Original Article

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Radiation-induced Xerostomia: Evaluation with ^{18}F-FDG PET/CT

Radyoterapi İlişkili Kserostominin ^{18}F-FDG PET/BT ile Değerlendirilmesi

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Abstract

Objectives: To investigate the relationship between radiation dose, metabolic changes in the salivary glands assessed by ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT), and xerostomia severity in patients with head and neck cancer following radiotherapy (RT).

Methods: We retrospectively analyzed 107 patients treated with intensity-modulated RT or volumetric modulated arc therapy for head and neck malignancies. Clinical xerostomia severity was evaluated at the time of post-treatment PET/CT. Mean gland doses and dose–volume parameters (V10–V50) were extracted from treatment plans. Metabolic changes were evaluated by $^{\Delta}$maximum standardized uptake value and $^{\Delta}$mean standardized uptake value between pre and post treatment PET/CT scans. The relationships between clinical, dosimetric, and metabolic variables were examined.

Results: Moderate-to-severe xerostomia occurred in 63.6% of patients. Both higher T and N stage were significantly associated with greater xerostomia severity ($p<0.05$). Patients with nodal metastases on pretreatment PET/CT demonstrated a higher prevalence of xerostomia. Dose–volume parameters (V10–V30 for parotids, V50 for submandibular glands) were significantly correlated with symptom severity. $^{\Delta}$SUV values were significantly associated with both mean dose and dose–volume parameters, particularly in the left parotid gland, where patients receiving >30 Gy showed markedly greater metabolic decline. Parotid glands demonstrated stronger dose-dependent metabolic changes compared with submandibular glands, consistent with their higher radiosensitivity.

Conclusion: Despite the use of advanced RT techniques, xerostomia remains a frequent toxicity. ^{18}F-FDG PET/CT reliably captured dose-dependent salivary gland impairment and reflected the impact of tumor burden on toxicity risk. These findings underscore the complementary role of PET-derived biomarkers as integrative tools for predicting salivary dysfunction beyond conventional dosimetric parameters.

Keywords: ^{18}F-FDG PET/CT, head and neck cancer, radiotherapy, xerostomia

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Öz

Amaç: Bu çalışmada, baş ve boyun kanseri nedeniyle radyoterapi (RT) uygulanan hastalarda, tükrük bezlerine ait radyasyon dozu, ^{18}F-florodeoksiglukoz pozitron emisyon tomografisi/bilgisayarlı tomografi (^{18}F-FDG PET/BT) ile değerlendirilen metabolik değişiklikler ve kserostomi şiddeti arasındaki ilişki araştırıldı.

Yöntem: Baş ve boyun kanseri tanısı ile RT alan 107 hasta retrospektif olarak incelendi. Post-RT PET/BT sırasında klinik kserostomi semptomları değerlendirildi. Tedavi planlarından ortalama bez dozları ve doz–hacim parametreleri (V10–V50) elde edildi. Pre- ve post-RT PET/BT arasındaki $^{\Delta}$maksimum standart tutulum değeri ve $^{\Delta}$ortalama standart tutulum değeri değerleri hesaplanarak metabolik değişiklikler değerlendirildi. Klinik, dozimetrik ve metabolik değişkenler arasındaki ilişkiler incelendi.

Bulgular: Hastaların %63,6'sında orta ve şiddetli kserostomi saptandı. İleri T ve N evreleri kserostomi şiddeti ile anlamlı ilişkiliydi ($p<0,05$). Pre-RT PET/BT'de nodal metastazı olan hastalarda şiddetli kserostomi daha sık izlendi. Parotis bezleri için V10–V30, submandibuler bezler için V50 parametreleri semptom şiddeti ile anlamlı ilişkiliydi. $^{\Delta}$SUV değerleri ortalama doz ve doz–hacim parametreleri ile korelasyon gösterdi; özellikle sol parotiste >30 Gy alan hastalarda belirgin metabolik azalma gözlendi. Parotis bezleri, submandibuler bezlere kıyasla daha güçlü doz bağımlı metabolik değişiklikler sergiledi.

