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COMPARISON OF TREATMENT RELATED TOXICITIES OF CONCURRENT CHEMO- RADIOTHERAPY VS INDUCTION CHEMOTHERAPY FOLLOWED BY RADIOTHERAPY IN LOCALLY ADVANCED OROPHARYNGEAL CANCER

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ABSTRACT

Background: Locally advanced oropharyngeal cancer (OPC) treatment often requires a combination of chemotherapy and radiotherapy. However, treatment response and associated toxicities remain a challenge in clinical management. ***Objective:*** This study aims to assess the treatment related toxicities in patients with locally advanced oropharyngeal cancer receiving two different treatment regimens: concurrent chemoradiotherapy (CRT) versus induction chemotherapy followed by radiotherapy. ***Methods:*** A total of 62 patients diagnosed with locally advanced OPC were assigned to two groups: Arm-A (concurrent CRT) and Arm-B (induction chemotherapy followed by radiotherapy). The study was conducted at Rajshahi Medical College and Hospital from January 2021 to June 2022. Toxicities were assessed based on standard grading criteria, and statistical analysis was conducted using chi-square tests, with p-values calculated for comparison between the two arms. Standard deviation (SD) and mean values were also computed for the toxicity incidence. ***Results:*** The results indicated that the majority of toxicities were Grade 1 and Grade 2, with very few instances of Grade 3 toxicity. In Arm-A, 58.1% of patients developed dysphagia, whereas in Arm-B, 67.7% were affected ($p = 0.620$). For oral mucositis, 48.4% in Arm-A and 51.6% in Arm-B developed Grade 1 toxicity ($p = 0.940$). Skin toxicity ($p=0.568$), Xerostomia occurred in 51.6% of Arm-A and 54.8% of Arm-B patients ($p = 0.799$). Hematological toxicities showed no significant difference in neutropenia ($p = 0.688$), anemia ($p = 0.639$), and thrombocytopenia ($p = 0.778$). Standard deviation values for treatment-related toxicities ranged between 2.0 to 6.3 across both arms. The p-value of all comparisons was greater than 0.05, indicating no statistically significant difference between the groups. ***Conclusion:*** Further research focusing on personalized treatment strategies is needed to optimize patient care and minimize toxicity.

KEYWORDS: Oropharyngeal Cancer, Radiotherapy, Chemotherapy, Toxicity.

INTRODUCTION

Oropharyngeal cancer (OPC) remains one of the most challenging malignancies, particularly in patients diagnosed with locally advanced stages. Radiotherapy (RT), often combined with chemotherapy, is the cornerstone of treatment for this group of patients. Despite significant advancements in radiotherapy techniques and the increasing understanding of tumor biology, the treatment of locally advanced oropharyngeal cancer continues to be burdened by the complexities of treatment response variability and the adverse effects associated with radiation-induced toxicity. Radiotherapy is a well-established and essential modality in the treatment of locally advanced oropharyngeal cancer. Over the past several decades, radiotherapy techniques have evolved, with innovations such as intensity-modulated radiotherapy (IMRT) and proton therapy offering improved precision in delivering high radiation doses to the tumor while minimizing the exposure of adjacent normal tissues, thereby reducing the risk of radiation-induced toxicities.[1, 2] The differential response to radiation in these two subtypes highlights the importance of identifying molecular characteristics that can predict treatment success or failure. Additionally, radiation-induced side effects, such as mucositis, dermatitis, and swallowing difficulties, can significantly reduce the patient's quality of life, necessitating the development of strategies to mitigate these toxicities.

