An Analysis of Post-Radiation Therapy and Clinical Disease Predictors in the Development of Xerostomia and Dysphagia in Head and Neck Cancer Patients

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Introduction

- Head and neck cancers (HNC) are the sixth most common types of cancers in the world[1].
- With more than 63,000 annually reported cases and a mortality rate of less than 3%, current studies suggest that HNCs are highly treatable and preventable[2 3].
- Cancer management through radiotherapy is a core mechanism for minimizing tumorigenesis.
- A major concern with the use of RT is the unintended targeting of normal soft tissues and other organs-at-risk (OAR).
- RT produces certain toxicities, or side effects, such as dysphagia (Figure 1) and xerostomia (Figure 2) that undermine the effectiveness of head and neck cancer treatments.

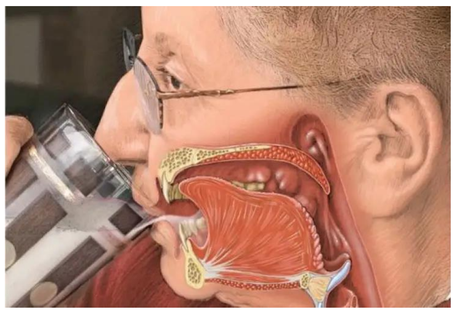


Figure 1. Clinical Presentation of Dysphagia[4]. Dysphagia is pain or difficulty with swallowing. It is often associated with head and neck cancers and leads to impairments in speech production and other swallowing mechanisms.

Problem

Research related to radiation-induced toxicities is mainly focused on patient experiences during radiation therapy. Limited knowledge on side effect development after radiation therapy poses short and long-term health concerns.

Objective

To analyze post-RT toxicity trends in working to identify social and clinical-based predictors of xerostomia and dysphagia in HNC patient populations.

Methods

- Forty-four patients (44), who had undergone radiation therapy between 2015 and 2021, were enrolled in this study.
- Eligibility criteria: age>18 years, history of external beam radiotherapy, evidence of xerostomia and dysphagia in soft tissues.
- Patients were assessed for xerostomia and dysphagia at the following time points: pre-therapy, mid-radiotherapy, end-radiotherapy, and 3-, 6-, 12-months post-therapy.
- The patient's objective and subjective outcome assessments were scored and cross-compared.
- Radiation therapy and clinical-based contributors to toxicity development were analyzed individually.

Results

Table 1. Patient Disease and Treatment Characteristics

Characteristics	N (%)
Sex	
Male	35 (79.55%)
Female	9 (20.45%)
Age at diagnosis, years: median (IQR)	59 (54-63)
Race	
White or Caucasian	38 (86.36%)
Black or African-American	4 (9.09%)
Other	2 (4.55%)
Smoking Status	
Current	2 (4.55%)
Former	22 (50%)
Never	20 (45.45%)
Tumor laterality	
Left	11 (25%)
Right	31 (70.45%)
Bilateral	2 (4.55%)
Oropharynx subsites	
Base of Tongue	16 (36.36%)
Tonsil	19 (40.91%)
Neck	2 (4.55%)
Others	7 (15.91%)
HPV Status	
Positive	23 (52.27%)
Negative	0 (%)
Not tested	21 (47.73%)
p16 Status	
Positive	30 (68.18%)
Negative	0 (0%)
Not tested	14 (31.82%)
Therapeutic Combination	
Radiation Therapy (RT) alone	5 (2.72%)
Concurrent Chemotherapy (CC)	21 (47.73%)
Induction Chemotherapy (IC) alone	2 (4.55%)
IC followed by CC	6 (13.64%)
Surgery followed by CC	5 (11.36%)
Surgery followed by RT	3 (6.82%)
Others	2 (2.72%)
Stage	
I	16 (36.36%)
II	7 (15.91%)
III	5 (11.36%)
IV	16 (36.36%)

