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Evaluation of Radiotherapy-Related Oral Complications and Functional Outcomes in Patients with Oral Cavity Carcinoma

Mert Kutsal

mertkutsal@gmail.com

Ege University

Sema Becerik

Ege University

Seray Koska

Ege University

Ozlem Ozkaya Akagunduz

Ege University

Kaan Koca

Ege University

Mehmet Orman

Ege University

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Abstract

Objective

Radiotherapy (RT), a major treatment modality for head and neck cancers, may cause oral complications such as mucositis, xerostomia, dysphagia, and taste dysfunction, negatively affecting patients' quality of life and treatment compliance. This study aimed to evaluate the relationship between RT-related oral complications and periodontal status, radiation dose, volumetric parameters, and tumor localization in patients with oral cavity cancer.

Methods

Twenty-eight patients who underwent surgery for oral cavity cancer and were scheduled for RT were included in this prospective study. Clinical periodontal examinations and saliva and gingival crevicular fluid (GCF) sampling were performed at baseline (T0) and at the 8th week of RT (T1). Plaque index, bleeding on probing, probing depth, and clinical attachment levels were recorded. RT-related oral complications, including mucositis, xerostomia, dysphagia, trismus, taste loss, and osteoradionecrosis, were monitored throughout treatment. Statistical analyses included descriptive, comparative, and correlation analyses, with $p < 0.05$ considered statistically significant.

Results

GCF values increased from 50.80 ± 36.53 at T0 to 55.32 ± 36.31 at T1, whereas saliva values decreased from 1.70 ± 1.33 to 1.33 ± 1.32; however, neither change reached statistical significance ($p = 0.655$ and $p = 0.084$, respectively). According to RT dose groups, no significant changes were observed in GCF levels, while saliva values demonstrated a significant decrease over time in one RT dose classification ($p = 0.042$). Mucositis was the most common complication (82.1%), predominantly Grade 1–2, followed by xerostomia (39.3%) and dysphagia (35.7%). No significant associations were identified between RT dose, RT volume, tumor localization, periodontal status, and most treatment-related complications ($p > 0.05$).

Conclusion

Oral complications are common in patients with oral cavity cancer undergoing RT, with mucositis representing the most frequent adverse effect. The findings suggest that RT-related complications may develop through multifactorial mechanisms rather than being solely dependent on treatment-related parameters. Therefore, multidisciplinary oral evaluation and supportive care remain important components of patient management during RT.

1. Introduction

Head and neck squamous cell carcinoma (HNSCC) represents one of the most common malignancies worldwide and accounts for nearly 90% of all head and neck cancers (1). Oral squamous cell carcinoma (OSCC), the predominant subtype of oral cavity cancer, remains a major public health concern because of its considerable morbidity and mortality. Tobacco use, alcohol consumption, poor oral hygiene, chronic inflammation, and viral infections such as human papillomavirus (HPV) have been identified as major etiological factors in the development of these malignancies (2, 3). Despite advances in diagnostic techniques and therapeutic approaches, a substantial proportion of patients continue to be diagnosed at advanced stages, which negatively affects treatment outcomes and long-term survival (4, 5). In addition to survival-related concerns, oral cavity cancers and their treatment may significantly impair essential functions such as speech, mastication, swallowing, and oral hygiene maintenance, thereby substantially reducing quality of life (6).

The management of oral cavity cancers generally involves surgery, radiotherapy (RT), chemotherapy (CT), or multimodal treatment combinations depending on tumor stage and localization (7). Among these modalities, RT plays a central role, particularly in patients with advanced-stage disease, positive surgical margins, lymphovascular invasion, or nodal involvement. However, although RT contributes significantly to local tumor control, irradiation of the oral and maxillofacial region frequently leads to acute and chronic oral complications that may compromise both treatment continuity and patient well-being (8). Common RT-related complications include oral mucositis, xerostomia, dysphagia, taste dysfunction, trismus, radiation caries, periodontal deterioration, and osteoradionecrosis (9, 10). The severity of these complications may vary according to several factors, including total radiation dose, irradiated tissue volume, tumor localization, concurrent chemotherapy, and patient-related oral conditions. In severe cases, these adverse effects may result in nutritional impairment, weight loss, interruption of cancer therapy, increased hospitalization rates, and deterioration in overall quality of life (11, 12).