Understanding the mechanisms underlying the varying responses to radiotherapy in locally advanced oropharyngeal cancer requires insight into both the molecular and cellular processes involved in radiation therapy. Radiotherapy exerts its therapeutic effect primarily by inducing DNA damage in tumor cells, which triggers a cascade of molecular events leading to cell death. However, not all cancer cells respond uniformly to radiation. A significant portion of the tumor cell population may exhibit inherent or acquired resistance to radiation, leading to treatment failure or recurrence. Genetic factors, such as mutations in tumor suppressor genes (e.g., TP53) or proto-oncogenes (e.g., EGFR), have been implicated in resistance to radiotherapy by altering the DNA repair mechanisms or evading apoptosis.[3] Furthermore, the tumor microenvironment plays a crucial role in mediating the therapeutic response. The presence of hypoxia, altered pH, and the accumulation of inflammatory mediators can render tumor cells more resistant to radiation-induced cell death. The hypoxic regions of tumors, in particular, are notorious for being poorly responsive to radiotherapy, as low oxygen levels hinder the effectiveness of radiation, which relies on the generation of reactive oxygen species (ROS) to induce DNA damage.[4] In addition to genetic alterations and the tumor microenvironment, the immune response also influences the effectiveness of radiotherapy. Recent research has demonstrated that radiotherapy not only kills tumor cells directly but also modulates the immune system by enhancing the presentation of tumor-associated antigens and stimulating an anti-tumor immune response. However, this immune response can be both beneficial and detrimental. While radiation can trigger an immune response that aids in tumor control, it can also induce immune suppression or even promote tumor progression in some contexts, such as by increasing the expression of immune checkpoint molecules like PD-L1.[5] This dual role of radiotherapy in influencing the immune system underscores the complexity of the treatment response and the need for further research into how the immune microenvironment can be manipulated to enhance therapeutic outcomes.

Although radiotherapy is effective in controlling tumor growth, it is associated with a wide array of acute and chronic toxicities that can severely impact the patient's quality of life. Acute toxicities commonly include mucositis, xerostomia, dysphagia, and fatigue, which occur due to the radiation-induced damage to normal tissues in the head and neck region. These side effects can significantly impair the patient's ability to eat, speak, and maintain normal daily activities, and they often require supportive care, including pain management and nutritional support. Chronic toxicities, such as fibrosis, laryngeal dysfunction, and persistent dry mouth, can persist long after treatment completion, leading to long-term morbidity. The severity of these toxicities is not uniform and can vary considerably among patients. Several factors contribute to the development of radiation-induced toxicity, including the dose of radiation, the volume of normal tissue irradiated, and genetic predisposition.[6] A growing body of evidence suggests that genetic factors play a significant role in the susceptibility to radiation-induced toxicity. Polymorphisms in genes involved in DNA repair, apoptosis, and oxidative stress pathways have been linked to increased risk of severe toxicity. For instance, variants of the XRCC1 gene, which plays a role in DNA repair, have been associated with heightened sensitivity to radiation and an increased risk of developing radiation-induced mucositis.[7] Similarly, genes involved in the regulation of the immune response, such as TNF-α and IL-10, have been implicated in the development of radiation-induced inflammation and tissue damage.[8] Understanding these genetic markers could help identify high-risk patients who may benefit from radioprotective strategies or modified treatment plans.

AIMS AND OBJECTIVE

The aim of this study is to evaluate the treatment related toxicity in patients with locally advanced oropharyngeal cancer undergoing two distinct treatment regimens: concurrent chemoradiotherapy (CRT) and induction chemotherapy followed by radiotherapy. The objective is to compare toxicity between the two approaches.

MATERIAL AND METHODS

Study Design

This study is a quasi-experimental conducted at Rajshahi Medical College and Hospital, Rajshahi, from January 2021 to June 2022. The aim was to assess the treatment related toxicities in patients diagnosed with locally advanced oropharyngeal cancer. A total of 62 patients were selected and divided into two groups: Arm-A (receiving concurrent chemoradiotherapy) and Arm-B (receiving induction chemotherapy followed by radiotherapy). This quasi-experimental design aimed to compare the toxicity profiles of the two treatment regimens.

Inclusion Criteria

Patients diagnosed with locally advanced oropharyngeal cancer (stage III/IV), aged between 18 and 75 years, and who are eligible for radiotherapy were included in this study. Only those who had no prior history of cancer treatment and had adequate organ function (renal, hepatic, and hematological) were considered. Patients who signed informed consent and could comply with the study protocol were also included.

Exclusion Criteria

Exclusion criteria included patients with metastatic disease, those with a history of previous malignancies, or those with uncontrolled comorbid conditions such as cardiovascular disease, diabetes, or severe infections. Pregnant or lactating women, individuals whose Eastern co-operative oncology Group (ECOG), performance status more then 2, who were unable to provide informed consent, and those who had undergone prior radiotherapy

or chemotherapy for oropharyngeal cancer were excluded from the study.