Sonuç: Gelişmiş RT tekniklerine rağmen kserostomi sık görülen bir yan etki olmaya devam etmektedir. 18F-FDG PET/BT, tükrük bezlerindeki doz bağımlı fonksiyon kaybını güvenilir şekilde gösterebilmekte ve tümör yükünün toksisite riskine etkisini yansıtmaktadır. Bu bulgular, PET tabanlı biyogöstergelerin geleneksel dozimetrik parametrelerin ötesinde kserostomi riskinin öngörülmesinde tamamlayıcı rol oynayabileceğini ortaya koymaktadır.

Anahtar kelimeler: ^{18}F-FDg PET/BT, baş ve boyun kanseri, radyoterapi, kserostomi

Introduction

Radiotherapy (RT) remains a fundamental treatment method for head and neck cancers (HNC), either as a primary treatment or in combination with chemotherapy (CT) and/or surgery. However, radiation-induced damage to surrounding normal tissues is a major limitation, with xerostomia being one of the most frequent and distressing side effects. Moreover, RT affects the composition of saliva, resulting in a thicker and more viscous secretion (1). Xerostomia occurs due to radiation-induced dysfunction of the salivary glands. Despite advances in RT techniques, radiation-induced damage to normal tissues remains a major concern. One of the most debilitating and common late toxicities is xerostomia, which substantially impairs patients' quality of life by affecting speech, mastication, taste, oral hygiene, and overall nutritional status (2). Stimulated salivary production is largely derived from the parotid glands, contributing approximately 60-70% of total saliva, whereas resting (unstimulated) salivary flow predominantly originates from the submandibular and sublingual glands as well as numerous minor oral salivary glands (3). This physiological distinction underlines the different clinical impact of radiation-induced dysfunction in these glands.

Previous studies have shown that both the occurrence and severity of xerostomia are closely associated with the mean radiation dose delivered to the parotid and submandibular glands. The parotid glands appear particularly radiosensitive due to their predominantly serous acinar structure. Dose–response relationships have demonstrated that when the mean dose to the parotid glands is maintained below approximately 26 Gy and to the submandibular glands below approximately 40 Gy, the incidence of xerostomia is significantly reduced. Furthermore, prospective data indicate that, provided these thresholds are not exceeded, a gradual recovery of salivary gland function may occur within two years following RT. In contrast, doses beyond these limits are often associated with persistent dysfunction and chronic symptoms. According to the Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC) guidelines, these thresholds form the basis of widely applied dose–volume constraints for organs at risk (OARs) in head and neck RT (3,4,5,6).

In addition to its established role in staging and treatment response assessment in HNC, ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) can also provide insights into radiation-induced changes in normal tissues. PET-derived metabolic parameters, such as maximum standardized uptake value (SUV_{max}) and mean standardized uptake value (SUV_{mean}), may therefore serve as objective biomarkers of salivary gland function and radiation-related injury (7). Nevertheless, the association between metabolic changes in salivary glands, radiation dose exposure, and clinical xerostomia symptoms has not been fully elucidated.

The present study aimed to investigate the relationship between radiation doses delivered to the salivary glands, metabolic changes assessed by pre- and post-RT ^{18}F-FDG PET/CT parameters, and the correlation of these factors with the severity of xerostomia symptoms in patients with head and neck malignancies.

Materials and Methods

Patient Selection

This retrospective study included 107 patients with histopathologically confirmed head and neck malignancies who underwent ^{18}F-FDG PET/CT in our institution between 2018 and 2023 for disease staging and subsequent treatment response evaluation after curative RT. Patients with distant metastases at baseline, a history of another malignancy, or prior surgical treatment for HNC were excluded. Patients with incomplete clinical, pathological, or imaging data were also not included in the analysis. None of the patients received any treatment specifically for xerostomia between the two PET/CT scans. The study protocol was reviewed and approved by the Health Sciences Ethics Committee of Manisa Celal Bayar University Faculty of Medicine (number: 20.478.486/3287, date: 16.07.2025). Written informed consent was obtained from all subjects.

