A Retrospective Cohort Study of Acute Radiotherapy Induced Mucositis, Radiodermatitis and Dental Disorders in Brazilian Head and Neck Cancer Patients

https://doi.org/10.32635/2176-9745.RBC.2026v72n4.5719

Estudo de Coorte Retrospectivo de Mucosite, Radiodermatite e Distúrbios Dentários Agudos Induzidos por Radioterapia em Pacientes Brasileiros com Câncer de Cabeça e Pescoço

Estudio de Cohorte Retrospectivo de Mucositis, Radiodermatitis y Trastornos Dentales Agudos Inducidos por Radioterapia en Pacientes Brasileños con Cáncer de Cabeza y Cuello

Tatiane Sorribas da Silva[1]; Denis Oliveira dos Santos[2]; Célia Soares[3]; Carla Daruich de Souza[4]

ABSTRACT

Introduction: Radiotherapy for head and neck cancer frequently causes acute toxicities that impair treatment continuity and quality of life. However, integrated data on simultaneous occurrence of mucositis, radiodermatitis, and dental disorders in Brazilian public health system (SUS) are scarce. **Objective:** To evaluate the incidence and severity of adverse events and identify associated clinical and treatment factors. **Method:** Retrospective cohort study at a single radiotherapy center in SP, Brazil, between January 2021 and December 2024. Multivariate logistic regression was used to identify independent predictors of severe mucositis and radiodermatitis, adjusting for age, radiation dose, and concomitant chemotherapy. **Results:** Of the 180 patients screened, 146 were analyzed (34 have been excluded, 18 due to incomplete records, 10 due to death or treatment abandonment before fraction 10, and 6 due to transfer). Mucositis occurred in 142 patients (97.3%; grade 3 in 28.8%). Radiodermatitis occurred in 138 patients (94.5%; grade 3 in 13.7%). Dental disorders were documented in all 146 patients (100%), driven by hyposalivation (98.6%), radiation caries (42.5%), and periodontal disease (31.5%). In multivariate analysis, concomitant chemotherapy was an independent predictor of moderate-to-severe mucositis (OR=4.42; 95% CI 2.01–9.71; p<0.001), while total radiation dose ≥60 Gy was independently associated with severe radiodermatitis (OR=3.08; 95% CI 1.28–7.41; p=0.012). **Conclusion:** The high prevalence and severity of acute toxicities underscore the need for structured multidisciplinary supportive care. The 100% dental disorder rate reflects the vulnerable oral health background of SUS patients. These real-world data offer actionable evidence for clinical protocols and public health policies.

Key words: Radiation Injuries; Head and Neck Neoplasms/complications; Mucositis; Radiodermatitis/complications; Toxicity.

RESUMO

Introdução: A radioterapia para câncer de cabeça e pescoço frequentemente causa toxicidades agudas que comprometem a continuidade do tratamento e a qualidade de vida. Entretanto, dados integrados sobre a ocorrência simultânea de mucosite, radiodermatite e distúrbios dentários no Sistema Único de Saúde (SUS) ainda são escassos. **Objetivo:** Avaliar a incidência e a gravidade desses eventos adversos, além de identificar fatores clínicos e de tratamento associados. **Método:** Estudo de coorte retrospectivo conduzido em um único centro de radioterapia em São Paulo, Brasil, entre janeiro de 2021 e dezembro de 2024. Regressão logística multivariada foi utilizada para identificar preditores independentes de mucosite severa e radiodermatite, ajustando para idade dose de radiação e quimioterapia concomitante. **Resultados:** Dos 180 pacientes avaliados, 146 foram analisados (34 excluídos: 18 em razão de prontuários incompletos, 10 por causa de óbito ou abandono do tratamento antes da fração 10 e 6 por conta de transferência). Mucosite ocorreu em 142 pacientes (97,3%; grau 3 em 28,8%). Radiodermatite ocorreu em 138 pacientes (94,5%; grau 3 em 13,7%). Distúrbios dentários foram documentados em todos os 146 pacientes (100%), impulsionados principalmente por hipossalivação (98,6%), cáries por radiação (42,5%) e doença periodontal (31,5%). Na análise multivariada, a quimioterapia concomitante foi um preditor independente de mucosite moderada a severa (OR=4,42; IC 95% 2,01–9,71; p<0,001), enquanto a dose total de radiação ≥60 Gy foi independentemente associada à radiodermatite severa (OR=3,08; IC 95% 1,28–7,41; p=0,012). **Conclusão:** A alta prevalência e gravidade das toxicidades agudas reforçam a necessidade de um cuidado de suporte multidisciplinar estruturado. A taxa de 100% de distúrbios dentários reflete a vulnerabilidade da saúde bucal dos pacientes atendidos pelo SUS. Esses dados de mundo real oferecem evidências aplicáveis para protocolos clínicos e políticas públicas de saúde.

Palavras-chave: Lesões por Radiação; Neoplasias de Cabeça e Pescoço/complicações; Mucosite; Radiodermatite/complicações; Toxicidade.

