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Accelerated Chemoradiation vs. Conventional Chemoradiation in Locally Advanced Head and Neck Cancer: A Retrospective Study

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ABSTRACT

Background: Head and neck squamous cell carcinoma (HNSCC) is the seventh most diagnosed malignancy worldwide. The standard approach for treating locally advanced HNSCC consists of concurrent chemoradiotherapy (CRT) utilizing a fractionated radiotherapy regimen, typically delivering 70 Gy over seven weeks, this conventional schedule is associated with extended overall treatment time (OTT), significant acute and late toxicities, and suboptimal locoregional control (LRC) outcomes. RTOG 90-03 and the DAHANCA protocols, as well as meta-analyses such as MARCH, supports the use of altered fractionation schedules compared to conventional once-daily radiotherapy, demonstrating modest but statistically significant improvements in LRC and overall survival (OS).

Objective: Our aim was to compare accelerated chemoradiation vs. conventional chemoradiation regarding late toxicity, recurrence rate, disease-free survival (DFS), progression-free survival (PFS), OS, and prognostic factors affecting survival.

Patients and Methods: Our study is a retrospective comparative study in which data were collected from 2012 to 2022. Patients were grouped into two arms: one (Arm A) for 60 patients who received accelerated radiotherapy with 1.8-2 Gy per fraction, 5 fractions per week, and a second (Arm B) for 50 patients who received conventional radiotherapy with 2 Gy per fraction, 6 fraction per week.

Results: There was a statistically significant lower percentage of RT interruption in arm A compared to arm B (3.3% vs. 18.0%, respectively). However, there was no statistically significant difference between the two arms regarding cranial nerve affection, taste alteration, trismus, hearing impairment, and RT completion. There was no statistically significant difference between the two arms regarding response to treatment. There was a statistically significant lower mortality rate in arm A compared to arm B (43.3% vs. 68.0%, respectively). There was a statistically significant higher median OS in arm A compared to arm B.

Conclusion: These findings suggest that accelerated radiotherapy offers a potential advantage in improving survival outcomes, with comparable toxicity profiles to conventional treatment.

Keywords: Accelerated fractionation, Squamous cell carcinoma, Chemoradiation, Altered fractionation.

INTRODUCTION

HNSCC is the seventh most commonly diagnosed malignancy worldwide, with an estimated 890,000 new cases and 450,000 deaths reported in 2020. The global incidence of HNSCC is steadily increasing and is projected to rise by approximately 30% by 2030, reaching an estimated 1.08 million new cases annually [1,2]. Squamous cell carcinoma represents approximately 90% of all head and neck cancers and exhibits a marked predominance in the male population [3,4]. More than three-quarters of these cases now occur in low- and middle-income countries, where patients most often present with loco-regionally advanced disease [5].

The increasing incidence of HNSCC is largely attributed to lifestyle-related factors, particularly tobacco and alcohol consumption [5,6]. In addition, infection with high-risk strains of human papillomavirus (HPV), notably HPV-16, has emerged as a critical etiological factor in the development of oropharyngeal cancers [7]. Unlike tumors associated with tobacco and alcohol, HPV-positive cancers generally demonstrate improved responses to therapy and more favorable prognoses [7,8].

Concurrent cisplatin-based chemoradiation remains a cornerstone of definitive treatment for HNSCC by enhancing radiosensitization. However, weekly and three-weekly cisplatin regimens differ in their toxicity profiles and influence treatment adherence [9,10]. Despite significant advances in diagnostic modalities and therapeutic strategies, the management of locally advanced HNSCC continues to present substantial challenges, owing to both the aggressive biological behavior of these tumors and the complex anatomical structures of the head and neck region [11].

The standard approach for treating locally advanced HNSCC consists of concurrent chemoradiotherapy (CRT) utilizing a fractionated radiotherapy regimen, typically delivering 70 Gy over seven weeks [12]. Nevertheless, this conventional schedule is associated with extended overall treatment time (OTT), significant acute and late toxicities, and suboptimal locoregional control (LRC) outcomes [12,13]. Additionally, biological factors such as tumor hypoxia and accelerated tumor cell repopulation during therapy further compromise treatment efficacy. These limitations highlight the urgent need for alternative therapeutic approaches that enhance tumor control while minimizing associated toxicities [13].