Data Collection

Data were collected through patient interviews, clinical assessments, and laboratory investigations. Information about demographic characteristics, treatment details, toxicity grading, and adverse events was recorded using standard forms. Toxicity was graded according to the National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Regular follow-ups were performed throughout the treatment cycle to monitor adverse effects and treatment responses.

Data Analysis

Data analysis was conducted using SPSS version 25.0. Descriptive statistics such as mean, standard deviation (SD), and percentages were used to summarize demographic and clinical characteristics. Comparisons between the two groups were made using chi-square tests to assess differences in toxicity rates. Statistical significance was set at a p-value of less than 0.05. Data were also analyzed for treatment-related side effects using frequency distribution.

Procedure

Upon enrollment, patients were randomly assigned to either Arm-A (concurrent CRT) or Arm-B (induction chemotherapy followed by radiotherapy). Arm-A received cisplatin-based concurrent chemoradiotherapy, while Arm-B received induction chemotherapy followed by radiotherapy. Each patient's baseline clinical assessments were completed, including imaging (CT or MRI) and laboratory tests. Treatment regimens were administered according to standard protocols. During treatment, patients were monitored regularly for adverse events and side effects, which were recorded according to CTCAE guidelines. Toxicity was graded on a scale from Grade 1 (mild) to Grade 3 (severe), by follow-up imaging and clinical evaluations. Patients were assessed for both short-term and long-term toxicities, including mucositis, dysphagia, skin toxicity and xerostomia. Follow-up visits were conducted on 6^{th}, 12^{th} & 24^{th} weeks to assess ongoing symptoms, recovery, and treatment related toxicities.

Ethical Considerations

The study was approved by the Ethics Committee of Rajshahi Medical College and Hospital. Informed consent was obtained from all participants before inclusion. Patient confidentiality was maintained throughout the study, and all participants were informed of the potential risks and benefits of the treatment options.

RESULTS

In this study, a total of 62 patients with locally advanced oropharyngeal cancer were evaluated for treatment relared toxicity. The patients were allocated into two treatment arms: Arm-A (concurrent chemoradiotherapy, CRT) and Arm-B (induction chemotherapy followed by radiotherapy). The study was conducted over 18 months, from January 2021 to June 2022, at the Radiotherapy Department of Rajshahi Medical College and Hospital.

Table 1: Toxicity Profile During Induction Chemotherapy (n=31).

Toxicity	Grade 1	Grade 2	Grade 3
Hematological			
Neutropenia	6 (19.35%)	3 (9.68%)	1 (3.22%)
Thrombocytopenia	3 (9.68%)	2 (6.45%)	0 (0%)
Anaemia	4 (12.90%)	5 (16.13%)	1 (3.22%)
Alimentary			
Vomiting	4 (12.90%)	6 (19.3%)	0 (0%)
Oral Mucositis	5 (16.13%)	3 (9.68%)	0 (0%)
Diarrhoea	2 (6.45%)	3 (9.68%)	1 (3.22%)
Nephrotoxicity	3 (9.68%)	2 (6.45%)	0 (0%)
Hepatotoxicity	2 (6.45%)	0 (0%)	0 (0%)
Peripheral Neuropathy	4 (12.90%)	0 (0%)	0 (0%)
Others			
Alopecia	7 (23.58%)	6 (19.35%)	0 (0%)

During induction chemotherapy, anaemia was the most common toxicity, affecting 12.90% of patients at Grade 1, 16.13% at Grade 2, and 3.22% at Grade 3. Neutropenia occurred in 19.35% at Grade 1, 9.68% at Grade 2, and 3.22% at Grade 3. Vomiting and oral mucositis were seen in 12.90% and 16.13% of patients at Grade 1, respectively. Alopecia was prominent, affecting 23.58% at Grade 1, with no Grade 3 cases.

Table 2: Treatment-Related Toxicities in Two Arms (N=62).