Table 2. Baseline to 12-Months Post-RT Xerostomia Trends

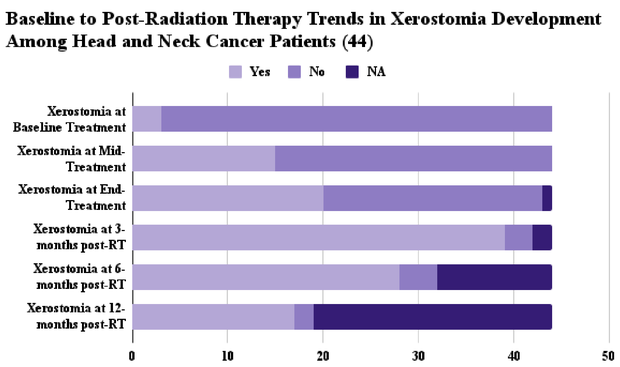
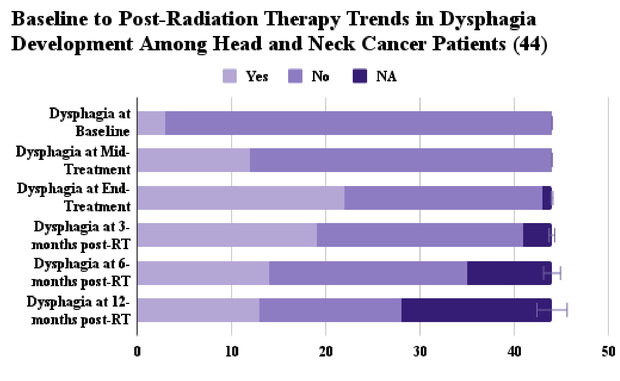


Table 3. Baseline to 12-Months Post-RT Dysphagia Trends



Discussion

Trend Summary

Only 6.82% of the study participants reported dysphagia and xerostomia (dry mouth) as symptoms of their cancer diagnosis. At three-months post-RT, 86% of patients identified with xerostomia, while 43% noted experiencing dysphagia. Twelve months post-RT, most patients were placed in the not-applicable (NA) category. Factors accounting for NA include death or a lack of follow-up appointments after RT. Most patients were in the "no follow-up (no FU)" subcategory. So, there is a need to identify possible characteristics that could contribute to an upward trend in xerostomia and dysphagia development after treatment (Tables 2 and 3).

Age

- Out of 44 study participants, the average age at the time of diagnosis was around fifty (50) to sixty (60) years old (Table 1).
- Delayed HNC diagnoses lead to higher probabilities of developing stage II, III, and stage IV cancer (Table 1).

Figure 2. Clinical Presentation of Xerostomia[5]. Xerostomia (or dry mouth) is caused by decreased fluidity in the salivary glands. It is often characterized by soreness, dry mucosal appearance, and a loss of gingival tissue.

Gender

- Epidemiological trends confirmed that males comprised 70.3% of all [HNC] cases from 2002 to 2012[6].
- Gender-based disparities become increasingly insignificant when both groups receive high-quality oral care.

Smoking Status

- Smoking is associated with higher cases of HNC recurrences that lead to more RT and a greater vulnerability to toxicities[7].

HNC Subsite and HPV status

- Patients with HPV-related HNSCC are at a lower risk of developing Secondary Primary Malignancies (SPM) than patients with non-HPV HNCs[2].
- For the 47.74% of patients, who had not been tested for HPV, an early diagnosis of the disease is advised as not to increase the potential for SPM risk and toxicity exposure.

Therapeutic Combination

- Exploratory studies on concurrent chemotherapy alone may decrease the likelihood of patients acquiring late radiation-induced toxicities (Figure 1).
- Surgery with chemotherapy and/or radiotherapy is often associated with "clinically worse dysphagia and xerostomia" outcomes for patients in treatment[8].

Conclusion

- Men over the age of fifty (50) are more susceptible to developing radiation-induced toxicities, so more research needs to be directed towards analyzing those trends and mitigating those risks in female populations as well.
- Head and neck cancer research should account for the variability in oropharyngeal subsites and therapeutic combinations.
- Smoking increases the likelihood of developing xerostomia and dysphagia.
- Addressing the lack of racial diversity in this study might offer less biased outcomes and greater representation of HNC patient populations.
- An increase in the population size may provide more variability in analyzing the toxicity database results and developing more preventive treatment methods.
- Attending follow-up appointments after HNC radiation therapy can mitigate the development of xerostomia and dysphagia in patient populations, while improving their overall quality of life.

Future Studies

- Increase the scope of the study to 24-months and 36-months after radiation therapy.
- Revise the eligibility criteria to accommodate for HNC survivorship patients.
- Investigate alcohol use, weight change, and nutritional status as contributing factors to post-RT toxicity development.
- Analyze trends in other HNC toxicities like osteoradionecrosis (ORN) (Figure 3).

Figure 3. ORN[9] Osteoradionecrosis is a condition of the mandibular region that arises from extreme radiation therapy to areas affected by head and neck cancers

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Responsibility of Research Conduct
As a Fuller Lab undergraduate trainee, I was required to complete the Radiation Oncology Mentorship Agreement Form to demonstrate my responsibility in conducting and analyzing this research study individually. I did so while complying to "institutional, state, regulatory, and [ethical] guidelines," of research conduct and patient confidentiality.