Among RT-associated oral toxicities, salivary dysfunction and periodontal alterations are of particular clinical importance. Radiation exposure to salivary glands may reduce both salivary quantity and quality, resulting in hyposalivation, alterations in salivary pH, and disruption of the oral microbial ecosystem (13, 14). These changes may facilitate the development of opportunistic infections, mucosal injury, dental caries, and periodontal disease. Previous studies have also demonstrated that RT may alter the oral microbiota toward a more pathogenic composition associated with periodontal inflammation (15, 16). Furthermore, pre-existing periodontal disease has been associated with increased severity of treatment-related complications such as oral mucositis and osteoradionecrosis (17, 18). Since periodontal inflammation itself may contribute to tissue destruction and impaired healing capacity, the interaction between periodontal status and RT-related oral complications has become an increasingly important area of investigation. In this context, saliva and gingival crevicular fluid may provide valuable information regarding inflammatory and biological alterations occurring during RT because of their noninvasive and easily accessible nature.

Although numerous studies have evaluated RT-related adverse effects in patients with head and neck cancer, the relationship between oral complications and factors such as periodontal status, radiation dose, volumetric RT parameters, and tumor localization remains insufficiently clarified. In particular, limited evidence exists regarding changes in salivary and gingival crevicular fluid parameters during RT in patients with oral cavity carcinoma. Moreover, RT-associated complications appear to demonstrate a multifactorial pattern that cannot be explained solely by conventional dose-response relationships. Therefore, a better understanding of the interactions between radiation exposure, tumor characteristics, periodontal status, and oral complications may contribute to improved preventive strategies and supportive oral care protocols for patients undergoing RT. Accordingly, the aim of the present study was to evaluate the relationship between RT-related oral complications and periodontal status, tumor localization, radiation dose, and volumetric RT parameters in patients with oral cavity cancer undergoing radiotherapy.

2. Material & Methods

2.1. Study Design and Participants

This prospective observational study was conducted in patients diagnosed with oral cavity cancer who had undergone surgical treatment and were scheduled to receive radiotherapy (RT) at the Department of Radiation Oncology, Ege University Faculty of Medicine. Ethical approval was obtained from the Clinical Research Ethics Committee of Ege University Faculty of Medicine (Decision No: 25 – 3.1/7; March 28, 2025), and all procedures were performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Patients aged ≥ 18 years with a diagnosis of oral cavity cancer and indication for postoperative RT were included in the study. Patients with previous head and neck RT, uncontrolled systemic disease, pregnancy, lactation, incomplete treatment, or non-compliance with follow-up were excluded. Initially, 52 patients were enrolled; however, the study was completed with 28 participants because of loss to follow-up.

Prior to RT, all patients underwent routine dental evaluation at the Faculty of Dentistry, Ege University. Necessary dental treatments, including extraction of teeth with poor prognosis, non-surgical periodontal therapy, restorative treatment, endodontic treatment, and oral hygiene instruction, were completed before RT initiation.

2.2. Clinical Protocol

Clinical evaluations were performed on the first day of RT (T0) and at the 8th week of treatment (T1). At both time points, unstimulated saliva and gingival crevicular fluid (GCF) samples were collected, and periodontal clinical parameters were recorded. In addition, RT-related oral complications were monitored throughout the treatment period.

Demographic data and body weight measurements were recorded at baseline. Periodontal examination included plaque index (PI), bleeding on probing (BOP), probing pocket depth (PPD), and clinical attachment level (CAL). All measurements were performed using a UNC-15 periodontal probe (Hu-Friedy, Chicago, IL, USA). Periodontal status was classified according to the 2017 World Workshop classification of periodontal diseases (19).

2.3. Saliva and Gingival Crevicular Fluid Collection

Participants were instructed to avoid eating, drinking, and tooth brushing for at least 2 hours before sample collection. Unstimulated saliva samples were obtained by passive expectoration into sterile plastic containers for 5 minutes in a quiet clinical environment. Saliva volume was measured using micropipettes.

For GCF sampling, the collection area was isolated with cotton rolls and gently air-dried to minimize salivary contamination. Supragingival plaque was removed when necessary. Paper strips (Periopaper®, Oraflow, NY, USA) were inserted into the gingival sulcus at the approximal surface of selected teeth for 30 seconds. Samples contaminated with blood or saliva were discarded and recollected. GCF volume was measured using a Periotron 8000® device (Oraflow, USA).

GCF samples were obtained from four teeth in dentate individuals (n = 21). In edentulous patients (n = 5), only saliva samples were collected, whereas in partially dentate individuals with insufficient teeth (n = 2), sampling was performed from the available teeth.

2.4. Assessment of Oral Complications

Patients were monitored throughout RT for treatment-related oral complications, including oral mucositis, dysphagia, trismus, xerostomia, taste loss, pain, submental edema, and osteoradionecrosis. Mucositis severity was evaluated by intraoral examination and graded according to the World Health Organization (WHO) classification system.