Evidence from randomized clinical trials, including RTOG 90-03 and the DAHANCA protocols,

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as well as meta-analyses such as MARCH, supports the use of altered fractionation schedules compared to conventional once-daily radiotherapy, demonstrating modest but statistically significant improvements in LRC and OS [14,15]. One particularly promising strategy involves the use of altered fractionation, especially accelerated radiotherapy (RT), which entails delivering more than the conventional 10 Gy per week [16,17]. Accelerated RT has been shown to offer a more favorable benefit-risk profile when total dose, dose per fraction, and OTT are appropriately balanced. By shortening the overall treatment duration without compromising the total radiation dose, these approaches aim to reduce the time available for tumor repopulation and improve locoregional control [17].

Clinical studies comparing accelerated hyperfractionated radiotherapy (AHRT) with conventional fractionated radiotherapy (CFRT) have demonstrated trends toward improved progression-free survival (PFS) and LRC, although improvements in OS have been less consistently observed. Importantly, concurrent cisplatin-based chemotherapy continues to serve as the backbone of definitive treatment, with both weekly and daily cisplatin schedules showing variable radiosensitization efficacy and differing toxicity profiles [13].

Beyond modifications in radiation delivery, there is a growing interest in incorporating systemic inflammatory markers as prognostic tools in HNSCC. Biomarkers such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) have been extensively investigated for their potential to predict treatment outcomes. Numerous retrospective studies have linked elevated pre-treatment NLR and PLR values with poorer OS, disease-free survival, and LRC outcomes. Given their simplicity, low cost, and accessibility through routine blood tests, these systemic markers represent attractive candidates for integration into clinical prognostic models [18].

Our aim was to compare accelerated chemoradiation vs. conventional chemoradiation regarding late toxicity, recurrence rate, DFS, PFS, OS, and prognostic factors affecting survival. DFS is determined from the complete response to treatment until recurrence or distant metastasis. PFS is determined from the time of achieving partial response or stationary disease until progression. OS is determined from the time of diagnosis until death. After completing treatment, follow-up was conducted every 3 months for 2 years, then every 6 months for 3 years, and annually thereafter.

PATIENTS AND METHODS

Our study is a retrospective comparative study in which data were collected from 2012 to 2022 from the medical files of cancer patients in both the Clinical Oncology Department at Assiut University Hospital and the Radiotherapy Department at the South Egypt Cancer Institute archives.

All patients were diagnosed with squamous cell carcinoma (SCC), aged 18 years or older, and had a performance status (ECOG PS) of 0-2.

Exclusion criteria included patients diagnosed with distant metastasis, those who had previous head and neck irradiation, and pregnant or lactating women. Disease staging was performed according to the American Joint Committee on Cancer (AJCC), with staging for patients treated prior to 2017 reconstructed according to the same edition [19].

Patients underwent endoscopic biopsy, radiological assessment (MSCT or MRI of the head, neck, and chest), nutritional assessment, dental care, and a full laboratory and chemical assessment (CBC, RFT, LFT). 3D simulation with MSCT slice thickness of 1.5 mm in the supine position, from vertex to carina, with a suitable headrest and thermoplastic mesh for immobilization, was performed.

Patients were grouped into two arms: one (Arm A) for 60 patients who received accelerated radiotherapy with 1.8-2 Gy per fraction, 5 fractions per week, and a second (Arm B) for 50 patients who received conventional radiotherapy with 2 Gy per fraction, 6 fractions per week. Patients received radiotherapy on a LINAC Elekta with 6 MV energy. Some patients received concurrent chemotherapy, which was documented, and any neoadjuvant chemotherapy was also recorded. Response assessment was done using RECIST criteria version 1.1, and toxicity was assessed using CTCAE V.4 and RTOG for radiotherapy toxicity assessment.

Ethical approval:

Ethical approval was obtained from the Assiut University Ethical Approval Committee (approval number 17101687). Signed consent was provided by all the participant to use their information for research purposes, at the entry of the hospital. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis

SPSS version 26.0 was used for data analysis. Both percentages and frequencies were used to display categorical data. The Shapiro-Wilk test was used to assess for normalcy of numerical data, which were then shown as either mean ± SD or median and 95% confidence interval (CI), depending on how they were distributed. The X^2-test or Fisher exact test was used to compare proportions across groups, while the independent sample t-test was used to analyze mean differences between two groups. The Log-rank test was used for survival analysis in order to determine OS and DFS. Prognostic factors linked to DFS were identified using univariate Cox regression analysis, and the adjusted hazard ratio was computed by entering relevant variables into a multivariate backward LR Cox regression analysis. When the P value was less than 0.05, the significance threshold was taken into account.

