tooth present. Restorations were indicated for 33 patients (15.9%, CI 10.9–20.9). In addition, it was observed that 104 (50.2%, CI 43.4–57.0) patients needed at least one extraction, with a mean of 11 teeth needing extraction per patient. Xerostomia was a complaint of 19 patients (9.1%, CI 5.2–13.1). Table 2 shows the most important oral findings found in the study before RT.

During radiotherapy

The charts of 131 patients who had completed the entire RT course while attending our service were analyzed. Table 2 summarizes the most important oral findings found in the study during RT. Sucralfate was correctly used by 93 (70.9%, CI 63.2–78.7) patients. Twenty-three out of 58 (39.6%, CI 27.0–52.2) dentate patients used sodium fluoride as recommended. Candidiasis was seen in 60 patients (45.8%, CI 37.2–54.3), with mean development in the 16th session. Out of these, 31 (51.6%, CI 39.2–64.3) patients presented a localized form of the disease. The remaining showed generalized candidiasis. Mucositis was found in 80 (61.7%, CI 52.7–69.4) patients (mean development in the 15th session). Out of these, 36 (45.0%, CI 34.1–55.9) developed greatest mucositis grade 1, 41 (51.2%, CI 40.3–62.2) grade 2, and three patients (3.7%, CI 0–7.9) developed grade 3. Regarding clinical sites affected, 28 patients (35.0%, CI 24.5–45.4) showed localized mucositis, while 52 (65.0%, CI 54.5–75.4) developed generalized mucositis. Xerostomia was a complaint of 82 (62.6%, CI 54.3–70.8) patients (mean development in the 11th session). Figure 1 shows the schematic progression of xerostomia, candidiasis, and mucositis throughout RT.

After radiotherapy

Table 2 presents the most important data found in the study after RT. A total of 109 patients were still being followed up at least 3 months after the end of RT, with mean time of follow-up 120 days (range 90–1,005 days). Of the 98

Table 2 Important oral mucosa, periodontal, and dental alterations observed in the study group

Study stage	Number of patients	Oral finding	Number of affected patients (%)	95% CI limits
Before radiotherapy	207	Periodontal disease	85 (41.0)	34.3–47.7
		Residual root	44 (21.2)	15.6–26.8
		Caries	25 (12.0)	7.6–16.5
		Xerostomia	19 (9.1)	5.2–13.1
		Candidiasis	15 (7.2)	3.7–10.7
		Unerupted tooth	12 (5.8)	2.6–8.9
During radiotherapy	131	Xerostomia	82 (62.6)	54.3–70.8
		Mucositis	80 (61.7)	52.7–69.4
		Candidiasis	60 (45.8)	37.2–54.3
After radiotherapy	109	Xerostomia	58 (53.2	43.8–62.5
		Candidiasis	23 (21.1)	13.4–28.7
		Mucositis	21 (19.2)	11.8–26.6
		Radiation caries	12 (11.0)	5.1–16.8
		Osteoradionecrosis	6 (5.5)	1.2–9.7

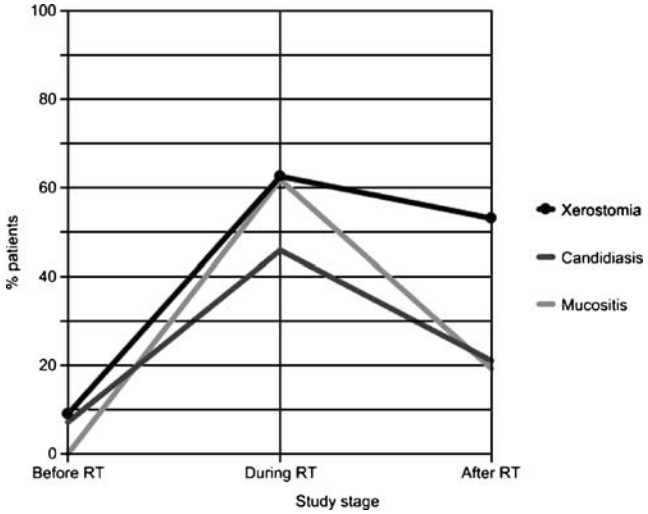

Fig. 1 Percentage of patients who developed mucositis, candidiasis, and xerostomia, in relation to the study stages

patients lost from the first stage of the study, 66 were deceased (67.3%, CI 58.0–76.6), and 32 (32.7%, CI 23.3–41.9) were lost to follow-up. Out of the 66 patients who were deceased, 55 (83.3%, CI 74.3–92.3) died from their disease, whereas 11 (16.6%, CI 7.6–25.6) died from other causes. Persistent mucositis was seen in 21 patients (19.2%, CI 11.8–26.6), with mean duration of 15 days. Candidiasis was found in 23 patients (21.1%, CI 13.4–28.7) after RT and persisted on average for 30 days. Xerostomia remained a complaint of 58 patients (53.2%, CI 43.8–62.5), with a mean duration 251 days (range 7–1,005 days). Figure 1 shows the schematic progression of xerostomia, candidiasis, and mucositis throughout RT. Radiation caries was found in 12 patients (11.0%, CI 5.1–16.8), with mean development time of 1.38 years post-RT. Six patients (5.5%, CI 1.2–9.7) developed osteoradionecrosis, on average 3.5 months post-RT.