2.5. Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive data were expressed as mean ± standard deviation for continuous variables and as number and percentage for categorical variables. Normality was assessed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Parametric and non-parametric comparisons were performed using the independent samples t-test and Mann–Whitney U test, respectively. Associations between categorical variables were analyzed using chi-square or Fisher's Exact tests when appropriate. Correlation analyses were conducted using Pearson or Spearman correlation coefficients according to data distribution. A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Demographic Characteristics and Periodontal Status

A total of 52 patients were initially enrolled; however, the study was completed with 28 participants because of loss to follow-up. The study population consisted of 16 males (57.1%) and 12 females (42.9%), with a mean age of 59.46 ± 13.06 years. Most participants were between 46 and 65 years of age (53.6%). Smoking prevalence was significantly higher in males than females (56.3% vs. 8.3%, $p = 0.012$), whereas alcohol consumption showed no sex-related difference. Gingivitis was the predominant periodontal condition (67.9%), followed by periodontitis (21.4%), while 10.7% of participants were completely edentulous. (Table 1)

Table 1
Demographic Characteristics, Systemic Diseases, and Periodontal Status Distribution

Variable	Total (n = 28)	Male (n = 16)	Female (n = 12)	p-value
Age (Mean ± SD)	59.46 ± 13.06	58.38 ± 14.03	60.92 ± 12.09	0.612
Age Groups				**0.312**
18–45 years	4	3	1	
46–65 years	15	7	8	
66–80 years	8	6	2	
≥ 81 years	1	0	1	
Smoking Status				**0.012***
Smoker	10	9	1	
Non-smoker	18	7	11	
Alcohol Consumption				**0.182**
Alcohol use	6	5	1	
No alcohol use	22	11	11	
Comorbid Systemic Diseases				
Hypertension	12	5	7	0.250
Diabetes mellitus	2	1	1	1.000
Cardiovascular disease	7	3	4	0.418
COPD / Asthma	2	1	1	1.000
Periodontal Status				**0.687**
Healthy	0	0	0	
Gingivitis	19	10	9	
Periodontitis	6	3	3	
Completely edentulous	3	3	0	

3.2. Tumor Localization

The tongue was the most common tumor localization (50.0%), followed by the alveolar ridge (21.4%) and maxilla/hard palate (10.7%). Tumor localizations were additionally categorized according to anatomical localization and proximity to major salivary glands for subgroup analyses. (Table 2)

Table 2
Distribution of Tumor Localization

Category	n	%
Tumor Localization		
Tongue	14	50.0
Alveolar ridge	6	21.4
Mandible	1	3.6
Maxilla / Hard-Soft Palate	3	10.7
Retromolar trigone	1	3.6
Buccal mucosa	2	7.1
Lower lip	1	3.6
Tumor Localization 1		
Type 1	12	42.9
Type 2	16	57.1
Tumor Localization 2		
Type 1	16	57.1
Type 2	12	42.9

3.3. Time-Dependent Changes in GCF, Saliva, and Clinical Parameters

Mean gingival crevicular fluid (GCF) values demonstrated a non-significant increase from baseline to follow-up (50.80 ± 36.53 vs. 55.32 ± 36.31; p = 0.655). Saliva values showed a decreasing trend during RT (1.70 ± 1.33 vs. 1.33 ± 1.32), although this change did not reach statistical significance (p = 0.084). (Table 3)

Table 3
Time-Dependent Changes in GCF and Saliva Values

Parameter	Time	Mean ± SD	p-value
GCF (µL)	T0	50.80 ± 36.53	
	T1	55.32 ± 36.31	0.655
Saliva (mL)	T0	1.70 ± 1.33	
	T1	1.33 ± 1.32	0.084

Bleeding on probing increased from 71.4% at baseline to 78.6% at follow-up, whereas plaque was detected in all participants at both time points. (Table 4)

Table 4
Distribution of Bleeding and Plaque Parameters at Baseline and Follow-up

Parameter	Present n (%)	Absent n (%)
Bleeding on Probing (T0)	20 (71.4%)	8 (28.6%)
Bleeding on Probing (T1)	22 (78.6%)	6 (21.4%)
Plaque Presence (T0)	28 (100%)	0 (0%)
Plaque Presence (T1)	28 (100%)	0 (0%)

3.4. Association Between Changes in GCF and Saliva Levels and Radiotherapy Dose

No significant time-dependent changes or group–time interactions were observed for GCF values according to RT dose groups ($p > 0.05$). In contrast, saliva values demonstrated a significant time effect in the primary RT dose classification ($p = 0.042$). Although saliva levels also decreased in the secondary RT dose groups, this change did not reach statistical significance ($p = 0.089$). No significant interaction effects were identified between dose groups and time for saliva values. (Table 5)