RESULTS

A retrospective comparative study was conducted with a total of 110 patients, who received accelerated radiotherapy (RTH) or conventional radiotherapy (RTH) in the proportions of 60 (54.5%) and 50 (45.5%), respectively. Table 1 shows that there was no statistically significant difference between both arms regarding mean age, gender, smoking status, and performance status (PS) group. The majority of patients in both arms were classified as PS 0 and PS 1. There was no statistically significant difference between both arms regarding the site of lesion and pathology. Regarding pathology, moderate differentiation was the most common in both arms. Regarding T stage in both arms, the majority of cases were in stage T2, followed by T1, and T3. Regarding N stage in both arms, there was a statistically significant higher percentage of N0 in arm A compared to arm B. Regarding tumor stage in both arms, there was a statistically significant higher percentage of stage II in arm A compared to arm B (18.3% vs. 0.0%, respectively) (Table 1).

Table (1): Characteristics of the studied patients in the two groups.

Variables	Arm A (n=60)	Arm B (n=50)	P-Value
Age (years): Mean ± SD	53.12±12.27	54.98±9.19	0.378*
Gender			
▪ Male	39 (65.0%)	26 (52.0%)	0.167
▪ Female	21 (35.0%)	24 (48.0%)	
Smoking			
▪ Current smoker	45 (75.0%)	39 (78.0%)	0.712
▪ Ex-smoker	7 (11.7%)	4 (8.0%)	0.751
▪ Non-smoker	8 (13.3%)	7 (14.0%)	0.919
PS			
▪ 0	21 (35.0%)	22 (44.0%)	0.335
▪ 1	27 (45.0%)	20 (40.0%)	0.597
▪ 2	10 (16.7%)	8 (16.0%)	0.925
▪ 3	2 (3.3%)	0 (0.0%)	0.500
Site of lesion			
▪ Larynx	22 (36.7%)	19 (38.0%)	0.885
▪ Oral cavity	15 (25.0%)	10 (20.0%)	0.693
▪ Nasopharyngeal	12 (20.0%)	9 (18.0%)	0.791
▪ Hypopharynx	7 (11.7%)	6 (12.0%)	0.957
▪ Maxillary	3 (5.0%)	2 (4.0%)	1.000
▪ Oropharynx	1 (1.7%)	4 (8.0%)	0.175
Pathology			
▪ Well differentiated	12 (20.0%)	7 (14.0%)	0.407
▪ Moderately differentiated	39 (65.0%)	34 (68.0%)	0.899
▪ Poorly differentiated	9 (15.0%)	9 (18.0%)	0.671
Clinical stage			
T stage			0.669
▪ T1	15 (25.0%)	15 (30.0%)	0.557
▪ T2	27 (45.0%)	19 (38.0)	0.458
▪ T3	13 (21.7%)	9 (18.0%)	0.814
▪ T4	5 (8.3%)	7 (14.0%)	0.344
N stage			0.081
▪ N0	17 (28.3%)	5 (10.0%)	**0.016**
▪ N1	19 (31.7%)	18 (36.0%)	0.632
▪ N2	21 (35.0%)	21 (42.0%)	0.452
▪ N3	3 (5.0%)	6 (12.0%)	0.295
Tumor stage			**0.002**
▪ Stage I	4 (6.7%)	1 (2.0%)	0.242
▪ Stage II	11 (18.3%)	0 (0.0%)	**<0.001**
▪ Stage III	25 (41.7%)	26 (52.0%)	0.279
▪ Stage IV A	18 (30.0%)	17 (34.0%)	0.654
▪ Stage IV B	21 (3.3%)	6 (12.0%)	0.138

** Independent sample t-test compared means between groups.Chi-square/Fisher exact test compared proportions between groups.*

There was no statistically significant difference between both arms regarding the type of radiotherapy, ccRTH, neoadjuvant CTH, whether patients underwent surgery, and pathological staging after surgery according to TNM staging. Regarding radiotherapy, either adjuvant or definitive, the majority of cases received definitive radiotherapy in both arms (70.0% vs. 82.0%, respectively). Regarding concurrent chemoradiotherapy (ccRTH), most patients in both arms received cisplatin (46.7% vs. 36.0%, respectively). For neoadjuvant chemotherapy (CTH), 13.3% and 10.0% of patients in arms A and B, respectively, received the TPF regimen. Surgery was required in 30.0% and 18.0% of patients in arms A and B, respectively (Table 2).

Table (2): Lines of treatment in the two studied groups.