PET/CT Acquisition and Image Analysis

All patients fasted for at least 4-6 hours prior to the examination, and serum glucose levels were confirmed to be <200 mg/dL before tracer administration. The standard intravenous dose of 370-555 MBq (10-15 mCi) of ^{18}F-FDG was injected, followed by a resting period of approximately 60 minutes in a quiet room. Imaging was performed using a General Electric Discovery IQ 3-Ring hybrid PET/CT scanner (GE Healthcare, Milwaukee, USA). A low-dose CT scan (16-slice; 120 kVp; 90 mA) was acquired first for attenuation correction and anatomical reference. Subsequently, PET data were obtained from the skull base to the mid-thigh in the supine position, with an acquisition time of 2 minutes per bed position (typically 8–10 beds per patient). PET images were reconstructed with the Q. Clear penalized-likelihood algorithm (β-value 500) to improve image quality. Images were generated on a 192 × 192 matrix with a field of view of 70 cm and a slice thickness of 3.26 mm, yielding a voxel size of approximately 3.65 mm³. Fusion PET/CT images were reviewed in axial, sagittal, and coronal planes using maximum intensity projection and attenuation-corrected datasets.

For quantitative analysis, regions of interest were manually drawn over the bilateral parotid and submandibular glands on attenuation-corrected PET/CT images. SUV_{max} and SUV_{mean} values were measured for each gland on both the pre-RT and the post-RT PET/CT scans. The second (post-RT) PET/CT examination was performed 3–6 months after completion of RT. Differences between pre-RT and post-RT values were calculated and expressed as $^{\Delta}SUV_{max}$ and $^{\Delta}SUV_{mean}$. At the time of the post-RT PET/CT examination, xerostomia-related symptoms were assessed using the Turkish validated version of the University of Washington Quality of Life Questionnaire version 4 (8). Based on patient-reported responses to the xerostomia domain, patients were categorized into three groups: no symptoms, mild symptoms, and moderate-to-severe symptoms.

Radiotherapy and Dosimetric Evaluation

All patients received curative-intent RT using intensity-modulated radiotherapy (IMRT) or volumetric modulated arc therapy (VMAT) techniques delivered with an Elekta Versa HD linear accelerator (Elekta AB, Stockholm, Sweden), according to institutional protocols. Treatment planning was performed on CT images, with target volumes and OARs delineated in accordance with international contouring guidelines (Figure 1). Dose–volume histograms were generated for each plan (Figure 2).

For dosimetric analysis, the mean radiation doses delivered to the bilateral parotid and submandibular glands were recorded. In addition, volumetric parameters were calculated to quantify the percentage of gland volume receiving specified dose levels. For the parotid glands,

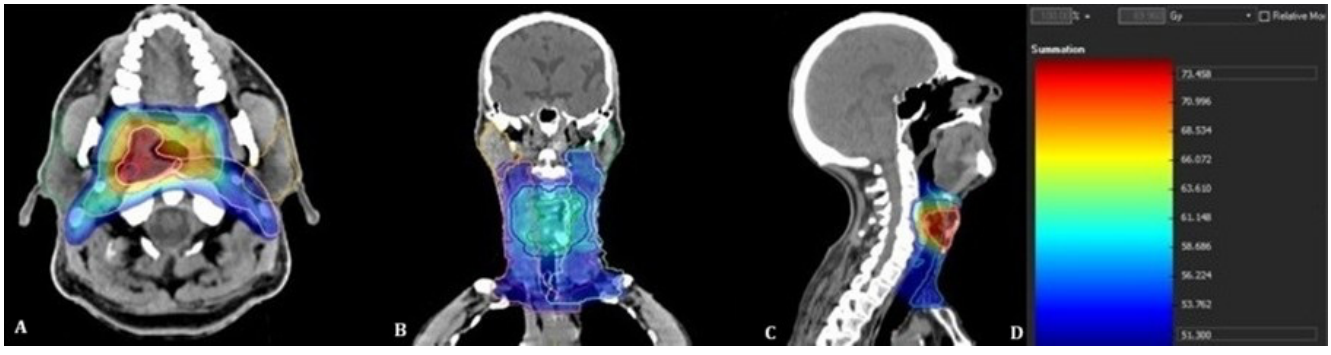

Figure 1. Representative radiotherapy planning computed tomography images of a patient with a right posterolateral oropharyngeal tumor. (A) Axial, (B) coronal, and (C) sagittal slices demonstrate in the slices target volumes and dose distributions, with delineation of parotid and submandibular glands as organs at risk. (D) Corresponding dose-color scale

