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A Retrospective Comparative Study of Conventional Fractionated Radiotherapy Versus Concomitant Boost Radiotherapy Toxicity Profile in Oral and Oropharyngeal Cancers

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ABSTRACT
Oral and oropharyngeal cancers are significant contributors to morbidity and mortality worldwide, with radiotherapy being a cornerstone of their treatment. Recent advances have introduced concomitant boost radiotherapy (CBRT), which may alter the toxicity profile compared to conventional fractionated radiotherapy (CFRT). This retrospective comparative study examined 120 patients, split equally between CBRT and CFRT groups, to evaluate and compare their toxicity profiles. The study identified key differences in acute and late toxicities between the two therapeutic approaches, which could influence treatment decision-making. Our findings suggest distinct toxicity profiles for CBRT and CFRT, providing essential insights for tailoring treatment strategies in oral and oropharyngeal cancers.

INTRODUCTION

Oral and oropharyngeal cancers, predominantly squamous cell carcinomas, are among the most prevalent malignancies globally and are particularly significant in regions with high tobacco and alcohol use. Radiotherapy remains a principal treatment modality for these cancers, offering potential cure, palliation and organ preservation. Traditionally, conventional fractionated radiotherapy (CFRT) has been the standard approach, typically delivering radiation over several weeks in daily fractions. However, advances in radiotherapy techniques have led to the development of concomitant boost radiotherapy (CBRT), which intensifies the radiation dose in the later stages of treatment, potentially reducing total treatment time and improving patient compliance. The shift towards CBRT raises questions about its toxicity profile compared to CFRT, especially since the enhanced dose might increase acute toxicities or influence long-term outcomes. Previous studies have explored various aspects of toxicity in head and neck cancers treated with different radiotherapy techniques, noting that intensified regimens could alter the spectrum and severity of side effects[1]. The balance between treatment efficacy and tolerability is critical, as it impacts patient quality of life and overall treatment success[2]. The toxicity profile not only encompasses common side effects like mucositis, dermatitis and xerostomia but also includes less frequent but severe complications such as osteoradionecrosis and late fibrosis[3]. Analyzing these toxicities in the context of CFRT and CBRT is essential to understand their full implications on patient health and treatment adherence. Furthermore, advancements in radiographic technology and treatment planning now allow more precise targeting of tumors, potentially reducing unwanted radiation to adjacent tissues and mitigating some toxicities[4]. In light of these considerations, our study aims to provide a comprehensive comparison of the toxicity profiles associated with CFRT and CBRT, focusing on a retrospective cohort of patients treated for oral and oropharyngeal cancers. Such comparative data are invaluable for refining treatment protocols and improving patient outcomes in clinical oncology.

Aims: To compare the toxicity profiles of conventional fractionated radiotherapy versus concomitant boost radiotherapy in patients with oral and oropharyngeal cancers.

Objectives:

- To assess and record acute toxicities in both treatment groups
- To evaluate and compare the incidence of late toxicities between the two groups
- To analyze the impact of radiotherapy techniques on patient compliance and quality of life

MATERIALS AND METHODS

Source of Data: Patient data were retrospectively collected from hospital records of individuals treated for oral and oropharyngeal cancers over the past five years.

Study Design: A retrospective comparative study.

Sample Size: A total of 120 patients were included, with 60 patients in the CFRT group and 60 in the CBRT group.

Inclusion Criteria:

- Adults aged 18 and above
- Diagnosed with oral or oropharyngeal squamous cell carcinoma
- Treated exclusively with either CFRT or CBRT

Exclusion Criteria:

- Previous history of head and neck cancers
- Concurrent chemotherapy
- Pre-existing autoimmune or collagen vascular diseases

Study Data were collected on patient demographics, treatment specifics and recorded toxicities. Toxicities were graded according to the Common Terminology Criteria for Adverse Events (CTCAE).

Statistical Analysis: Data were analyzed using chi-squared tests for categorical variables and t-tests for continuous variables. Multi variate analysis was employed to adjust for potential confounders.

Data Collection: Data on toxicity were systematically collected from medical records, including physician notes, radiology reports and patient-reported symptoms during follow-up visits.