Variables	**Arm A (n=60)**	**Arm B (n=50)**	**P-Value***
Type of Radiotherapy			
▪ Post-operative	18 (30.0%)	9 (18.0%)	0.145
▪ Definitive	42 (70.0%)	41 (82.0%)	
ccRTH			
▪ No	28 (46.7%)	30 (60.0%)	0.365
▪ Cisplatin	28 (46.7%)	18 (36.0%)	
▪ Taxotere	4 (6.7%)	2 (4.0%)	
Neo adjuvant CTH			
▪ TPF	8 (13.3%)	5 (10.0%)	0.568
▪ No	52 (86.7%)	45 (90.0%)	
Surgery			
▪ Yes	18 (30.0%)	9 (18.0%)	0.145
▪ No	42 (70.0%)	41 (82.0%)	
Pathological staging after surgery	**N=18**	**N=9**	
T stage			
▪ T1	4 (22.3%)	0 (0.0%)	0.124
▪ T2	9 (50.0%)	4 (44.4%)	0.376
▪ T3	3 (16.7%)	2 (22.2%)	1.000
▪ T4	2 (11.1%)	3 (33.3%)	0.658
N stage			
▪ N0	4 (22.2%)	0 (0.0%)	0.124
▪ **N1**	6 (33.3%)	1 (11.1%)	0.124
▪ N2	6 (33.3%)	4 (44.4%)	0.753
▪ N3	2 (11.1%)	4 (44.4%)	0.408

Chi-square/Fisher exact test was used to compare proportions between groups.

There was a statistically significant lower percentage of grade 1 odynophagia in arm A compared to arm B (84.7% vs. 98.0%, respectively). However, there was no statistically significant difference between the two arms regarding renal toxicity, grades of mucositis, skin toxicity, and xerostomia.
Grade 1 renal toxicity occurred in 5% of patients in arm A and 2% in arm B. The majority of mucositis cases were classified as grade 2 or 3 in both groups. Nearly all patients in both arms experienced grade 1 skin toxicity. Additionally, more than two-thirds of patients in both arms had grade 1 xerostomia. There was a statistically significant lower percentage of RT interruption in arm A compared to arm B (3.3% vs. 18.0%, respectively). However, there was no statistically significant difference between the two arms regarding cranial nerve affection, taste alteration, trismus, hearing impairment, and RT completion (Table 3).

Table (3): Comparison of toxicity between the two studied arms.

Variables	Arm A (n=60)	Arm B (n=50)	P-Value*
Renal toxicity			
▪ No	57 (95.0%)	49 (98.0%)	0.403
▪ Gr1	3 (5.0%)	1 (2.0%)	
Mucositis			
▪ Gr1	3 (5.0%)	2 (4.0%)	1.000
▪ Gr2	25 (41.7%)	20 (40.0%)	0.859
▪ Gr 3	30 (50.0%)	25 (50.0%)	1.000
▪ Gr4	2 (3.3%)	3 (6.0%)	0.658
Skin toxicity			
▪ No	1 (1.7%)	0 (0.0%)	1.000
▪ Gr1	59 (98.3%)	49 (100.0%)	
Odynophagia			
▪ No	**9 (15.3%)**	**1 (2.0%)**	**0.02**
▪ Gr1	**50 (84.7%)**	**48 (98.0%)**	
Xerostomia			
▪ No	16 (26.7%)	10 (20.0%)	0.413
▪ Gr1	44 (73.3%)	40 (80.0%)	
Cranial nerve affection	1 (1.7%)	1 (2.0%)	1.000
Presence of taste alteration	29 (48.3%)	19 (38.0%)	0.227
Trismus			
▪ No	58 (96.7%)	48 (96.0%)	1.000
▪ Gr1	2 (3.3%)	2 (4.0%)	
Hearing impairment	6 (10.2%)	5 (10.0%)	0.977
RT interruption	**2 (3.3%)**	**9 (18.0%)**	**0.022**
RT completion	56 (94.9%)	43 (86.0%)	0.108

Chi-square/Fisher exact test was used to compare proportions between groups.

There was no statistically significant difference between the two arms regarding response to treatment. The majority of patients in both groups achieved a complete response (86.7% vs. 90.0%, respectively) (Table 4).

Table (4): Response to treatment between the two studied arms.

Variables	Arm A (n=60)	Arm B (n=50)	P-Value*
Response to treatment			0.231
▪ CR	52 (86.7%)	45 (90.0%)	0.590
▪ PR	1 (1.7%)	3 (6.0%)	0.328
▪ SD	3 (5.0%)	0 (0.0%)	0.249
▪ PD	4 (6.7%)	2 (4.0%)	0.687

Chi-square/Fisher exact test was used to compare proportions between groups.