Discussion

The purpose of the pre-RT screening is to identify any oral infectious foci and determine the patient's level of oral hygiene and dental awareness [24]. Most of our patients were poorly educated low-income individuals, with minimal oral hygiene and level of dental awareness. Many patients had never undergone dental treatment. Previous studies have shown that between 68 and 97% of the patients examined just before RT need immediate dental care [14, 15]. Similarly, 58% of our sample required dental treatment when first assessed. Table 2 shows the most common alterations found in our study before RT: periodontal disease (41%), residual roots (22%), and caries (12%). Others verified a much greater incidence of periodontal disease and caries, in comparison to our findings (93 vs 41% and 43 vs 12%, respectively) [4]. Our data confirm that most oral cancer patients present with poor oral health, yet the severity of alterations may vary according to the population studied [4, 15, 17]. Thus, health professionals should have extensive knowledge on the specific characteristics and needs of their patients, so that the quality of care can be enhanced.

The criteria used for dental extractions before RT are not universally accepted and are subject to clinical judgment [10]. In our service, we try to employ a conservative approach, yet we still found a striking mean of 11 teeth needing to be removed per patient. This is higher than previous reports, where between six and nine teeth needed to be extracted per patient [4, 7]. Around 50% of our patients needed at least one extraction before RT. In previous studies, this ranged from 68 to 82% [8, 14]. In any case, it is important to consider that the dental treatment in a patient planning to receive RT is unique and may include the extraction of a tooth that otherwise would receive a more conservative treatment [8, 14].

In the next stage of the study, we first assessed our patients' compliance with our protocol during RT. Compliance is a major problem when dealing with HNC patients; one study showed that 81% of patients do not follow the indicated treatments [15]. In our service, all patients are prescribed sucralfate and sodium fluoride (when dentulous) to be used concomitant with RT, aiming to reduce mucositis and caries, respectively. We verified that more patients complied with the sucralfate than with the sodium fluoride (70 and 40%, respectively). Although we could not assess the reasons for noncompliance, we believe this occurred because mucositis' course is much more acute, painful, and debilitating. In addition, patients may not perceive cavities as an important issue, especially because these are normally late side effects of RT. The fact that patients undergoing RT are prescribed multiple drugs may also contribute to low compliance. Lastly, a diagnosis of cancer may impact the patients' ability to assimilate the proposed dental treatment plan [16].

With the initiation of RT, a variety of oral complications may arise. Among these, xerostomia is the most common oral sequelae. This disorder develops early, and up to 80% of patients will complaint of dry mouth during RT [5]. In our sample, the xerostomia prevalence increased from 9.1% before RT to 62.6% during RT, with a mean development in the 11th session (Fig. 1). Current therapies for the management of RT-induced xerostomia include saliva substitutes to relieve symptoms and systemic sialogogues to stimulate saliva production [6]. Of the latter, pilocarpine is most widely used. However, because pilocarpine tablets are not commercially available in Brazil, our patients can only rely on topical saliva substitutes.

Mucositis is defined as an inflammation of the mucosa, in this case initiated by direct cellular damage secondary to radiation [27]. The pathogenesis of mucositis is still unclear. Cell death and inhibition of mitosis in the basal cell population, in addition to cell loss from the mucosal surface, are factors involved in the mucosal thinning. Furthermore, inflammatory cells, including granulocytes, play an important role [3]. Up to 80% of irradiated patients will develop mucositis, with the onset usually occurring at the end of the first week [13]. In addition, between 20 and 30% of the patients will need artificial feeding [28]. In our study, mucositis was identified in 61% of our sample, developing on average in the 15th session (third week; Fig. 1 and Table 2). Regarding severity of mucositis, 97% of our patients developed relatively mild alterations namely, stages I/II. Artificial feeding was not required for any patient in our study. We believe that the smaller frequency and severity of mucositis we observed could be related to the use of sucralfate, although its clinical efficacy is not consistent in the literature. In that case, our data favor the use of sucralfate as an agent for the prevention of mucositis [9]. However, caution should be taken when interpreting this finding, as this was not the primary aim of this study. Alternatively, mucositis could have been positively influenced by the weekly prophylaxis sessions our patients underwent, as it has been suggested that there is an association between mucositis and oral hygiene status [23].