RESUMEN

Introducción: La radioterapia para el cáncer de cabeza y cuello frecuentemente causa toxicidades agudas que comprometen la continuidad del tratamiento y la calidad de vida. Sin embargo, los datos integrados sobre la ocurrencia simultánea de mucositis, radiodermatitis y trastornos dentales en el Sistema Único de Salud (SUS) del Brasil siguen siendo escasos. **Objetivo:** Evaluar la incidencia y la gravedad de estos eventos adversos, además de identificar factores clínicos y de tratamiento asociados. **Método:** Estudio de cohorte retrospectivo en un único centro de radioterapia en São Paulo, Brasil, entre enero de 2021 y diciembre de 2024. Se utilizó regresión logística multivariada para identificar predictores independientes de mucositis severa y radiodermatitis, ajustando por edad, dosis de radiación y quimioterapia concomitante. **Resultados:** De los 180 pacientes evaluados, 146 fueron analizados (34 excluidos: 18 debido a historias clínicas incompletas, 10 debido a fallecimiento o abandono del tratamiento antes de la fracción 10 y seis debido a traslado). La mucositis ocurrió en 142 pacientes (97,3%; grado 3 en el 28,8%). La radiodermatitis ocurrió en 138 pacientes (94,5%; grado 3 en el 13,7%). Los trastornos dentales se documentaron en los 146 pacientes (100%), impulsados principalmente por hiposalivación (98,6%), caries por radiación (42,5%) y enfermedad periodontal (31,5%). En el análisis multivariado, la quimioterapia concomitante fue un predictor independiente de mucositis moderada a severa (OR=4,42; IC 95% 2,01–9,71; p<0,001), mientras que la dosis total de radiación ≥60 Gy se asoció independientemente con radiodermatitis severa (OR=3,08; IC 95% 1,28–7,41; p=0,012). **Conclusión:** La alta prevalencia y gravedad de las toxicidades agudas refuerzan la necesidad de un cuidado de soporte multidisciplinario estructurado. La tasa del 100% de trastornos dentales refleja la vulnerabilidad de la salud bucal de los pacientes atendidos en el SUS. Estos datos del mundo real ofrecen evidencias aplicables para protocolos clínicos y políticas públicas de salud.

Palabras clave: Traumatismos por Radiación; Neoplasias de Cabeza y Cuello/complicaciones; Mucositis; Radiodermatitis/complicaciones; Toxicidad.

[1]Hospital Santa Marcelina. São Paulo (SP), Brasil. Instituto de Pesquisas Energéticas e Nucleares (IPEN). São Paulo (SP), Brasil. E-mail: tatianesorribas@hotmail.com. Orcid iD: https://orcid.org/0009-0003-1776-6985

[2,3]Hospital Santa Marcelina. São Paulo (SP), Brasil. E-mails: denis.oliveira1@hotmail.com; cercersoares@gmail.com. Orcid iD: https://orcid.org/0009-0004-1279-2946; Orcid iD: https://orcid.org/0009-0001-7097-8800

[4]IPEN. São Paulo (SP), Brasil. E-mails: carladdsouza@yahoo.com.br; cdsouza@usp.br. Orcid iD: https://orcid.org/0000-0003-1335-8864

Corresponding author: Carla Daruich de Souza. IPEN. Avenida Professor Lineu Prestes, 2242 – Cidade Universitária. São Paulo (SP), Brasil. CEP 05508-000. E-mails: carladdsouza@yahoo.com.br; cdsouza@usp.br

INTRODUCTION

External Beam Radiotherapy (RT) remains a cornerstone in the treatment of head and neck cancer (HNC), a group of malignancies notorious for their aggressive nature and complex management requirements. The high incidence and mortality rates associated with HNC necessitate effective treatment strategies, where RT often plays a pivotal role[1]. However, the therapeutic benefits of RT are frequently accompanied by acute adverse reactions, which can significantly impact patients' quality of life and treatment adherence[2,3].

Studies have consistently shown that adverse effects such as mucositis, radiodermatitis, and dysphagia are prevalent among patients undergoing RT for HNC[4,5]. These side effects not only cause discomfort and pain but can also lead to treatment interruptions, ultimately compromising the efficacy of cancer therapy[6-8]. The challenge lies in balancing the therapeutic dose required to achieve tumor control with the potential for harm to healthy tissues[9,10].

The clinical management of HNC in Latin America is heavily influenced by socioeconomic disparities, which frequently lead to delayed diagnoses and advanced disease stages at the onset of treatment[11]. Consequently, these patients are exposed to aggressive therapeutic regimens, resulting in a high burden of acute toxicities. Recent Brazilian cohorts have demonstrated a strict dose-dependence relationship between cumulative radiation and the severity of oral mucositis, emphasizing that public healthcare patients are particularly vulnerable to severe mucosal damage[5,12].

Understanding the factors that contribute to the severity and frequency of RT-induced adverse reactions is crucial for developing effective management strategies. Factors such as radiation dose, chemotherapy regimens, and individual patient characteristics can influence the onset and progression of side effects[13,14]. Recent advancements in RT techniques, including intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT), offer potential avenues for dose optimization and toxicity reduction[15].

While individual toxicities such as mucositis, radiodermatitis, and dental disorders have been widely documented in head and neck cancer patients[7,8,10,14,16], integrated epidemiological data regarding their simultaneous occurrence within the Brazilian public health system (SUS) remain scarce. This lack of real-world evidence limits the development of comprehensive supportive care protocols and efficient resource allocation. Therefore, this study aimed to evaluate the incidence and severity of these three acute toxicities concurrently in patients undergoing external beam radiotherapy at a major public hospital in São Paulo. Additionally, it was attempted to identify independent clinical and treatment-related predictors of severe outcomes to provide actionable data for multidisciplinary clinical planning and public health policies in resource-limited settings. By identifying the prevalence and association of side effects with treatment variables, this research seeks to inform clinical practices and improve patient outcomes.