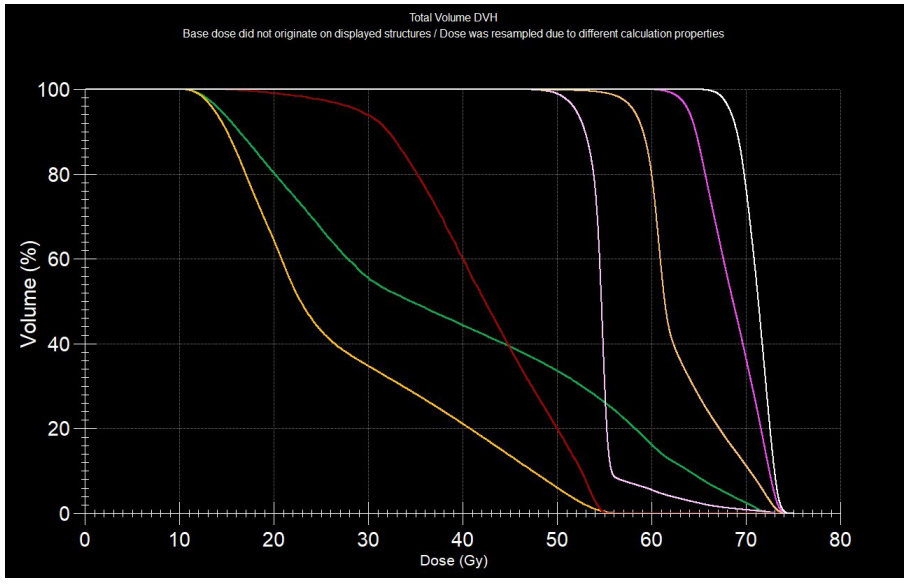

Figure 2. Representative dose–volume histogram from the same patient shown in Figure 1. Due to the right posterolateral location of the oropharyngeal tumor, the right parotid gland (green line) received substantially higher radiation doses compared with the contralateral parotid gland (yellow line). Dose–volume histograms of target volumes are also displayed for reference
DVH: Dose–volume histogram

V10, V20, and V30 were determined, representing the proportions of gland volume exposed to ≥10 Gy, ≥20 Gy, and ≥30 Gy, respectively. For the submandibular glands, V50 was calculated as the proportion of gland volume exposed to ≥50 Gy. These parameters, together with mean gland doses, were subsequently analyzed in relation to xerostomia severity and PET-derived metabolic changes ($^{\Delta}SUV_{max}$ and $^{\Delta}SUV_{mean}$).

Statistical Analysis

Descriptive statistics were expressed as mean, standard deviation, and range for continuous variables, and as frequency and percentage for categorical variables. The association between xerostomia severity and continuous parameters such as age was assessed using Spearman's rank correlation test. Correlations between PET/CT-derived metabolic parameters ($^{\Delta}SUV_{max}$, $^{\Delta}SUV_{mean}$) and both mean doses and dose–volume parameters (V10, V20, V30 for the parotid glands and V50 for the submandibular glands) were also evaluated using Spearman's rank correlation. Differences in $^{\Delta}SUV$ values across xerostomia severity groups (0, 1, 2) were analyzed with the Kruskal-Wallis test. Categorical variables, including sex, tumor stage, and lateralization, were compared with xerostomia severity using the chi-square test. For cut-off analysis, patients were stratified according to a 30 Gy threshold for parotid mean dose, and intergroup differences were assessed using the Mann–Whitney U test. Statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA), and a p-value <0.05 was considered statistically significant.

Results

A total of 107 patients who underwent RT for head and neck malignancies were included in the study. The cohort consisted of 95 men (88.8%) and 12 women (11.2%), with a mean age of 61.3 years (range: 25–84 years). Primary tumor sites were the larynx (n=63), nasopharynx (n=13), oral cavity (n=11), hypopharynx (n=8), oropharynx (n=6), paranasal sinus (n=3), and HNC of unknown primary (n=3). In 56 patients (52.3%), the tumor was located in the midline, while 26 patients (24.3%) had left-sided and 25 patients (23.4%) had right-sided tumors. At the time of post-RT PET/CT imaging, xerostomia symptoms were absent in 9 patients (8.4%), mild in 30 patients (28.0%), and moderate-to-severe in 68 patients (63.6%) (Table 1).