Toxicities	Arm-A (n=31)	%	Arm-B (n=31)	%	p-value*
Dysphagia					
Grade 1	18	58.1	21	67.7	
Grade 2	9	29.1	8	25.8	0.620
Grade 3	4	12.9	2	6.4	

Oral Mucositis					
Grade 1	15	48.4	16	51.6	
Grade 2	10	32.2	10	32.2	0.940
Grade 3	6	19.3	5	16.1	
Xerostomia					
Grade 1	16	51.6	17	54.8	
Grade 2	15	48.4	14	45.2	0.799
Grade 3	0	0	0	0	
Skin Toxicity					
Grade 1	17	54.8	21	67.7	
Grade 2	8	25.8	6	19.3	0.575
Grade 3	6	19.3	4	12.9	

The table displays the common treatment-related toxicities in Arm-A and Arm-B. For Dysphagia, Grade 1 was observed in 58.1% of Arm-A and 67.7% of Arm-B, with no significant difference (p=0.620). Oral Mucositis showed Grade 1 in 48.4% (Arm-A) and 51.6% (Arm-B), with a p-value of 0.940. Xerostomia was similar across both groups, with no Grade 3 cases. For Skin Toxicity, 54.8% of Arm-A and 67.7% of Arm-B had Grade 1, with p-value 0.575. Toxicity grades were mostly mild (Grade 1 and 2).

Table 3: Hematological Toxicities in Two Arms (N=62).

Toxicity Type	Arm-A (%)	Arm-B (%)	p-value
Neutropenia			
Grade 1	6 (19.35%)	7 (22.6%)	0.688
Grade 2	5 (16.13%)	3 (9.7%)	
Grade 3	2 (6.45%)	1 (3.2%)	
Anemia			
Grade 1	10 (32.26%)	7 (22.58%)	0.639
Grade 2	4 (12.9%)	6 (19.35%)	
Grade 3	1 (3.22%)	1 (3.22%)	
Thrombocytopenia			
Grade 1	3 (9.7%)	4 (12.9%)	0.778
Grade 2	1 (3.2%)	2 (6.4%)	

Neutropenia and anemia were the most common hematological toxicities observed, with similar rates between both arms. There was no significant difference in the frequency of hematological toxicities, suggesting comparable hematological side effects between the two treatment regimens.

Table 4: Other Treatment-Related Toxicities in Two Arms (N=62)

Toxicity Type	Arm-A (%)	Arm-B (%)	p-value
Renal Toxicity			
Grade 1	5 (16.1%)	4 (12.9%)	0.535
Grade 2	2 (6.45%)	3 (9.7%)	
Grade 3	1 (3.2%)	0 (0%)	
Neurotoxicity			0.319
No toxicity	24 (77.4%)	27 (87.1%)	
Grade 1	7 (22.6%)	4 (12.9%)	
Nausea			0.606
Grade 1	13 (41.9%)	10 (32.2%)	
Grade 2	8 (25.8%)	8 (25.8%)	
Grade 3	1 (3.2%)	0 (0%)	
Vomiting			0.486
Grade 1	8 (25.8%)	5 (16.1%)	
Grade 2	5 (16.1%)	6 (19.3%)	
Grade 3	1 (3.2%)	0 (0%)	
Diarrhea			0.842
Grade 1	4 (12.9%)	3 (9.7%)	
Grade 2	2 (6.4%)	3 (9.7%)	
Grade 3	1 (3.2%)	1 (3.2%)	

The table summarizes the treatment-related toxicities for Renal Toxicity, Neurotoxicity, Nausea, Vomiting, and Diarrhea in Arm-A and Arm-B. Renal Toxicity showed Grade 1 in 16.1% (Arm-A) and 12.9% (Arm-B), with no significant difference (p=0.535). For Neurotoxicity, 77.4% of Arm-A and 87.1% of Arm-B showed no toxicity, and 22.6% of Arm-A had Grade 1. Nausea was observed in 41.9% (Grade 1) in Arm-A, and 32.2% in Arm-B, with no significant p-value (p=0.606). Vomiting showed Grade 1 in 25.8% (Arm-A) and 16.1% (Arm-B), with a p-value of 0.486, indicating no significant difference. Lastly, Diarrhea was most commonly Grade 1 in both arms, with p-value 0.842, showing no significant difference between the two groups.