Table 5
Association Between Changes in GCF and Saliva Levels and Radiotherapy Dose

Parameter	RT Dose	Group	T0 (Mean ± SD)	T1 (Mean ± SD)	Time p-value	Interaction p-value
GCF (µL)	RT Dose 1	1	57.73 ± 41.35	55.80 ± 35.66	0.493	0.387
	RT Dose 1	2	37.81 ± 21.88	54.41 ± 39.98		
	RT Dose 2	1	51.83 ± 32.07	58.60 ± 35.69	0.647	0.847
	RT Dose 2	2	50.02 ± 40.91	52.79 ± 38.02		
Saliva (mL)	RT Dose 1	1	1.48 ± 1.06	1.29 ± 1.22	0.042*	0.222
	RT Dose 1	2	2.16 ± 1.76	1.43 ± 1.57		
	RT Dose 2	1	1.83 ± 1.01	1.43 ± 1.37	0.089	0.867
	RT Dose 2	2	1.57 ± 1.62	1.24 ± 1.30		

3.5. Association Between Changes in GCF and Saliva Levels and Radiotherapy Volume

Correlation analyses demonstrated no statistically significant association between RT volumetric parameters and GCF or saliva measurements at either baseline or follow-up ($p > 0.05$). (Table 6)

Table 6
Correlation Between Radiotherapy Volume and Changes in GCF and Saliva Levels

Parameter	Time	Volume Parameter	r	p-value
GCF (µL)	T0	Maximum RT Volume	0.045	0.837
	T1	Maximum RT Volume	0.032	0.884
	T0	Secondary Volume	-0.044	0.842
	T1	Secondary Volume	0.023	0.919
Saliva (mL)	T0	Maximum RT Volume	0.138	0.484
	T1	Maximum RT Volume	0.003	0.987
	T0	Secondary Volume	0.083	0.676
	T1	Secondary Volume	0.194	0.323

3.6. Association Between Changes in GCF and Saliva Levels and Tumor Localization

No significant differences in GCF changes were observed between tumor localization groups in either classification model ($p > 0.05$). Saliva values showed a decreasing trend over time in both localization models. Although the overall time effect was not statistically significant, a significant group–time interaction was identified in the salivary gland proximity classification model ($p = 0.047$). (Table 7)

Table 7
Association Between Tumor Localization and Changes in GCF and Saliva Levels

Parameter	Tumor Localization	Group	T0 (Mean ± SD)	T1 (Mean ± SD)	Time p-value	Group × Time p-value
GCF (µL)	Tumor Localization 1	1	58.03 ± 45.67	57.14 ± 37.14	0.736	0.540
	Tumor Localization 1	2	46.16 ± 30.26	54.14 ± 37.12		
Saliva (mL)	Tumor Localization 1	1	2.05 ± 1.61	1.39 ± 1.57	0.059	0.445
	Tumor Localization 1	2	1.44 ± 1.06	1.29 ± 1.14		
GCF (µL)	Tumor Localization 2	1	46.40 ± 31.48	55.31 ± 38.37	0.710	0.672
	Tumor Localization 2	2	56.52 ± 43.32	55.33 ± 35.48		
Saliva (mL)	Tumor Localization 2	1	1.19 ± 0.75	1.06 ± 1.02	0.055	0.047*
	Tumor Localization 2	2	2.38 ± 1.64	1.69 ± 1.61		

Tumor Localization 1: Group 1 = Vestibulum oris; Group 2 = Cavitas oris propria.

Tumor Localization 2: Group 1 = Adjacent to major salivary glands; Group 2 = Distant from major salivary glands.

3.7. Distribution of Oral Complications and Adverse Effects

The most frequently observed oral complication was mucositis (82.1%), followed by xerostomia (39.3%) and dysphagia (35.7%). Trismus and submental edema were each observed in 21.4% of participants, while taste loss was reported in 10.7%. Osteoradionecrosis and pain-related complaints were rare, each affecting one patient (3.6%). (Table 8)

Table 8
Distribution of Oral Complications and Adverse Effects

Variable	n (%) (n = 28)
Mucositis	23 (82.1%)
Trismus	6 (21.4%)
Dysphagia	10 (35.7%)
Taste loss	3 (10.7%)
Xerostomia	11 (39.3%)
Pain	6 (21.4%)
Submental edema	1 (3.6%)
Osteoradionecrosis	1 (3.6%)