Oral candidiasis is common in individuals with HNC, especially during RT. Both *C. albicans* and nonalbicans species are involved in the colonization and infection of patients that undergo RT [21, 22]. The acute form usually presents as erythema, but the diagnosis may be missed, as this may be mistaken for radiation mucositis. In chronic forms of candidiasis, the infection most commonly occurs in the corners of the mouth or beneath prosthesis [3]. In our service, patients who developed infections that we do not consider significantly severe are initially treated with only oral hygiene improvement, to avoid antifungal resistance. When medications are necessary, systemic ketoconazole (100 mg/day, 21 days) is initially prescribed. Fluconazole is employed as a second option or for very severe and persistent infections, mainly because the drug is expensive in Brazil and our patients can not bear the costs. In our study, we detected candidiasis in 46% of the patients during RT (Fig. 1 and Table 2). This is higher than rates reported elsewhere (17–29%) [20, 21] yet consistent with one of our previous studies with a similar sample (52%) [12]. The higher rates found in both of our studies could be due to the fact that our patients are mainly low-income individuals. In addition, our patients are often unable to maintain adequate nutritional status and oral hygiene during RT, in spite of receiving instructions and care.

Lastly, we assessed the oral health status of patients after completion of RT. Xerostomia persisted in 53.2% of our patients after RT, with mean duration of 251 days. Others have found that 64% of long-term HNC survivors (at least 3 years after RT) experienced a moderate to severe degree of xerostomia [31]. Some recovery is possible until 12 to 18 months after RT, depending on the dose received by the salivary glands and the volume of the glandular tissue included in the irradiation fields. However, xerostomia generally develops into an irreversible, life-long problem [6]. It is also known that candidiasis may be seen post-RT, especially with persistent xerostomia [2]. Candidiasis was still present in 21% of our patients after RT and persisted on average for 30 days. Likewise, Schwarz et al. [25] found that 42% of previously irradiated patients had candidiasis on follow-up sessions. Mucositis may persist for 3–6 weeks after therapy is completed [13, 27], but in 90–95% of the patients, it subsides before the fourth week post-RT [2]. In our study, mucositis persisted for 2 weeks in 19% of the patients, consistent with the published literature (Fig. 1 and Table 2).

With the end of RT, new complications may arise. Radiation caries is a highly destructive form of dental caries with rapid onset and progression. Lesions start on the labial surface at the cervical areas of the teeth, including mandibular anterior teeth, which are usually very resistant to caries in nonirradiated populations. The main risk factor is hyposalivation, in addition to alterations in microbial, chemical, immunologic, and dietary parameters [13, 29]. Dental caries can begin to develop as early as 3–6 months after treatment and progresses to complete destruction of all the teeth over a period of 3–5 years [27]. We verified that radiation caries developed in 11% of our sample, on average 1.4 years after RT (Table 2). However, it should be kept in mind that our study's mean follow-up period after RT (4 months) is too short to thoroughly evaluate caries activity.

Osteoradionecrosis is also an important late side effect of RT. Osteoradionecrosis incidence varies widely in the literature, ranging from to 0.4 to 56% [11]. Development usually occurs within 1 year after RT, ranging from 2 weeks to 34 months [30]. In our study, 5% of the patients in the last stage of the study developed osteoradionecrosis, on average 3.4 months post-RT (Table 2). A possible explanation for this low rate is the early extraction of nonrestorable teeth before RT. As with radiation caries, it should be remembered that 4 months is a short follow-up period to evaluate the development of osteoradionecrosis.

The major drawback of our study was that the information was collected retrospectively, thus being subject to inherent inaccuracies, including the inability to control bias and cofounders. Observation bias in the collection of the original data by different clinical observers

may have occurred. An additional limitation was that 47% (98 of 207) of the patients initially enrolled in the study were excluded throughout the study stages because of death (67.3%) or loss to follow-up (32.7%). Further, we were unable to objectively measure the dropout reasons, as such information was not recorded in the charts. Still, we believe dropouts occurred primarily because our service is not hospital based, thus making it more difficult for subjects to comply with their appointment schedules.

In conclusion, we described the oral health status of a large sample of HNC patients before, during, and after RT. The demographic profile of ST herein presented will be useful as baseline data to provide additional epidemiological information and to determine future measures for prevention and treatment of RT-induced complications and sequelae.

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