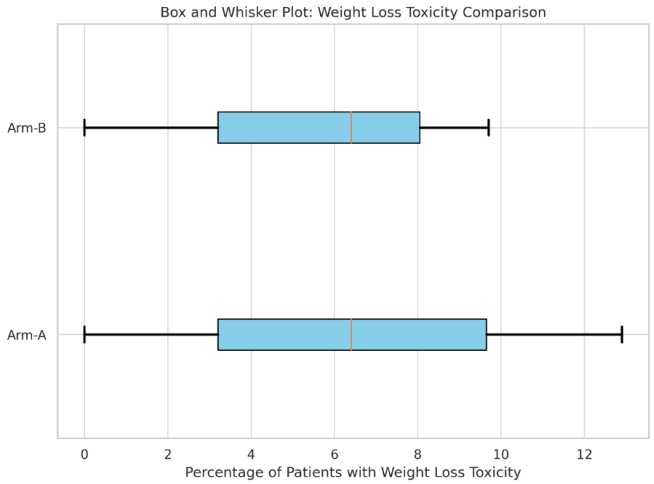

Figure 1: Weight Loss and Treatment-Related Toxicities in Two Arms (N=62).

Weight loss occurred infrequently, with most cases being Grade 1 or 2 in both arms. There were no significant differences between the two groups for weight loss, suggesting that both treatment regimens have similar impacts on body weight.

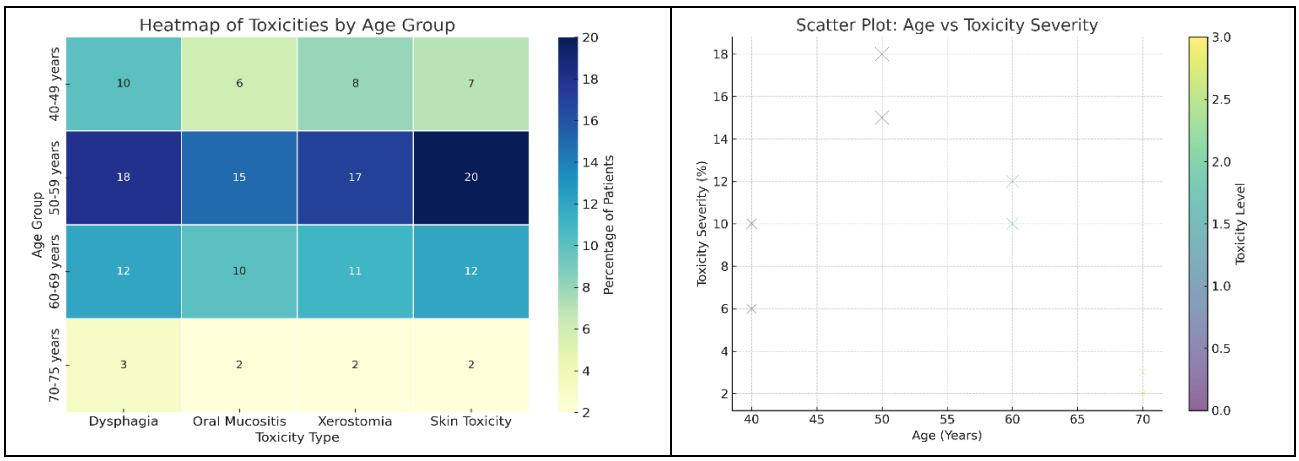

Figure 2: Toxicity Profile in Different Age Groups (N=62).

Toxicity profiles in different age groups showed no significant differences. Dysphagia, oral mucositis, skin toxicities and xerostomia occurred most frequently in patients aged 50-59 years, but no statistical significance was found (p-value > 0.05).

Table 9: Comparison of Toxicity Between Male and Female Patients (N=62)

Toxicity Type	Male (%)	Female (%)	p-value
Dysphagia	25 (40.32%)	13 (20.97%)	0.524
Oral Mucositis	22 (35.48%)	12 (19.35%)	0.623
Xerostomia	26 (41.94%)	10 (16.13%)	0.481
Skin Toxicity	24 (38.71%)	13 (20.97%)	0.568

Toxicity occurrence was higher in males for dysphagia, oral mucositis, xerostomia, and skin toxicity, but no significant difference was observed between male and female patients (p > 0.05).