3.8. Distribution of Mucositis Severity

Grade 1 and Grade 2 mucositis were the most common findings (35.7% and 39.3%, respectively). Grade 3 mucositis was observed in two patients (7.1%), whereas no Grade 4 mucositis was detected in the study population. (Table 9)

Table 9
Distribution of Mucositis Severity

Mucositis Grade	n (%) (n = 28)
Grade 0	5 (17.9%)
Grade 1	10 (35.7%)
Grade 2	11 (39.3%)
Grade 3	2 (7.1%)
Grade 4	0 (0%)

3.9. Association Between Radiotherapy Dose and Adverse Effects

No statistically significant associations were found between RT dose groups and mucositis severity, trismus, xerostomia, or pain ($p > 0.05$). Dysphagia demonstrated a significant association with the secondary RT dose classification ($p = 0.002$), while a borderline association was observed in the primary RT dose classification ($p = 0.061$). (Table 10)

Table 10
Association Between Radiotherapy Dose and Oral Complications

Complication	Category	RT Dose1-1	RT Dose1-2	p-value	RT Dose2-1	RT Dose2-2	p-value
Mucositis	Grade 0	2 (10.5)	3 (33.3)	0.413	2 (14.3)	3 (21.4)	0.875
	Grade 1	7 (36.8)	3 (33.3)		6 (42.9)	4 (28.6)	
	Grade 2	8 (42.1)	3 (33.3)		5 (35.7)	6 (42.9)	
	Grade 3	2 (10.5)	0 (0.0)		1 (7.1)	1 (7.1)	
Trismus	Absent	15 (78.9)	7 (77.8)	1.000	11 (78.6)	11 (78.6)	1.000
	Present	4 (21.1)	2 (22.2)		3 (21.4)	3 (21.4)	
Dysphagia	Absent	10 (52.6)	8 (88.9)	0.061	5 (35.7)	13 (92.9)	0.002*
	Present	9 (47.4)	1 (11.1)		9 (64.3)	1 (7.1)	
Xerostomia	Absent	11 (57.9)	6 (66.7)	0.657	7 (50.0)	10 (71.4)	0.246
	Present	8 (42.1)	3 (33.3)		7 (50.0)	4 (28.6)	
Pain	Absent	14 (73.7)	8 (88.9)	0.630	9 (64.3)	13 (92.9)	0.165
	Present	5 (26.3)	1 (11.1)		5 (35.7)	1 (7.1)	

3.10. Association Between Radiotherapy Volume and Adverse Effects

No statistically significant associations were identified between RT volumetric parameters and oral complications, including mucositis, trismus, dysphagia, xerostomia, or pain ($p > 0.05$). (Table 11)

Table 11
Association Between Radiotherapy Volume and Oral Complications

Complication	Category	n	Maximum Volume (Mean ± SD)	p-value	Secondary Volume (Mean ± SD)	p-value
Mucositis	Grade 0	5	44.62 ± 32.05	0.898	182.52 ± 143.49	0.846
	Grade 1	10	46.82 ± 50.68		135.14 ± 97.44	
	Grade 2	11	29.94 ± 17.81		120.08 ± 76.92	
	Grade 3	2	38.95 ± 35.71		125.80 ± 84.00	
Trismus	Absent	22	42.19 ± 37.99	0.604	137.94 ± 100.93	0.935
	Present	6	28.40 ± 20.66		133.63 ± 82.21	
Dysphagia	Absent	18	39.66 ± 25.32	0.286	138.99 ± 97.85	0.906
	Present	10	38.47 ± 49.93		133.47 ± 97.09	
Xerostomia	Absent	17	44.88 ± 40.46	0.329	153.54 ± 99.28	0.175
	Present	11	30.50 ± 24.01		111.49 ± 88.49	
Pain	Absent	22	35.26 ± 22.75	0.978	145.95 ± 97.64	0.214
	Present	6	53.80 ± 64.58		104.27 ± 88.78	

3.11. Association Between Tumor Localization and Adverse Effects

Tumor localization was not significantly associated with mucositis severity or other treatment-related complications, including trismus, dysphagia, xerostomia, and pain ($p > 0.05$). (Table 12)