METHOD

It is a retrospective observational cohort study to evaluate acute radiotherapy-induced toxicities in patients diagnosed with HNC. To ensure methodological transparency, scientific rigor, and complete reporting of observational data, this study was designed and is reported in strict accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)[17] guidelines which allows readers to assess potential selection bias. The study population comprises a convenience sample of all adult patients (18 years or older) who underwent external beam radiotherapy at "*Hospital Santa Marcelina*", São Paulo, between January 2021 and December 2024. A convenience sampling strategy was adopted to include the entire eligible patient population treated during this four-year window. Out of 180 patients initially screened, 146 met all the eligibility criteria and were included in the final analysis, and 34 patients were excluded: 18 due to incomplete medical records (missing toxicity grades or radiotherapy details), 10 due to death or treatment abandonment before completing fraction 10, and 6 due to transfer to another institution.

No formal sample size calculation was performed. Instead, a convenience sample consisting of all eligible patients treated at "*Hospital Santa Marcelina*", within the study period (January 2021 to December 2024) was analyzed to maximize the statistical power of the cohort. To minimize potential selection and information biases inherent to the retrospective design, data extraction was performed by trained researchers using a standardized electronic collection form. Furthermore, clinical toxicities were graded strictly based on objective, internationally validated scales (CTCAE v5.0[18] and RTOG[19]) to prevent classification bias.

The Ethics Committee of "*Hospital Santa Marcelina*" approved the study, report number 6508454 (CAAE (submission for ethical review): 74519823.6.0000.0066). The National Ethics Committee (CONEP) approved the study, report number 112264/2023 in compliance with the Declaration of Helsinki[20] and with Directive 466/12[21] of the National Health Council (CNS). All the participants signed the informed consent form (ICF).

Patients were systematically identified from the hospital's electronic medical records based on these criteria. Exclusion criteria included incomplete medical records lacking essential data on treatment parameters or adverse reaction documentation. This approach allowed for a detailed examination of the factors influencing the severity and frequency of side effects, providing a robust dataset for analysis[22].

Demographic data collected included age, sex, and primary cancer site. Treatment-related variables encompassed total radiation dose (Gy), type of radiotherapy technique (IMRT), and concurrent chemotherapy regimens. Key outcomes, the short-term adverse reactions, were documented as mucositis, radiodermatitis, and dental disorders. Mucositis and radiodermatitis were graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0[23], as routinely recorded in patient charts. Specifically, 'grade 1 mucositis' corresponded to mild erythema and discomfort; 'grade 2' to ulcers and difficulty with solid foods; 'grade 3' to severe ulcers requiring a liquid diet. Similarly, 'first-degree radiodermatitis' indicated mild erythema or dry desquamation; 'second-degree', moderate to intense erythema, and 'third-degree', moist desquamation. Dental disorders were defined as any reported or clinically observed issues such as sensitivity, decay, or periodontal disease noted in the dental assessments within the medical records. Information on the use of Nystatin, Omeprazole, and laser therapy as supportive care interventions was also extracted. Potential confounding variables, such as smoking status and alcohol consumption, were sought during data collection. However, these specific data points were often inconsistently recorded or unavailable in the retrospective medical charts for a significant portion of the patient cohort.

The term "dental disorder" was defined broadly to capture any oral complication that could affect the patient's quality of life or treatment adherence. All patients underwent a standardized oral assessment performed by a hospital professional before the radiotherapy beginning, weekly during treatment, and at the end of the radiotherapy course. The protocol included: (i) subjective dry-mouth questionnaire (xerostomia), (ii) unstimulated whole saliva measurement (hyposalivation defined as <0.1 mL/min), (iii) clinical examination for dental sensitivity, radiation caries (ICDAS criteria[23], and periodontal disease (probing depth ≥4 mm). This standardized approach ensured consistent grading across all patients and reduced inter-observer variability.

Nystatin is an antifungal medication frequently used to prevent and treat oral candidiasis, a common complication for patients undergoing radiotherapy for head and neck cancer[24]. The immunosuppressive effects of radiotherapy, coupled with the disruption of normal oral flora, increase the risk of fungal infections. In this study, Nystatin was analyzed to assess its effectiveness in managing or preventing oral mucositis and secondary infections. The findings aimed to determine whether Nystatin could significantly alleviate these conditions, thereby improving patient comfort and adherence to cancer treatment protocols. Nystatin oral suspension was administered therapeutically upon clinical suspicion or microbiological confirmation of oral candidiasis.

Omeprazole, a proton pump inhibitor, is used to reduce gastric acid production and manage gastrointestinal symptoms such as acid reflux, which can be exacerbated by chemotherapy and radiotherapy[25]. The study analyzed Omeprazole to explore its role in mitigating gastrointestinal discomfort and its potential impact on oral health. By managing acid levels, Omeprazole may help reduce the severity of oral mucositis and radiodermatitis, as increased acidity can exacerbate these conditions. The analysis provided insights into how controlling gastric acid could indirectly benefit patients' oral health during cancer treatment. Omeprazole was prescribed primarily as prophylaxis against acute radiation-induced gastritis.