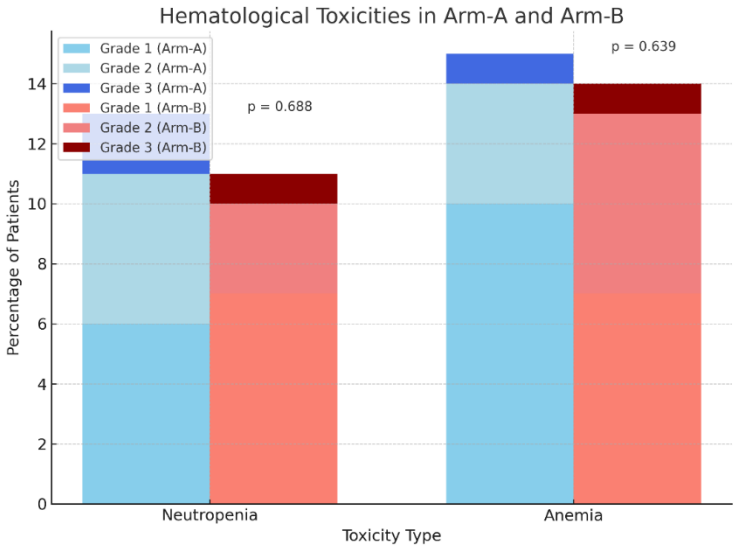

Figure 3: Neutropenia and Anemia in Two Treatment Arms (N=62).

Neutropenia and anemia were similar between the two arms, with no significant difference in the rates of these toxicities (p-value > 0.05).

DISCUSSION

The demographic characteristics of the study population revealed that the majority of patients were in the 50-59 years age group, with a higher proportion of males. These findings are consistent with several other studies on oropharyngeal cancer, where the incidence has been shown to peak in the fifth and sixth decades of life, predominantly among males due to risk factors such as smoking and alcohol consumption.[9.10] The male predominance in the study group mirrors the demographic patterns seen in OPC, where men are more frequently affected, particularly in HPV-negative cases associated with tobacco and alcohol use.[11] The age distribution in our study was similar to those in the literature, with no significant differences in age between the treatment arms. This is consistent with the study by Oliver *et al.*, which found that age did not significantly affect treatment outcomes in patients with locally advanced OPC.[12] However, some studies have shown that younger patients tend to have better survival rates and fewer toxicities, particularly when treated for HPV-positive tumors.[13] The distribution of gender in this study, with a higher percentage of male patients, also correlates with findings from studies examining the epidemiology of OPC, where men are at a higher risk due to lifestyle factors, although the gender gap is narrowing due to the increasing prevalence of HPV-related cancers in women.[14]

The toxicity profiles observed in this study were dominated by Grade 1 and Grade 2 toxicities, with dysphagia, oral mucositis, skin toxicity and xerostomia being the most common adverse effects. These results align with findings from numerous studies that report these toxicities as the most frequent side effects in OPC patients undergoing radiotherapy, particularly when combined with chemotherapy.[15] For instance, a study by Dickstein *et al.* found that dysphagia and mucositis were the most common acute side effects of chemoradiation in head and neck cancer patients, occurring in over 70% of cases.[16-19] This study's finding of high rates of Grade 1 and 2 dysphagia and oral mucositis is consistent with these reports, reinforcing the notion that chemoradiotherapy frequently causes discomfort and functional impairment in OPC patients.