Additional analyses were performed to evaluate the association between xerostomia severity and baseline clinical variables. Older age was significantly correlated with higher xerostomia severity (p=-0.27, p=0.005). Sex and tumor lateralization (right, left, or midline) were not significantly related to xerostomia severity (p>0.05). In contrast, both T stage and N stage were significantly associated with xerostomia, with more advanced stages corresponding to more moderate-to-severe symptoms (p<0.001 and p=0.004, respectively).

Table 1. Distribution of descriptive characteristics	
Variable	**n (%) or mean ± SD (range)**
Total patients	107
Age (years)	61.3±10.9 (25–84)
Sex	Male: 95 (88.8%) Female: 12 (11.2%)
Primary tumor lateralization	Midline: 56 (52.3%) Left: 26 (24.3%) Right: 25 (23.4%)
T stage	T1: 8 (7.5%) T2: 14 (13.1%) T3: 35 (32.7%) T4: 49 (45.8%)
N stage	N0: 46 (43.0%) N1: 17 (15.9%) N2: 32 (29.9%) N3: 11 (10.3%)
Mean radiation dose (Gy)	Right parotid: 24.8 Left parotid: 26.2 Right submandibular: 52.5 Left submandibular: 52.7
Xerostomia severity	None: 9 (8.4%) Mild: 30 (28.0%) Moderate-to-severe: 68 (63.6%)
SD: Standard deviation	

A significant relationship was observed between tumor lateralization and N stage (p=0.0046), largely driven by the predominance of N0 cases in midline tumors. When right- and left-sided tumors were compared, no statistically significant differences were observed in N stage distribution (p=0.478). However, right-sided tumors more frequently presented as N0 (28.0%) compared with left-sided tumors (19.2%), whereas higher nodal stages were relatively more common in left-sided tumors. When patients were stratified according to primary tumor site, those with oropharyngeal, oral cavity, nasopharyngeal, or hypopharyngeal cancers exhibited a markedly higher rate of moderate-to-severe xerostomia compared with patients with laryngeal, paranasal sinus, or HNC of unknown primary origin (92.1% vs. 47.8%, p<0.001).

The mean radiation doses delivered to the salivary glands were 24.8 Gy, 26.2 Gy, 52.5 Gy, and 52.7 Gy for the right parotid, left parotid, right submandibular, and left submandibular glands, respectively. Statistically significant associations were observed between the mean doses to the salivary glands and the severity of xerostomia symptoms (p<0.05). In addition to mean gland doses, volumetric dose parameters were also analyzed. Kruskal-Wallis tests demonstrated that V10, V20, and V30 for both parotid glands, as well as V50 for both submandibular glands, were significantly associated with xerostomia severity (all p<0.001).

Pre-treatment SUV_{max} and SUV_{mean} values of the salivary glands showed no significant association with xerostomia severity (all p>0.05). $^{\Delta}SUV_{max}$ and $^{\Delta}SUV_{mean}$ values of the parotid and submandibular glands were calculated between pre- and post-RT PET/CT scans (Figure 3). When compared across xerostomia severity groups, statistically significant associations were observed only for the left parotid gland (p=0.031 and p=0.044, respectively). In contrast, no significant associations were found for the right parotid or for either submandibular gland (all p>0.05).