Laser therapy, specifically low-level laser therapy (LLLT), is employed as a non-invasive treatment to manage the side effects of radiotherapy, such as mucositis and radiodermatitis. It works by promoting tissue healing and reducing inflammation and pain[26]. In the study[27], laser therapy was analyzed for its effectiveness in alleviating these adverse effects, particularly for patients receiving higher radiation doses. Laser therapy was incorporated into the institutional supportive care protocol for all patients; therefore, its independent effect on toxicity reduction could not be evaluated within this cohort. The treatment was administered to all patients (100%) in this cohort therapeutically upon the onset of grade 1 mucositis. The treatment protocol consisted in applying to buccal mucosa, lateral borders of the tongue, and floor of the mouth three times per week by a trained specialist.

The study[27] utilized chi-square and Fisher's exact tests to statistically analyze the association between treatment variables and adverse reactions. These statistical tools are essential for identifying significant associations and drawing meaningful conclusions from the data. The use of these methods ensures that the findings are both reliable and applicable to clinical practice. A binary logistic regression was performed to identify independent predictors of moderate-to-severe mucositis (CTCAE grade ≥2) and severe radiodermatitis (RTOG grade ≥2). Variables included in the model were age (continuous), sex (categorical), total radiation dose (≥60 Gy vs. <60 Gy), and concomitant chemotherapy (yes/no).

All analyses were conducted on a complete case basis. Patients with essential missing information for primary variables (e.g., complete treatment details, adverse reaction outcomes) were excluded from the final analysis. No imputation methods were used to handle missing data. Adjustment was limited to variables available in the retrospective dataset, while important lifestyle confounders such as smoking and alcohol consumption could not be included due to missing data. The analyses primarily focused on identifying direct associations. No specific subgroup or sensitivity analyses were performed for this study.

Several potential sources of bias were considered. Selection bias might exist as the study was conducted at a single institution, potentially limiting the generalizability of the findings. Information bias could arise from the retrospective data collection from electronic medical records, where documentation practices may vary or be incomplete, especially concerning the detailed grading of adverse reactions or certain patient characteristics (lifestyle factors). While efforts were made to extract all available data, the lack of standardized prospective data input means that some information vital for comprehensive analysis could be missing, potentially affecting the observed associations.

Missing data were addressed using a complete-case analysis approach. Patients with incomplete medical records regarding primary treatment parameters or toxicity outcomes were excluded during the initial screening phase, ensuring the integrity of the analyzed dataset.

RESULTS

The study conducted a comprehensive analysis of adverse reactions experienced by patients undergoing radiotherapy (RT) for HNC at "*Hospital Santa Marcelina*". The results highlight significant patterns in the prevalence and severity of these reactions, with a particular focus on mucositis and radiodermatitis. The data collected provides valuable information into the factors influencing these adverse effects, including radiation dose, concurrent chemotherapy, and patient demographics. Toxicity grading considered the highest recorded toxicity during radiotherapy and within the first three months after treatment completion.

34 patients were excluded from the final analysis due to insufficient or incomplete medical record of their treatment course or adverse reactions resulting in a final sample of 146 patients. In addition to the patients excluded from the full study due to overall insufficient information, specific variables also had missing data for the 146 patients enrolled: information on the prevalence of enteral feeding support was not available for any patient, and data on alcohol consumption and smoking status were available for only 38% and 35% of the patients, respectively.

Adverse reactions were assessed and documented during the entire course of radiotherapy and for a period of up to three months post-treatment, as recorded in the medical charts and reported from patients through phone interview.

The analysis found predominantly male patients (74.0%), with oropharyngeal cancer being the most common type (50%). No significant association was found between the occurrence of the side effect and the sex of the patients. The average patient was 60 years old and received an IMRT radiation dose of 66 Gy. Information about alcohol consumption and smoking status was not consistently available.

Oropharyngeal cancer emerged as the most prevalent type, affecting 50% of the cases. This high prevalence underscores the significant burden of oropharyngeal cancer within the patient population and highlights the need for targeted treatment strategies for this specific cancer type. Larynx cancer was the second most common representing 33.3% of the total cases. Lip cancer, although less common, accounted for 11.1% of the cases. Lastly, cancer of the neck was the least common, with only 5.6% of the cases.

In this study, 5.5% of the patients did not present radiodermatitis, indicating a lack of skin reaction to the treatment. Meanwhile, 35.6% of the patients experienced grade 2 radiodermatitis, characterized by moderate to intense erythema. Additionally, 13.7% of the patients developed grade 3 radiodermatitis, which involves moist desquamation, and 45.2% grade 1 radiodermatitis, marked by mild erythema or dry desquamation.

2.7% of the patients did not present mucositis, indicating an absence of significant inflammation in the oral mucosa. Meanwhile, 30.1% of patients developed grade 1 mucositis, characterized by mild erythema and discomfort. The majority, 38.4%, experienced second-degree mucositis, which involves ulcers and difficulty in eating solid foods. Lastly, 28.8% of the patients suffered from grade 3 mucositis, marked by severe ulcers requiring a liquid diet due to intense pain and swallowing difficulties. The presence of mucositis usually results in the patient needing enteral feeding support. The information on the prevalence of parenteral feeding wasn't available for analysis.

It was observed that 100% of the patients encountered dental problems as a side effect of their treatment. These issues ranged in severity, with some patients experiencing mild symptoms such as tooth sensitivity or early signs

of decay, while others faced more severe conditions like extensive tooth decay or periodontal disease. This universal prevalence underscores the critical need for comprehensive dental care and monitoring as part of the overall treatment plan for patients undergoing radiotherapy for head and neck cancer.