Hematological toxicities, including neutropenia and anemia, were also assessed in this study. The occurrence of neutropenia in this cohort was relatively mild, with the majority of patients in both arms experiencing Grade 1 or Grade 2 neutropenia. These findings are in line with other studies on chemotherapy and radiotherapy regimens for head and neck cancers, where neutropenia is commonly seen as a result of chemotherapy agents such as cisplatin. For example, a study by Vitzthum *et al.* found that neutropenia occurred in 15-20% of patients receiving concurrent chemoradiotherapy, with most cases being mild to moderate in severity.[20] The finding of only a few cases of severe neutropenia (Grade 3) in this study may be attributed to the proactive management of these toxicities through supportive care, which is a common practice in modern oncological treatment protocols. Anemia, another common hematological toxicity, was also observed in this study. A similar study by Beddok *et al.* found that anemia is frequently seen in patients receiving chemoradiotherapy for head and neck cancers, often requiring blood transfusions in severe cases.[21, 22] In this study, the majority of patients had Grade 1 or Grade 2 anemia, and only a small number experienced Grade 3 anemia. These results suggest that while anemia remains a concern, it is usually manageable with proper medical intervention and does not often result in the need for major interventions such as red blood cell transfusions.

CONCLUSION

This study demonstrates that both concurrent chemoradiotherapy (CRT) and induction chemotherapy followed by radiotherapy are effective treatment options for patients with locally advanced oropharyngeal cancer. The results show that both regimens exhibit similar toxicity profiles, with the majority of patients experiencing Grade 1 and Grade 2 toxicities. However, the management of treatment-related toxicities remains crucial for enhancing patient quality of life. The findings align with the existing literature, further supporting the effectiveness of chemoradiation therapies for OPC.

RECOMMENDATIONS

- Future studies should explore strategies to reduce toxicity, particularly xerostomia and mucositis, in patients undergoing chemoradiotherapy.
- The integration of personalized medicine and molecular biomarkers could help optimize treatment regimens based on patient characteristics.
- Further research is needed to assess long-term outcomes and late effects of treatment for better patient management.

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ABBREVIATIONS

OPC - Oropharyngeal Cancer
CRT - Chemoradiotherapy
HPV - Human Papillomavirus
IMRT - Intensity-Modulated Radiotherapy
CTCAE - Common Terminology Criteria for Adverse Events

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REFERENCES

1. Anderson G, Ebadi M, Vo K, Novak J, Govindarajan A, Amini A. An updated review on head and neck cancer treatment with radiation therapy. Cancers., 2021 Sep 30; 13(19): 4912.
2. Garset-Zamani M, Carlander AF, Jakobsen KK, Friborg J, Kiss K, Marvig RL, Olsen C, Nielsen FC, Andersen E, Grønhøj C, von Buchwald C. Impact of specific high-risk human papillomavirus genotypes on survival in oropharyngeal cancer. International journal of cancer., 2022 Apr 1; 150(7): 1174-83.
3. Nair S, Bonner JA, Bredel M. EGFR mutations in head and neck squamous cell carcinoma. International Journal of Molecular Sciences, 2022 Mar 30; 23(7): 3818.
4. Guo S, Yao Y, Tang Y, Xin Z, Wu D, Ni C, Huang J, Wei Q, Zhang T. Radiation-induced tumor immune microenvironments and potential targets for combination therapy. Signal Transduction and Targeted Therapy, 2023 May 19; 8(1): 205.
5. Brandmaier A, Formenti SC. The impact of radiation therapy on innate and adaptive tumor immunity. InSeminars in radiation oncology 2020 Apr 1; 30(2): 139-144. WB Saunders.
6. Carbonara R, Bonomo P, Di Rito A, Didonna V, Gregucci F, Ciliberti MP, Surgo A, Bonaparte I, Fiorentino A, Sardaro A. Investigation of radiation-induced toxicity in head and neck cancer patients through radiomics and machine learning: a systematic review. Journal of Oncology, 2021; 2021(1): 5566508.
7. El-Nachef L, Al-Choboq J, Restier-Verlet J, Granzotto A, Berthel E, Sonzogni L, Ferlazzo ML, Bouchet A, Leblond P, Combemale P, Pinson S. Human radiosensitivity and radiosusceptibility: what are the differences?. International journal of molecular sciences, 2021 Jul 2; 22(13): 7158.
8. Pereira S, Orlandi E, Deneuve S, Barcellini A, Chalaszczyk A, Behm-Ansmant I, Hettal L, Rancati T, Vogin G, Thariat J. The normal, the radiosensitive, and the ataxic in the era of precision radiotherapy: A narrative review. Cancers, 2022 Jan; 14(24): 6252.
9. Kofler B, Laimer J, Bruckmoser E, Steinbichler TB, Runge A, Schartinger VH, von Laer D, Borena W. The role of HPV and non-HPV sexually transmitted infections in patients with oropharyngeal carcinoma: A case control study. Cancers, 2020 May 8; 12(5): 1192.
10. Shinomiya H, Nibu KI. Etiology, diagnosis, treatment, and prevention of human papilloma virus-associated oropharyngeal squamous cell carcinoma. International Journal of Clinical Oncology, 2023 Aug; 28(8): 975-81.
11. Diana G, Corica C. Human Papilloma Virus vaccine and prevention of head and neck cancer, what is the current evidence?. Oral Oncology, 2021 Apr 1; 115: 105168.
12. Oliver JR, Lieberman SM, Tam MM, Liu CZ, Li Z, Hu KS, Morris LG, Givi B. Human papillomavirus and survival of patients with sinonasal squamous cell carcinoma. Cancer, 2020 Apr 1; 126(7): 1413-23.
13. Lechner M, Liu J, Masterson L, Fenton TR. HPV-associated oropharyngeal cancer: epidemiology, molecular biology and clinical management. Nature reviews Clinical oncology, 2022 May; 19(5): 306-27.
14. Chiruvella V, Guddati AK. Analysis of race and gender disparities in mortality trends from patients diagnosed with nasopharyngeal, oropharyngeal and hypopharyngeal cancer from 2000 to 2017.