Significant correlations were observed between $^{\Delta}SUV$ values and radiation dose metrics of the salivary glands. For the parotid glands, $^{\Delta}SUV_{max}$ and $^{\Delta}SUV_{mean}$ demonstrated moderate inverse correlations with both mean dose and dose–volume parameters (V10, V20, V30), with the strongest associations observed in the left parotid gland (p=-0.34 to -0.44, p<0.05). For the submandibular glands, weaker but statistically significant correlations were identified between $^{\Delta}SUV$ values and V50 (p=-0.20 to -0.31,

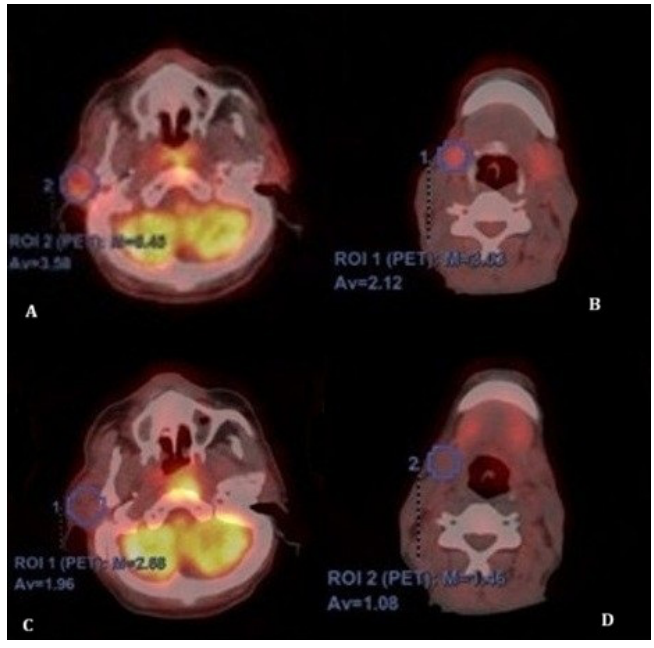

Figure 3. Representative pre-and post-radiotherapy ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography images from a patient included in the study. (A, B) Pre-treatment scans demonstrate preserved metabolic activity in the parotid and submandibular glands. (C, D) Follow-up scans performed 3-6 months after radiotherapy show a marked reduction in tracer uptake within the glands, reflecting radiation-induced functional impairment. Regions of interest (ROIs) used for maximum standardized uptake value and mean standardized uptake value measurements are indicated
PET: Positron emission tomography

p<0.05). These findings indicate that larger gland volumes exposed to higher radiation doses were associated with greater reductions in metabolic activity. When patients were stratified according to a 30 Gy cut-off for parotid dose–volume parameters, statistically significant differences were found only in the left parotid gland, where both $^{\Delta}SUV_{max}$ (p=0.013) and $^{\Delta}SUV_{mean}$ (p=0.024) showed greater reductions in the high-dose group.

Discussion

Despite the widespread adoption of advanced RT techniques such as IMRT and image-guided RT, xerostomia remains among the most common and distressing late toxicities in patients with HNC, significantly diminishing quality of life. Studies have consistently shown that sparing the major salivary glands, particularly by maintaining mean parotid doses below 26 Gy and submandibular doses below 40-50 Gy, can effectively reduce the incidence and severity of xerostomia, without compromising tumor control (4,9,10,11). In line with this evidence, the present study aimed to explore the relationship between radiation dose to the salivary glands, metabolic changes visualized on ^{18}F-FDG PET/CT, and the clinical manifestation of xerostomia in patients treated for head and neck malignancies.

In our study cohort, 63.6% of patients developed moderate-to-severe xerostomia following RT, despite the use of advanced techniques such as IMRT and VMAT. This finding underscores the persistent clinical burden of xerostomia as a late toxicity in HNC treatment. Notably, the observed prevalence rate is in line with previously reported data, where the incidence of moderate-to-severe xerostomia ranged between 40% and 70%, even in studies employing parotid-sparing RT approaches (9, 12).

Our results demonstrated that patients with moderate-to-severe xerostomia had significantly higher mean radiation doses to both the parotid and submandibular glands. This finding reinforces the well-established dose–response relationship between salivary gland irradiation and the development of xerostomia. Moiseenko et al. (4) demonstrated a clear correlation between increased mean dose and higher patient-reported xerostomia severity. Our findings are consistent with these results and highlight the importance of adhering to gland-specific dose constraints during treatment planning.