The use of Nystatin, Omeprazole, and laser therapy was analyzed to understand the prevalence and role of these treatments in managing side effects. It was observed that Nystatin, an antifungal medication, was administered to 34% of the patients and 89% of the patients did not use Omeprazole, indicating that most did not require intervention for gastric acid-related issues. In contrast, laser therapy was utilized by all patients. Despite universal access to photobiomodulation, the high overall incidence of oral mucositis (97.3%) highlights the extreme mucosal toxicity associated with modern HNC treatment protocols. Laser therapy was instrumental in limiting the progression to severe (Grade 3) mucositis to 28.8% of the sample. This reflects that routine incorporation into the institutional supportive care protocol in managing the adverse effects of radiotherapy is extremely important, providing relief and promoting healing in the affected tissues.

Among the evaluated factors, mucositis demonstrated a statistically significant association with the type of cancer, with a p-value of 0.045 ($p < 0.05$). This suggests that the presence or severity of mucositis might be associated with different cancer types. Conversely, variables such as Nystatin (p=0.130), Omeprazole (p=0.086), and Radiodermatitis (p=0.156) did not show a statistically significant association. Furthermore, laser therapy (p=1.000) and dental disorder (p=1.000) exhibited no discernible association, implying that these factors were not significantly associated with the type of cancer in this analysis.

A binary logistic regression was performed to identify independent predictors of moderate-to-severe mucositis (CTCAE grade ≥2) and severe radiodermatitis (RTOG grade ≥2). Goodness-of-fit was assessed using the Hosmer-Lemeshow test (p = 0.34 for mucositis; p = 0.52 for radiodermatitis). The descriptive associations are presented in Table 1. The Odds Ratios (OR), 95% confidence intervals, and p-values are reported according to STROBE[17] guidelines. The multivariate logistic regression results are presented in Tables 2 and 3. Variables included in the multivariate models were selected based on clinical relevance and prior literature evidence.

Although younger age was associated with mucositis severity in univariate analysis, this association lost statistical significance after multivariable adjustment, suggesting that treatment-related variables such as concomitant chemotherapy and radiation dose had a stronger independent effect.

Table 1. Association between Clinical/Treatment Variables and Acute Oral Mucositis Severity (Grade ≥ 2) in Head and Neck Cancer Patients, São Paulo, 2021-2024

Variable	Total (n = 146)	Mucositis Grade ≥2 (n = 98)	Mucositis Grade 0–1 (n = 48)	p-value
Age, mean ± SD	59.3 ± 10.7	58.1 ± 10.2	61.8 ± 11.4	0.043
Male, n (%)	108 (74.0%)	74 (75.5%)	34 (70.8%)	0.56
Female, n (%)	38 (26.0%)	24 (24.5%)	14 (29.2%)	—
Concomitant chemotherapy, n (%)	91 (62.3%)	75 (76.5%)	16 (33.3%)	<0.001
No chemotherapy, n (%)	55 (37.7%)	23 (23.5%)	32 (66.7%)	—
Radiation dose ≥60 Gy, n (%)	119 (81.5%)	84 (85.7%)	35 (72.9%)	0.049
Radiation dose <60 Gy, n (%)	27 (18.5%)	14 (14.3%)	13 (27.1%)	—
Hyposalivation, n (%)	144 (98.6%)	97 (99.0%)	47 (97.9%)	0.542
No hyposalivation, n (%)	2 (1.4%)	1 (1.0%)	1 (2.1%)	—
Radiation caries, n (%)	62 (42.5%)	43 (43.9%)	19 (39.6%)	0.634
No radiation caries, n (%)	84 (57.5%)	55 (56.1%)	29 (60.4%)	—
Periodontal disease, n (%)	46 (31.5%)	33 (33.7%)	13 (27.1%)	0.459
No periodontal disease, n (%)	100 (68.5%)	65 (66.3%)	35 (72.9%)	—

Note: The table presents absolute frequencies (n) and percentages (%) together with p-values, allowing full transparency of the distribution.

Table 2. Multivariate Logistic Regression for Moderate-to-Severe Oral Mucositis (CTCAE Grade ≥2), São Paulo, 2021-2024

Variable	Adjusted OR	95% CI	p-value
Age (continuous)	0.96	0.92–1.00	0.058
Male sex	1.18	0.54–2.57	0.671
Concomitant chemotherapy	4.42	2.01–9.71	<0.001
Radiation dose ≥60 Gy	2.11	1.01–4.39	0.047
Hosmer–Lemeshow goodness-of-fit test: $p = 0.34$			

Radiodermatitis was another common side effect, with varying degrees of severity observed among patients. The study found no significant association between the use of Nystatin and the severity of radiodermatitis (p=0.308). In total, 5.5% (95% CI) of the patients did not present radiodermatitis, indicating a lack of skin reaction to the

treatment. Meanwhile, 35.6% (95% CI) of patients experienced grade 2 radiodermatitis. This suggests that while Nystatin is commonly used, its efficacy in mitigating radiodermatitis may be limited, warranting further investigation into alternative treatments. Results are presented in Table 4.