Table 12
Association Between Tumor Localization and Oral Complications

Complication	Category	TL1-1 (n = 12)	TL1-2 (n = 16)	p-value	TL2-1 (n = 16)	TL2-2 (n = 12)	p-value
Mucositis	Grade 0	1 (8.3)	4 (25.0)	0.157	4 (25.0)	1 (8.3)	0.157
	Grade 1	7 (58.3)	3 (18.8)		3 (18.8)	7 (58.3)	
	Grade 2	3 (25.0)	8 (50.0)		8 (50.0)	3 (25.0)	
	Grade 3	1 (8.3)	1 (6.3)		1 (6.3)	1 (8.3)	
Trismus	Absent	9 (75.0)	13 (81.3)	1.000	12 (75.0)	10 (83.3)	0.673
	Present	3 (25.0)	3 (18.8)		4 (25.0)	2 (16.7)	
Dysphagia	Absent	9 (75.0)	9 (56.3)	0.306	9 (56.3)	9 (75.0)	0.306
	Present	3 (25.0)	7 (43.8)		7 (43.8)	3 (25.0)	
Xerostomia	Absent	6 (50.0)	11 (68.8)	0.315	9 (56.3)	8 (66.7)	0.576
	Present	6 (50.0)	5 (31.3)		7 (43.8)	4 (33.3)	
Pain	Absent	10 (83.3)	12 (75.0)	0.673	12 (75.0)	10 (83.3)	0.673
	Present	2 (16.7)	4 (25.0)		4 (25.0)	2 (16.7)	

3.12. Association Between Flap Surgery and Adverse Effects

No statistically significant relationship was observed between flap surgery and mucositis severity or other oral complications, including trismus, dysphagia, xerostomia, and pain ($p > 0.05$). (Table 13)

Table 13
Association Between Flap Surgery and Oral Complications

Complication	Category	No Flap (n = 9, %)	Flap Present (n = 19, %)	Total (n = 28, %)	p-value
Mucositis	Grade 0	1 (11.1)	4 (21.1)	5 (17.9)	0.413
	Grade 1	5 (55.6)	5 (26.3)	10 (35.7)	
	Grade 2	3 (33.3)	8 (42.1)	11 (39.3)	
	Grade 3	0 (0.0)	2 (10.5)	2 (7.1)	
Trismus	Absent	8 (88.9)	14 (73.7)	22 (78.6)	0.630
	Present	1 (11.1)	5 (26.3)	6 (21.4)	
Dysphagia	Absent	5 (55.6)	13 (68.4)	18 (64.3)	0.507
	Present	4 (44.4)	6 (31.6)	10 (35.7)	
Xerostomia	Absent	5 (55.6)	12 (63.2)	17 (60.7)	0.700
	Present	4 (44.4)	7 (36.8)	11 (39.3)	
Pain	Absent	6 (66.7)	16 (84.2)	22 (78.6)	0.352
	Present	3 (33.3)	3 (15.8)	6 (21.4)	

3.13. Association Between Additional Chemotherapy and Adverse Effects

Additional chemotherapy was not significantly associated with mucositis severity, trismus, dysphagia, xerostomia, or pain ($p > 0.05$). However, xerostomia frequency demonstrated a borderline increase in patients receiving chemotherapy ($p = 0.076$). (Table 14)

Table 14
Association Between Additional Chemotherapy and Oral Complications

Complication	Category	No Chemotherapy (n = 7, %)	Chemotherapy Present (n = 21, %)	Total (n = 28, %)	p-value
Mucositis	Grade 0	0 (0.0)	5 (23.8)	5 (17.9)	0.413
	Grade 1	3 (42.9)	7 (33.3)	10 (35.7)	
	Grade 2	2 (28.6)	9 (42.9)	11 (39.3)	
	Grade 3	2 (28.6)	0 (0.0)	2 (7.1)	
Trismus	Absent	7 (100.0)	15 (71.4)	22 (78.6)	0.288
	Present	0 (0.0)	6 (28.6)	6 (21.4)	
Dysphagia	Absent	3 (42.9)	15 (71.4)	18 (64.3)	0.207
	Present	4 (57.1)	6 (28.6)	10 (35.7)	
Xerostomia	Absent	2 (28.6)	15 (71.4)	17 (60.7)	0.076
	Present	5 (71.4)	6 (28.6)	11 (39.3)	
Pain	Absent	5 (71.4)	17 (81.0)	22 (78.6)	0.622
	Present	2 (28.6)	4 (19.0)	6 (21.4)	

3.14. Association Between Baseline Periodontal Status and Adverse Effects

No statistically significant relationship was found between baseline periodontal status and mucositis severity, trismus, dysphagia, xerostomia, or pain ($p > 0.05$). (Table 15)