The relatively high prevalence of moderate-to-severe xerostomia in our cohort is likely attributable to the high rate of nodal involvement as detected on pretreatment ^{18}F-FDG PET/CT with 60 out of 106 patients (56.6%) presenting with nodal metastases (N1–N3). Patients with advanced N-stage disease often require more extensive target volumes and elective nodal irradiation, which reduces the possibility of sparing adjacent salivary glands, particularly the parotid and submandibular glands (13). In addition, T-stage was significantly associated with xerostomia severity in our cohort, with more advanced stages corresponding to more severe symptoms. Taken together, these findings suggest that tumor burden, reflected by both primary tumor size and nodal involvement, plays a critical role in salivary gland toxicity by limiting the feasibility of gland preservation during RT.

In our cohort, older age was significantly associated with higher xerostomia severity (p=0.005). This finding is consistent with the results of Beetz et al. (13), who reported that patients aged over 70 years had a substantially increased risk of persistent xerostomia despite meeting QUANTEC dose constraints, reflecting the limited recovery potential of elderly salivary glands. However, Pan et al. (14) did not identify age as a significant predictor of xerostomia in their study, which included nasopharyngeal carcinoma patients, where the median patient age was relatively young (47 years). Overall, these observations suggest that age is an important clinical factor influencing salivary gland recovery, although its impact may vary depending on patient demographics and tumor distribution.

When stratified by primary tumor site, the severity of xerostomia differed markedly across subsites. Moderate-to-severe xerostomia was observed in all patients with oropharyngeal and oral cavity cancers (100%) and in the majority of those with nasopharyngeal (84.6%) and hypopharyngeal (87.5%) primaries. In contrast, the prevalence was significantly lower in patients with laryngeal cancers (49.2%) and in those with paranasal sinus tumors (exact prevalence not specified, p<0.001). These findings underscore the importance of tumor location in determining the risk of xerostomia. Beetz et al. (13) reported that parotid-sparing with IMRT was considerably more difficult in oropharyngeal and oral cavity cancers due to their proximity to the major salivary glands. Likewise, nasopharyngeal and hypopharyngeal tumors frequently require large bilateral nodal irradiation volumes, further limiting the potential for gland sparing. However, laryngeal tumors are generally located in the midline and in a more caudal position, thereby reducing dose exposure to the parotid and submandibular glands, and resulting in a substantially lower prevalence of xerostomia compared with nasopharyngeal, hypopharyngeal, oropharyngeal, and oral cavity cancers. Overall, these findings emphasize that anatomical and tumor-related factors, in addition to dosimetric constraints, play a critical role in determining the risk of radiation-induced xerostomia.

In addition to the mean dose, our analysis demonstrated that dose–volume parameters were also significantly associated with xerostomia severity. Specifically, V10, V20, and V30 for both parotid glands, as well as V50 for the submandibular glands, correlated with increased xerostomia symptoms. This underlines the relevance of dose–volume parameters beyond mean dose alone in predicting xerostomia, as radiation exposure of larger gland volumes can significantly contribute to salivary gland dysfunction. Importantly, previous studies have shown that sparing at least one parotid and submandibular gland reduces the risk of xerostomia while improving both stimulated and unstimulated salivary function (3, 4).

Van Dijk et al. (15) demonstrated that textural radiomics features extracted from ^{18}F-FDG PET images significantly improved the prediction of late xerostomia, particularly one year after RT, highlighting the value of PET-derived image biomarkers for toxicity risk stratification. More recently, Li et al. (16) validated such a PET-based biomarker model in an independent cohort, confirming the independent prognostic value of PET-derived imaging features beyond conventional clinical and dosimetric parameters. In our study, metabolic changes in the salivary glands were evaluated using pretreatment and post-treatment ^{18}F-FDG PET/CT. SUV values showed significant correlations with both mean gland dose and dose–volume parameters, demonstrating that ^{18}F-FDG PET/CT can reliably detect the dose-dependent functional impairment of salivary glands following RT. These findings highlight the value of PET-based metabolic imaging as an adjunct to the conventional dose–volume predictor.