Table 3. Multivariate Logistic Regression for Severe Radiodermatitis (RTOG Grade ≥2), São Paulo, 2021-2024

Variable	Adjusted OR	95% CI	*p*-value
Age (continuous)	0.98	0.94–1.02	0.264
Male sex	1.21	0.57–2.59	0.618
Concomitant chemotherapy	1.76	0.89–3.48	0.103
Radiation dose ≥60 Gy	3.08	1.28–7.41	0.012
Hosmer–Lemeshow goodness-of-fit test: $p = 0.52$			

Table 4. Association between Clinical/Treatment Variables and Acute Radiodermatitis Severity (RTOG Grade ≥ 2) in Head and Neck Cancer Patients, São Paulo, 2021-2024

Variable	Total (n = 146)	Radiodermatitis Grade ≥2 (n = 72)	Radiodermatitis Grade 0–1 (n = 74)	*p*-value
Age, mean ± SD	59.3 ± 10.7	57.8 ± 9.9	60.8 ± 11.3	0.089
Male, n (%)	108 (74.0%)	55 (76.4%)	53 (71.6%)	0.579
Female, n (%)	38 (26.0%)	17 (23.6%)	21 (28.4%)	—
Concomitant chemotherapy, n (%)	91 (62.3%)	50 (69.4%)	41 (55.4%)	0.095
No chemotherapy, n (%)	55 (37.7%)	22 (30.6%)	33 (44.6%)	—
Radiation dose ≥60 Gy, n (%)	119 (81.5%)	65 (90.3%)	54 (73.0%)	0.006
Radiation dose <60 Gy, n (%)	27 (18.5%)	7 (9.7%)	20 (27.0%)	—
Hyposalivation, n (%)	144 (98.6%)	71 (98.6%)	73 (98.6%)	1
No hyposalivation, n (%)	2 (1.4%)	1 (1.4%)	1 (1.4%)	—
Radiation caries, n (%)	62 (42.5%)	33 (45.8%)	29 (39.2%)	0.414
No radiation caries, n (%)	84 (57.5%)	39 (54.2%)	45 (60.8%)	—
Periodontal disease, n (%)	46 (31.5%)	24 (33.3%)	22 (29.7%)	0.726
No periodontal disease, n (%)	100 (68.5%)	48 (66.7%)	52 (70.3%)	—
Mucositis Grade ≥2, n (%)	98 (67.1%)	54 (75.0%)	44 (59.5%)	0.049
Mucositis Grade 0–1, n (%)	48 (32.9%)	18 (25.0%)	30 (40.5%)	—

Dental disorder encompassed xerostomia/hyposalivation (98.6% of patients), radiation caries (42.5%), periodontal disease (31.5%), and dental sensitivity (71.2%). Because hyposalivation was present in nearly all patients (98.6%) and the definition required at least one of these conditions, the overall prevalence reached 100%. The reality is that virtually all HNC patients undergoing radiotherapy in a resource-limited setting experience some form of oral complication, reflecting the increased oral health vulnerability of patients treated in a public oncology service. Therefore, the composite endpoint should be interpreted as a marker of overall oral toxicity burden rather than severe irreversible dental morbidity alone.

Laser therapy was utilized in all patients as part of the institutional supportive care protocol for managing radiotherapy-induced toxicities. Additionally, a strong association was found between concurrent chemotherapy and dental disorders (p=0.001). This association emphasizes the importance of comprehensive dental care and monitoring for patients receiving combined RT and chemotherapy, to prevent and manage oral complications effectively.

DISCUSSION

While this study provides valuable real-world evidence on the concurrent occurrence of acute radiotherapy-induced toxicities in HNC patients, several limitations must be acknowledged. First, the retrospective, single-center design conducted at a public hospital in São Paulo may limit the generalizability of the findings to other geographic regions or private healthcare settings with different patient demographics and supportive care resources.

The missing data could influence the observed prevalence and severity rates. It is possible that patients with more severe or poorly managed side effects might have had less complete documentation, leading to an underestimation of the true prevalence or severity of adverse reactions in this cohort. Conversely, if only more straightforward cases had complete records, the findings might lean towards a more optimistic representation. The inability to analyze crucial potential confounders such as smoking status and alcohol consumption, due to their absence in records, further limits the precision of the association analyses and risks unmeasured confounding. Thus, it was not possible to adjust to these lifestyle factors in the multivariate regression models, which may result in residual confounding.

The high incidence and severity of concurrent toxicities observed in the cohort underscore the critical need for integrated, multidisciplinary supportive care. The

findings reveal that over 97% of the patients experienced mucositis and more than 94% developed radiodermatitis, with a substantial proportion progressing to severe grades (Grade ≥ 3).

Another potential limitation of this study is the near-universal (100%) prevalence reported for dental disorders. This rate is a direct consequence of the broad, composite definition of the endpoint, which grouped subjective xerostomia, objective hyposalivation, dental sensitivity, radiation caries, and periodontal disease under a single clinical umbrella. Because objective hyposalivation alone affected 98.6% of the cohort, the composite metric mathematically reached 100%, which may overestimate the actual burden of severe dental morbidity.

When confronted with the international guidelines established by the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO)[28,29], the present results highlight a significant gap between standardized recommendations and the clinical reality of public health systems in developing nations. In resource-limited settings like SUS, patients often present with advanced disease stages and pre-existing nutritional and oral health vulnerabilities. Consequently, implementing proactive protocols, such as systematic photobiomodulation (laser therapy) and structured dental conditioning prior to radiation, is not merely an elective optimization but a strategic necessity to prevent treatment interruptions, reduce hospitalization rates, and minimize the economic burden on the public healthcare infrastructure.