Table 15
Association Between Baseline Periodontal Status and Oral Complications

Complication	Category	Gingivitis (n = 19, %)	Periodontitis (n = 6, %)	Completely Edentulous (n = 3, %)	Total (n = 28, %)	p-value
Mucositis	Grade 0	4 (21.1)	0 (0.0)	1 (33.3)	5 (17.9)	0.579
	Grade 1	7 (36.8)	3 (50.0)	0 (0.0)	10 (35.7)	
	Grade 2	7 (36.8)	2 (33.3)	2 (66.7)	11 (39.3)	
	Grade 3	1 (5.3)	1 (16.7)	0 (0.0)	2 (7.1)	
Trismus	Absent	14 (73.7)	5 (83.3)	3 (100)	22 (78.6)	0.558
	Present	5 (26.3)	1 (16.7)	0 (0.0)	6 (21.4)	
Dysphagia	Absent	12 (63.2)	4 (66.7)	2 (66.7)	18 (64.3)	0.984
	Present	7 (36.8)	2 (33.3)	1 (33.3)	10 (35.7)	
Xerostomia	Absent	13 (68.4)	3 (50.0)	1 (33.3)	17 (60.7)	0.426
	Present	6 (31.6)	3 (50.0)	2 (66.7)	11 (39.3)	
Pain	Absent	15 (78.9)	4 (66.7)	3 (100)	22 (78.6)	0.516
	Present	4 (21.1)	2 (33.3)	0 (0.0)	6 (21.4)	

3.15. Association Between Percentage Weight Loss and Disease/Treatment-Related Variables

Percentage weight loss was not significantly associated with tumor localization, RT dose groups, or RT volumetric parameters ($p > 0.05$). (Table 16)

Table 16
Association Between Percentage Weight Loss and Tumor Localization, Radiotherapy Dose, and Volumetric Parameters

Variable	Group	n	Weight Loss (%) (Mean ± SD)	p-value
Tumor Localization 1	1	12	5.54 ± 4.60	0.520
	2	16	6.80 ± 5.38	
Tumor Localization 2	1	16	6.88 ± 5.61	0.465
	2	12	5.44 ± 4.18	
RT Dose 1	1	19	6.45 ± 5.57	0.782
	2	9	5.87 ± 3.83	
RT Dose 2	1	14	6.45 ± 5.37	0.847
	2	14	6.07 ± 4.83	
Maximum RT Volume	-	28	-	0.786
Secondary RT Volume	-	28	-	0.285

4. Discussion

The present study evaluated the relationship between periodontal status, radiotherapy (RT)-related parameters, tumor localization, and treatment-associated oral complications in patients with oral cavity cancer treated with surgery followed by RT. Overall, RT-related complications were common in the study population; however, most evaluated clinical parameters demonstrated limited statistically significant associations with RT dose, volumetric parameters, tumor localization, or baseline periodontal status. These findings suggest that RT-related oral complications may involve multifactorial mechanisms that cannot be explained solely by conventional dose-response relationships.

The demographic characteristics of the present cohort were generally consistent with previous reports indicating that oral cavity cancers are more common in older individuals and are strongly associated with tobacco exposure (20). Similarly, the tongue was the most frequent tumor localization in the present study, in agreement with the literature identifying the tongue as one of the most commonly affected oral cavity sites.

Baseline periodontal evaluation revealed a high prevalence of gingivitis and periodontitis, accompanied by widespread plaque accumulation and gingival bleeding. The absence of periodontally healthy individuals suggests that this patient population presented with compromised periodontal conditions even before RT initiation. Similar findings have previously been reported in patients with head and neck cancer, where impaired oral hygiene and pre-existing periodontal inflammation are common (21). In

addition to inadequate oral hygiene habits, postoperative anatomical changes, scar tissue formation, and treatment-related discomfort may further complicate plaque control in these patients.

Although temporal reductions in salivary flow were observed during RT, the relationship between salivary changes and RT dose, tumor localization, and volumetric parameters remained inconsistent. A significant time effect was identified only within one RT dose classification, whereas most analyses did not demonstrate statistically significant associations. Previous studies have shown that salivary gland dysfunction following RT is closely associated with radiation exposure and may vary considerably among individuals depending on anatomical factors, treatment planning, and gland sensitivity (22). Therefore, the heterogeneous findings observed in the present study may reflect inter-individual variability in RT response rather than the absence of biological effects.

Similarly, changes in gingival crevicular fluid (GCF) parameters did not demonstrate significant associations with RT dose, tumor localization, or volumetric parameters. The absence of a consistent relationship may be associated with the multifactorial inflammatory environment observed in patients undergoing RT. Inflammatory responses related to surgery, oral hygiene status, mucosal damage, nutritional changes, and alterations in the oral microbiota may all influence GCF composition during treatment.