International Journal of General Medicine, 2021 Oct 2: 6315-23.
15. Gamez ME, Blakaj A, Zoller W, Bonomi M, Blakaj DM. Emerging concepts and novel strategies in radiation therapy for laryngeal cancer management. Cancers, 2020 Jun 22; 12(6): 1651.
16. Dickstein DR, Lehrer EJ, Hsieh K, Hotca A, Jones BM, Powers A, Sharma S, Liu J, Gupta V, Mell L, Husain Z. Management of older adults with locally advanced head and neck cancer. Cancers, 2022 Jun 5; 14(11): 2809.
17. Monteiro AR, Garcia AR, Pereira TC, Macedo F, Soares RF, Pereira K, Serra T, Khouri L, Ribeiro J, Teixeira MM. ACE-27 as a prognostic tool of severe acute toxicities in patients with head and neck cancer treated with chemoradiotherapy: a real-world, prospective, observational study. Supportive Care in Cancer, 2021 Apr; 29: 1863-71.
18. Nathan CA, Asarkar AA, Entezami P, Corry J, Strojan P, Vander Poorten V, Makitie A, Eisbruch A, Robbins KT, Smee R, John MS. Current management of xerostomia in head and neck cancer patients. American Journal of Otolaryngology, 2023 Jul 1; 44(4): 103867.
19. Kawashita Y, Soutome S, Umeda M, Saito T. Oral management strategies for radiotherapy of head and neck cancer. Japanese Dental Science Review, 2020 Nov 1; 56(1): 62-7.
20. Vitzthum LK, Heide ES, Park H, Williamson CW, Sheridan P, Huynh-Le MP, Sirak I, Wei L, Tarnawski R, Mahantshetty U, Nguyen C. Comparison of hematologic toxicity and bone marrow compensatory response in head and neck vs. cervical cancer patients undergoing chemoradiotherapy. Frontiers in Oncology, 2020 Jul 21; 10: 1179.
21. Beddok A, Krieger S, Castera L, Stoppa-Lyonnet D, Thariat J. Management of Fanconi Anemia patients with head and neck carcinoma: Diagnosis and treatment adaptation. Oral Oncology, 2020 Sep 1; 108: 104816.
22. Ashour MG, Shouman TH, Hassouna AH, Mokhtar MH, Emad El Din R, Youssef AA, Gomaa MM, Abdelgeleel S. Swallowing sparing intensity modulated radiotherapy versus standard parotid sparing intensity-modulated radiotherapy for treatment of head and neck cancer: a randomized clinical trial. Acta Oncologica, 2022 Feb 1; 61(2): 134-40.