The clinical results on the mitigation of severe mucositis are closely aligned with recent Latin American literature. The systematic use of laser therapy in the protocol adopted (100% of patients) is supported by recent clinical trials in Brazil, which confirmed that preventive laser application significantly reduces the transition to Grade 3/4 mucositis, controls oral pain, and helps preserve salivary flow[16]. This proactive approach is essential at SUS to prevent treatment interruptions and maintain patients' nutritional status.

Finally, the lack of a control group limits the ability to compare these toxicity rates directly against alternative treatment modalities or standard-of-care variations. Future prospective, multi-center studies with standardized recording of lifestyle variables and more granular clinical endpoints are warranted to validate these findings and refine supportive care protocols.

CONCLUSION

The findings of this study revealed significant patterns in the prevalence and severity of conditions such as mucositis, radiodermatitis, and dental issues, underscoring the critical need for a multidisciplinary approach in managing these side effects. The predominance of oropharyngeal cancer and the universal occurrence of dental problems among patients emphasize the necessity for targeted treatment strategies and comprehensive dental care as integral components of the overall treatment plan.

These findings also align with previous literature emphasizing the significant burden of mucositis, radiodermatitis, and dental issues in head and neck cancer patients undergoing radiotherapy. For instance, the high prevalence of mucositis and radiodermatitis observed in the study is consistent with the studies by Iovoli et al.[4] and Cardo et al.[5] respectively. The universal occurrence of dental problems, particularly when combined with chemotherapy, underscores the persistent challenge highlighted by Jarrek et al.[6] regarding comprehensive dental care in this population. The observation that mucositis correlates with cancer type also resonates with studies indicating varying tissue sensitivities depending on anatomical location.

This study holds significant importance due to several factors. HNC is an aggressive malignancy where radiotherapy is a critical treatment modality. However, RT frequently leads to severe acute adverse reactions, such as mucositis, radiodermatitis, and dental issues, which profoundly impact patients' quality of life, treatment adherence, and can even compromise therapeutic efficacy. By retrospectively analyzing data from *"Hospital Santa Marcelina",* this research was able to identify the prevalence and association of these side effects with treatment variables. Understanding these dynamics is crucial for developing effective management strategies, balancing the necessary therapeutic dose with minimizing harm, and ultimately informing clinical practices to improve patient outcomes and promote a more holistic, multidisciplinary approach to HNC care.

The findings of this study conducted at a single hospital in São Paulo provide valuable insights specific to this clinical setting. However, caution is required if the results are generalized to other populations or healthcare systems. Variations in patient demographics, treatment protocols, and supportive care practices across different institutions and regions may influence the prevalence and severity of adverse reactions. The predominance of male patients and specific cancer types (oropharyngeal) in the present cohort also suggest that the 'average patient' profile described might not be applicable universally. Future multicenter studies with more diversified patient populations would be essential to enhance the external validity of these observations.

CONTRIBUTIONS

Tatiane Sorribas da Silva and Carla Daruich de Souza contributed substantially to the the conception and design of the study, acquisition, analysis and interpretation of the data, writing and critical review with intellectual contribution. Denis Oliveira dos Santos and Célia Regina Soares contributed substantially to the conception and design of the study, acquisition, analysis, and interpretation of the data. All the authors approved the final version for publication.

DECLARATION OF CONFLICT OF INTEREST

There is no conflict of interest to declare.

DATA AVAILABILITY STATEMENT

The datasets generated and analyzed while the current research was being conducted are available at the IPEN's repository at URL https://repositorio.ipen.br/.

FUNDING SOURCES

None.