The initial decline in salivary flow largely mirrors the intensity of treatment delivery. Among the major salivary glands, the parotids exhibit the highest radiosensitivity, with flow reduction determined by both the radiation dose and the volume of gland tissue encompassed within the treatment field (17). In our study, the parotid glands demonstrated stronger dose-dependent metabolic changes compared with the submandibular glands, as reflected by significant correlations of $^{\Delta}$SUV with both mean dose and low-to-intermediate dose–volume parameters (V10–V30). In contrast, correlations for the submandibular glands were weaker and limited to higher dose exposure (V50). This observation is consistent with the well-established higher radiosensitivity of the parotid glands, which are predominantly composed of serous acinar cells; whereas the mixed serous–mucous composition of the submandibular glands renders them relatively more resistant to radiation-induced injury.

In our cohort, primary tumor sites were relatively homogeneously distributed between the right and left sides, with more than half located in the midline. Tumor lateralization itself was not significantly associated with xerostomia severity. However, nodal involvement was more frequent in left-sided tumors compared with right-sided tumors. Specifically, right-sided tumors more frequently presented as N0 (28.0%) compared with left-sided tumors, (19.2%), whereas higher nodal stages were more common in left-sided tumors. This asymmetry in nodal distribution explains the more pronounced metabolic impairment observed in the left parotid gland, as greater nodal burden on the left side necessitated higher radiation exposure to the ipsilateral salivary gland. Consistent with this clinical observation, significant PET-based metabolic changes were also predominantly seen in the left parotid gland. Both $^{\Delta}SUV_{max}$ and $^{\Delta}SUV_{mean}$ were significantly associated with xerostomia severity and demonstrated dose–response correlations with mean dose and dose–volume parameters (V10–V30). In contrast, the submandibular glands showed weaker associations, which were limited to higher dose exposure (V50). Importantly, correlation strength was greatest in the left parotid gland, in line with its higher radiation burden. Furthermore, patients receiving mean parotid doses above 30 Gy, exhibited significantly greater reductions in $^{\Delta}SUV_{max}$ and $^{\Delta}SUV_{mean}$ in the left parotid, supporting the concept that doses beyond the QUANTEC threshold are linked to persistent metabolic dysfunction (3).

Study Limitations

Our study has several limitations. First, it was a single-institution, retrospective analysis. Second, although ^{18}F-FDG PET/CT provided valuable information on salivary gland metabolism, only SUV-based parameters were analyzed, whereas advanced textural features might have offered additional predictive power. Finally, the relatively short follow-up period precluded evaluation of long-term recovery dynamics of salivary gland function beyond the early post-treatment phase.

Conclusion

Despite widespread adoption of advanced RT techniques such as IMRT and VMAT, xerostomia remains a common and clinically significant late toxicity in HNC. Our findings demonstrate that advanced T and N stage, older age, and tumor location, particularly nasopharyngeal, hypopharyngeal, oropharyngeal, and oral cavity cancers, are associated with a higher risk of moderate-to-severe xerostomia, while laryngeal tumors show substantially

lower rates. Parotid glands exhibited greater radiosensitivity compared with submandibular glands, and ^{18}F-FDG PET/CT reliably captured dose-dependent metabolic impairment, highlighting its value as a functional biomarker complementing conventional dose–volume metrics.

From a clinical standpoint, careful treatment planning is especially warranted in patients with large tumors, salivary gland–adjacent nodal metastases, and high-risk subsites, where the risk of toxicity is greatest. These results reinforce the need for more personalized toxicity prediction models that go beyond dosimetric constraints alone.

Ethics

Ethics Committee Approval: The study protocol was reviewed and approved by the Health Sciences Ethics Committee of Manisa Celal Bayar University, Faculty of Medicine (number: 20.478.486/3287, date: 16.07.2025).

Informed Consent: Written informed consent was obtained from all patients.

Footnotes

Authorship Contributions

Surgical and Medical Practices: G.M., B.Ç.B., Ö.K.Ç., G.B., Concept: G.M., B.Ç.B., Ö.K.Ç., G.B., G.G., Design: G.M., B.Ç.B., Ö.K.Ç., Y.P., E.S.B., Data Collection or Processing: G.M., B.Ç.B., E.Ç., Ö.Y., M.K., Analysis or Interpretation: G.M., B.Ç.B., N.A., A.F.S., Y.P., G.B., Literature Search: G.M., B.Ç.B., N.A., Y.P., G.G., E.S.B., Writing: G.M., B.Ç.B., Ö.K.Ç., E.S.B.

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