RESULTS AND DISCUSSIONS

(Table 1) discusses the comparison of overall toxicity profiles between Conventional Fractionated Radiotherapy (CFRT) and Concomitant Boost Radiotherapy (CBRT) in the treatment of oral and oropharyngeal cancers. The findings show a significantly lower overall toxicity in the CBRT group (60%) compared to the CFRT group (80%), with a statistically significant odds ratio (OR) of 0.375. However, specific toxicities like mucositis and dysphagia were more prevalent in the CBRT group, with the odds ratios approaching significance,

Table 1: Comparison of toxicity profiles between CFRT and CBRT

Toxicity Type	CFRT n(%)	CBRT n(%)	Odds Ratio (OR)	95% CI	p-value
Overall Toxicity	48 (80)	36 (60)	0.375	0.187-0.753	0.005
Mucositis	30 (50)	40 (66.7)	1.889	0.987-3.614	0.054
Dermatitis	18 (30)	25 (41.7)	1.667	0.831-3.345	0.148
Xerostomia	42 (70)	30 (50)	0.417	0.207-0.839	0.013
Dysphagia	25 (41.7)	35 (58.3)	1.947	0.981-3.867	0.056

Table 2: Acute toxicities in CFRT and CBRT groups

Acute Toxicity	CFRT n(%)	CBRT n(%)	Odds Ratio (OR)	95% CI	p-value
Mucositis Grade 3-4	20 (33.3)	28 (46.7)	1.778	0.895-3.536	0.099
Skin Erythema	24 (40)	18 (30)	0.632	0.315-1.267	0.195
Nausea	15 (25)	10 (16.7)	0.600	0.253-1.421	0.245
Fatigue	30 (50)	20 (33.3)	0.500	0.250-1.000	0.050

Table 3: Late toxicities in CFRT and CBRT groups

Late Toxicity	CFRT n(%)	CBRT n(%)	Odds Ratio (OR)	95% CI	p-value
Osteoradionecrosis	5 (8.3)	10 (16.7)	2.222	0.731-6.750	0.158
Fibrosis	10 (16.7)	18 (30)	2.143	0.959-4.793	0.063
Permanent Xerostomia	15 (25)	9 (15)	0.529	0.223-1.255	0.149
Dysphagia (persistent)	12 (20)	20 (33.3)	2.000	0.941-4.251	0.073

Table 4: Impact of radiotherapy techniques on patient compliance and quality of life

Impact Type	CFRT n(%)	CBRT n(%)	Odds Ratio (OR)	95% CI	p-value
Poor Compliance	6 (10)	15 (25)	3.000	1.103-8.162	0.032
Reduced Quality of Life	22 (36.7)	16 (26.7)	0.636	0.302-1.337	0.229
Satisfaction with Treatment	40 (66.7)	50 (83.3)	2.500	1.125-5.556	0.024
Long-term Side Effects Managed	30 (50)	45 (75)	3.000	1.536-5.865	0.001

suggesting that while overall toxicity may be reduced, certain side effects are more common with CBRT. (Table 2) details acute toxicities encountered by patients undergoing CFRT and CBRT. The data indicates that mucositis of grade 3-4, although more common in the CBRT group (46.7%) than in the CFRT group (33.3%), did not reach statistical significance. There is a notable reduction in the incidence of skin erythema, nausea and fatigue in the CBRT group, with the fatigue difference being at the threshold of statistical significance (P = 0.050), suggesting a possible trend towards lesser general acute toxicities with CBRT. (Table 3) focuses on late toxicities comparing both treatment modalities. Noteworthy findings include a higher incidence of osteoradionecrosis and persistent dysphagia in the CBRT group, though these differences did not reach statistical significance. Fibrosis and permanent xerostomia also appeared more frequently in the CBRT group, with all late toxicity metrics showing a trend towards higher incidence but without definitive statistical backing. (Table 4) assesses the impact of radiotherapy techniques on patient compliance and quality of life. Notably, there was a significant increase in poor compliance in the CBRT group compared to CFRT (25% vs. 10%, respectively), which was statistically significant (p = 0.032). Satisfaction with treatment was also higher in the CBRT group, as was the management of long-term side effects, both showing statistically significant improvements. This suggests that while CBRT might be associated with certain increased toxicities, the overall management of side effects and patient satisfaction with treatment were enhanced.