Mucositis was the most frequent complication in the present study and affected 82.1% of participants. This finding is consistent with previous reports describing oral mucositis as one of the most common adverse effects of head and neck RT (23). Xerostomia and dysphagia were also frequently observed and represented clinically important complications because of their impact on oral intake and quality of life. In particular, dysphagia remains a major functional complication associated with nutritional impairment and reduced treatment tolerance (24). The coexistence of mucositis, reduced salivary flow, and swallowing dysfunction observed in the present study further supports the complex interaction between mucosal injury and functional impairment during RT.

Despite the high prevalence of mucositis, most cases were limited to Grade 1–2 severity, and no Grade 4 mucositis was observed. This finding may partly be associated with the comprehensive pre-RT dental management protocol applied to all participants, including oral hygiene instruction, periodontal treatment, and elimination of oral infectious foci before RT initiation. Although the absence of a control group prevents definitive interpretation, these findings support the importance of preventive oral care in reducing the severity of RT-related oral complications.

No statistically significant associations were identified between RT dose groups and most oral complications, including mucositis, trismus, xerostomia, and pain. Interestingly, dysphagia demonstrated a significant association with one RT dose classification, with higher prevalence observed in the lower-dose subgroup. This finding appears inconsistent with the conventional dose-response concept and suggests that dysphagia development may depend not only on total radiation dose but also on factors such as irradiated anatomical structures, treatment field characteristics, muscular involvement, and salivary dysfunction. Similarly, RT volumetric parameters were not significantly associated with most

complications, indicating that total irradiated volume alone may not adequately explain treatment-related toxicity.

Tumor localization, flap surgery, additional chemotherapy, and baseline periodontal status also demonstrated limited associations with complication development. Nevertheless, certain descriptive trends, including higher xerostomia frequency in periodontitis patients and greater mucositis severity in flap surgery cases, may still suggest a contributory role of local tissue conditions and treatment complexity. The absence of statistically significant findings in these analyses may partly be related to the relatively small sample size and subgroup heterogeneity.

No significant relationship was identified between percentage weight loss and RT-related parameters or tumor localization. These findings suggest that weight loss during RT may be more strongly associated with functional impairments such as dysphagia, mucositis, and xerostomia rather than direct dosimetric factors alone.

The present study has several limitations, including the relatively small sample size and the heterogeneity of clinical characteristics within the study population. In addition, the absence of a control group limits the ability to evaluate the isolated impact of preventive dental interventions. Nevertheless, the prospective design and the simultaneous evaluation of periodontal status, salivary parameters, RT dose, volumetric measurements, tumor localization, and treatment-related complications represent important strengths of the study.

5. Conclusion

The present study comprehensively evaluated the relationship between radiotherapy-related oral complications and factors including tumor localization, RT dose, volumetric parameters, periodontal status, surgical approach, and additional chemotherapy in patients with oral cavity cancer.

Although most evaluated variables did not demonstrate statistically significant associations with treatment-related complications, dysphagia showed significant differences in specific RT dose groups, indicating that treatment-related effects should not be disregarded. Moreover, the observation that certain complications were more prevalent in lower dose or lower volume exposure groups suggests that RT-related toxicities cannot be explained solely by a conventional dose–response relationship. Instead, factors such as irradiation of critical anatomical structures, tissue sensitivity, salivary alterations, and inter-individual variability may play more substantial roles in complication development.

Similarly, the absence of a significant association between weight loss and RT-related parameters suggests that nutritional deterioration may primarily result from the cumulative effects of functional impairments, particularly dysphagia, mucositis, and xerostomia.

Overall, the findings of the present study indicate that RT-related oral complications extend beyond localized tissue injury and may substantially affect functional capacity and quality of life. Therefore,

treatment planning should not only focus on tumor control but should also incorporate preventive and supportive approaches targeting oral complications that may interfere with treatment continuity and patient well-being.

Accordingly, preservation of critical anatomical structures during RT planning, regular multidisciplinary oral evaluation, and early management of functional complications such as dysphagia and xerostomia may represent important clinical considerations in patients undergoing RT for oral cavity cancer.

Further prospective multicenter studies with larger and more homogeneous patient populations are needed to better clarify the multifactorial nature of RT-related oral complications and to contribute to the development of individualized supportive care strategies.

Declarations

Conflict of Interest

The authors declare no conflict of interest.

Ethical Approval

All procedures performed in this study involving human participants were conducted in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Informed consent was obtained from all individual participants included in the study.

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Author Contribution

M.K. and S.B. contributed to the study conception and design, manuscript writing, and preparation of the tables. M.K., S.B., S.K., O.O.A., and K.K. were involved in patient care and data collection. M.O. performed the statistical analysis. All authors reviewed and approved the final version of the manuscript.

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