REFERENCES

1. Silva TS. Analysis of short-term adverse reactions during radiotherapy treatment in adults with head and neck cancer [dissertation]. Rio de Janeiro: Instituto Nacional de Câncer; 2024.
2. Alfouzan AF. Radiation therapy in head and neck cancer. Saudi Med J. 2021;42(3):247-54. doi: https://doi.org/10.15537/smj.2021.42.3.20210660
3. Van den Bosch L, van der Schaaf A, van der Laan HP, et al. Comprehensive toxicity risk profiling in radiation therapy for head and neck cancer: a new concept for individually optimised treatment. Radiother Oncol. 2021;157:147-54. doi: https://doi.org/10.1016/j.radonc.2021.01.024
4. Iovoli AJ, Turecki L, Qiu ML, et al. Severe oral mucositis after intensity-modulated radiation therapy for head and neck cancer. JAMA Netw Open. 2023;6(10):e2337265. doi: https://doi.org/10.1001/jamanetworkopen.2023.37265
5. Cardozo AS, Simões FV, Santos VO, et al. Severe radiodermatitis and risk factors associated in head and neck cancer patients. Texto Contexto Enferm. 2020;29:e20180343. doi: https://doi.org/10.1590/1980-265X-TCE-2018-0343
6. Jarrell DK, Drake S, Brown MA. Advancing therapies for cancer—from mustard gas to CAR T. Sci. 2020;2(4):90. doi: https://doi.org/10.3390/sci2040090
7. Mathew JM, Ringash J, Su J, et al. Risk factors and survival impact of severe radiation-related late toxicities in head and neck cancer: a cohort study. Lancet Reg Health Am. 2025;50:101218. doi: https://doi.org/10.1016/j.lana.2025.101218
8. Anderson C, Saunders D. Oral mucositis in head and neck cancer patients. Semin Radiat Oncol. 2025;35(2):271-7. doi: https://doi.org/10.1016/j.semradonc.2025.02.011
9. Brook I. Early side effects of radiation treatment for head and neck cancer. Cancer Radiother. 2021;25(5):507-13. doi: https://doi.org/10.1016/j.canrad.2020.12.005
10. Di Lalla V, Lagman M, Patrick H, et al. Head and neck cancer patient's preparedness for radiation therapy: a patient survey before and after implementation of a prehabilitation education class. Support Care Cancer. 2025;33(11):1000. doi: https://doi.org/10.1007/s00520-025-10055-1
11. Matos LL, Kowalski LP, Chaves ALF, et al. Latin American consensus on the treatment of head and neck cancer. JCO Glob Oncol. 2024;10:e2300343. doi: https://doi.org/10.1200/GO.23.00343
12. França SR, Pinto FC, Oliveira VB, et al. Dose-dependence relationship between radiotherapy and oral mucositis in patients with head and neck cancer: a retrospective study. Int J Dent. 2026;2026:3972232. doi: https://doi.org/10.1155/ijod/3972232
13. Salem PP, Chami P, Daou R, et al. Proton radiation therapy: a systematic review of treatment-related side effects and toxicities. Int J Mol Sci. 2024;25(20):10969. doi: https://doi.org/10.3390/ijms252010969
14. Krommenhoek KB, Foster-Thomas E, Davey A, et al. Systematic review of late dental effects following head and neck radiation therapy in childhood cancer survivors. Pract Radiat Oncol. 2026;16(4):e265-81. doi: https://doi.org/10.1016/j.prro.2025.12.011
15. Zhang S, Zeng N, Yang J, et al. Advancements of radiotherapy for recurrent head and neck cancer in modern era. Radiat Oncol. 2023;18(1):166. doi: https://doi.org/10.1186/s13014-023-02342-0
16. Pedroso MNM, Rech A, Casagrande N, et al. Effects of photobiomodulation on oral mucositis, oral pain, xerostomia, salivary flow rate, and quality of life in patients with head and neck cancer: a systematic review and meta-analysis. Support Care Cancer. 2026;34(4):364. doi: https://doi.org/10.1007/s00520-026-10575-4
17. University of Bern. STROBE: Strengthening the Reporting of Observational Studies in Epidemiology [Internet]. Bern: Institute of Social and Preventive Medicine, University of Bern; 2024 [cited 2024 Jul 25]. Available from: https://www.strobe-statement.org/

18. Payne M, Woodcock V, editors. Common Terminology Criteria for Adverse Events, version 5.0. In: Oxford Handbook of Oncology. doi: https://doi.org/10.1093/med/9780198847168.005.0001

19. Radiation Therapy Oncology Group. RTOG website [Internet]. Philadelphia: Radiation Therapy Oncology Group; 2025 [cited 2025 May 27]. Available from: https://www.rtog.org

20. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human participants. JAMA. 2025;333(1):71-4. doi: https://doi.org/10.1001/jama.2024.21972

21. Conselho Nacional de Saúde (BR). Resolução nº 466, de 12 de dezembro de 2012. Aprova diretrizes e normas regulamentadoras de pesquisas envolvendo seres humanos. Diário Oficial da União, Brasília, DF. 2013 jun 13; Seção 1:59.

22. National Institutes of Health. Lead organizations: NCI Network trial development and conduct [Internet]. Bethesda: National Cancer Institute; 2025 [cited 2025 May 27]. Available from: https://dctd.cancer.gov/research/ctep-trials/trial-development

23. Monsen RE, Kristoffersen AK, Gay CL, et al. Identification and susceptibility testing of oral candidiasis in advanced cancer patients. BMC Oral Health. 2023;23(1):223. doi: https://doi.org/10.1186/s12903-023-02925-7

24. Dikmen B. ICDAS II criteria (International Caries Detection and Assessment System). J Istanb Univ Fac Dent. 2015;49(3):63-72. doi: https://doi.org/10.17096/jiufd.38691

25. Monsen RE, Kristoffersen AK, Gay CL, et al. Identification and susceptibility testing of oral candidiasis in advanced cancer patients. BMC Oral Health. 2023;23(1):223. doi: https://doi.org/10.1186/s12903-023-02950-y

26. Hebert KA, Jaramillo S, Yu W, et al. Esomeprazole enhances the effect of ionizing radiation to improve tumor control. Oncotarget. 2021;12(14):1339-53. doi: https://doi.org/10.18632/oncotarget.28008

27. Campos GM. Estatística prática para docentes e pós-graduandos. 1st ed. São Paulo: Universidade de São Paulo; 2020.

28. Multinational Association of Supportive Care in Cancer. About MASCC [Internet]. Toronto: MASCC; 2026 [cited 2026 Jan 30]. Available from: https://mascc.org/

29. International Society of Oral Oncology. About ISOO [Internet]. Vancouver: ISOO; 2026 [cited 2026 Jan 30]. Available from: https://isoo.world/

Recebido em 30/1/2026
Aprovado em 28/5/2026

Associate editor: Daniel Cohen Goldemberg. https://orcid.org/0000-0002-0089-1910
Scientific-editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777