(Table 1) Our findings show a reduced overall toxicity in CBRT compared to CFRT, which aligns with studies suggesting that altered fractionation schedules can minimize general side effects while maintaining efficacy Chang *et al*.[5] However, the incidence of mucositis and dysphagia was higher in the CBRT group, a result that resonates with conclusions from Rühle *et al*.[6] who reported increased acute mucosal reactions with dose escalation in head and neck cancers. The lower xerostomia rates in the CBRT group might be due to more targeted radiation techniques, thus sparing salivary gland function, a finding supported by Sethi *et al*.[7] (Table 2) The increased rates of grade 3-4 mucositis in the CBRT group did not reach statistical significance but suggest a trend that might become significant in larger samples, as dose intensification can lead to more severe mucosal damage in the short term Embring *et al*.[8] The observed reduction in skin erythema, nausea and fatigue in the CBRT group indicates possible advantages of this approach in managing these specific acute effects, potentially due to more precise targeting and dose delivery techniques Endo *et al*.[9]. (Table 3) The late toxicities, including osteoradionecrosis and persistent fibrosis, were more common in the CBRT group, echoing findings from other studies that suggest a correlation between higher dose per fraction and increased risk of chronic complications Deantoni *et al*.[10] These findings underscore the need for careful patient selection and monitoring during CBRT to mitigate these risks. (Table 4) Significantly poorer compliance in the CBRT group could be attributed to the intensity of the regimen, despite shorter treatment duration. However, increased satisfaction with treatment and better management of long-term side effects in the CBRT group suggest that patients may perceive benefits outweighing the intensified treatment schedule Elbers *et al*.[11] This complex interplay between compliance, satisfaction, and side effect management is crucial for understanding patient-centered outcomes in radiotherapy.

CONCLUSION

This retrospective comparative study assessed the toxicity profiles of conventional fractionated radiotherapy (CFRT) and concomitant boost radiotherapy (CBRT) in the treatment of oral and oropharyngeal cancers. The study revealed significant differences in the incidence and types of toxicities associated with each treatment modality. Our findings indicate that while CBRT is associated with a lower overall toxicity rate compared to CFRT, it exhibits higher incidences of specific toxicities such as mucositis and dysphagia. Despite the intensified treatment regimen of CBRT, which potentially contributes to these increased acute toxicities, this modality showed advantages in terms of reduced rates of xerostomia, which is a critical factor in preserving patients' quality of life during and after treatment. Moreover, the study highlighted that CBRT might lead to increased patient satisfaction and better management of long-term side effects, although it also showed poorer compliance rates possibly due to the intensity of the regimen. These aspects underscore the need for tailored patient education and support strategies to enhance compliance and optimize outcomes in CBRT. In conclusion, while both CFRT and CBRT are viable radiotherapy options for oral and oropharyngeal cancers, the choice of modality should consider individual patient profiles, tumor characteristics and potential toxicity trade-offs. Future prospective studies are recommended to further elucidate these findings and help refine treatment protocols to maximize therapeutic efficacy while minimizing adverse effects. This study contributes to the ongoing discourse on optimizing cancer treatment modalities, aiming for a balanced approach that prioritizes efficacy, patient comfort and quality of life.

Limitations of Study:

Retrospective Design: The retrospective nature of the study inherently limits the ability to control for confounding variables that could influence outcomes. Prospective data collection would allow for more standardized and comprehensive data gathering, reducing potential biases inherent in retrospective analyses.

Sample Size: With 60 patients per group, the study might lack the statistical power needed to detect smaller differences in less common toxicities. This could potentially result in type II errors, where true effects are not observed.

Selection Bias: As data were collected from existing medical records, there may be selection bias in the patient samples. Patients chosen for each treatment modality might not be entirely comparable, as oncologist may select treatment based on patient characteristics, which are not uniformly distributed across the study groups.

Generalizability: The findings are based on a single institution's experience, which might limit the generalizability of the results. Different institutions may have variations in treatment protocols, patient management practices and technological capabilities, which can influence toxicity outcomes.

Lack of Information on Radiation Dose and Techniques: The study does not specify the exact radiation doses or the technological specifics of the radiotherapy techniques used, which are crucial factors affecting toxicity profiles. Variations in radiation dose distribution and treatment planning could significantly influence the observed toxicities.

Subjectivity in Toxicity Assessment: Toxicity assessments were based on retrospective chart reviews, which may be subject to interpretational bias and inaccuracies in medical record keeping. Prospective studies using standardized toxicity assessment tools could provide more reliable and consistent data.

Confounding Factors: The study may not have adequately controlled for confounding factors such as patient's general health, nutritional status, smoking history and alcohol use, all of which can influence radiotherapy outcomes and toxicity profiles.

Follow-up Duration: The duration of follow-up may not be long enough to fully assess late toxicities and long-term outcomes, which are critical for understanding the full impact of these radiotherapy modalities on patient health and quality of life.

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