The study revealed that the median OS among all patients was 48.0 months. According to the log-rank test, there was a statistically significant higher median OS in arm A compared to arm B (64.0 vs. 24.0 months, respectively). Regarding DFS, the median DFS among all patients was 24.0 months. The log-rank test also demonstrated a statistically significant higher median DFS in arm A compared to arm B (60.0 vs. 20.0 months, respectively), as shown in table 5.

Table (5): Comparison of OS and DFS between the two studied arms.

Variables	OS in months (median, 95% CI)	DFS in months (median, 95% CI)
Total (n=110)	**48.0 (33.47-62.52)**	**24.0 (9.84-38.16)**
Arm A (n=60)	**64.0 (47.51-66.65)**	**60.0 (37.08-62.45)**
Arm B (n=50)	**24.00 (20.58-27.41)**	**20.00 (17.74-22.25)**
P-Value*	**0.002**	**0.007**

***Log-rank test.*

As shown in table (6)**,** there were statistically significant higher levels of NLR, PLR, and PNR among patients with DFS < 24 months compared to those with DFS ≥ 24 months. There were statistically significant higher levels of NLR, PLR, and PNR among patients with OS < 48 months compared to those with OS ≥ 48 months.

Table (6): Comparison of NLR, PLR, and PNR according to DFS and OS among patients with squamous cell carcinoma of the head and neck

Variables	NLR	PLR	PNR
DFS < 24 Ms.	1.79 ± 0.59	136.40 ± 66.54	78.47 ± 43.25
DFS ≥ 24 Ms.	1.47 ± 0.69	81.59 ± 28.82	59.64 ± 21.95
DFS P-Value	**0.036**	**< 0.001**	**0.027**
OS < 48 Ms.	1.81 ± 0.60	127.79 ± 60.04	76.60 ± 38.32
OS ≥ 48 Ms.	1.11 ± 0.50	61.41 ± 16.40	47.68 ± 16.94
OS P-Value	**< 0.001**	**< 0.001**	**0.005**

Independent Sample T-test was used to compare means between groups.

Table (7) shows prognostic factors related to DFS among the studied patients. The significant prognostic factors associated with DFS in the univariate Cox regression analysis were: higher age, PS stage 2 or 3, definitive radiotherapy, conventional radiotherapy group, hearing impairment, higher levels of NLR, PLR, and PNR, and response to treatment (PR/SD/PD).

These significant variables were entered into a multivariate Cox regression model, and the significant prognostic variables identified were: PS stage 2 or 3 (HR = 2.71), conventional radiotherapy group (HR = 1.96), higher level of PLR (HR = 1.10), and response to treatment (PR/SD/PD) (HR = 6.32).

Table (7): Prognostic factors related to DFS among the studied patients.

Predictors	Univariate		Multivariate	
	HR (95% CI)	**P-value**	**HR (95% CI)**	**P-value**
Age (years)	**1.03 (1.01-1.11)**	**0.031**		
Gender				
▪ Male	Reference	0.575		
▪ Female	1.16 (0.68-1.97)			
Smoker				
▪ Positive	Reference	0.935		
▪ Smoker	1.0 (0.53-1.78)			
PS				
▪ 0-1	Reference	**0.006**	Reference	
▪ 2-3	**2.34 (1.28-4.26)**		**2.71 (1.26-5.77)**	**0.010**
Pathology				
▪ Well differentiated	Reference			
▪ Moderately differentiated	1.29 (0.55-2.99)	0.551		
▪ Poorly differentiated	0.89 (0.44-1.81)	0.753		
Tumor stage				
▪ Early stage (I, II)	Reference			
▪ Late stage (III, IV)	2.09 (0.89-4.92)	0.090		
Type of Radiotherapy				
▪ Adjuvant	Reference	**0.022**		
▪ Definitive	**1.91 (1.09-3.32)**			
CCRTH				
▪ No	Reference	0.816		
▪ Yes	0.94 (0.55-1.54)			
Groups				
▪ Accelerated	Reference	**0.019**	Reference	**0.045**
▪ conventional Radiotherapy	**1.91 (1.11-3.28)**		**1.96 (1.10-4.19)**	
Taste alteration				
▪ No	Reference	0.266		
▪ Yes	1.34 (0.79-2.26)			
Hearing impairment				
▪ No	Reference	**0.009**		
▪ Yes	**1.43 (0.67-3.03)**			
Xerostomia				
▪ No	Reference	0.075		
▪ Yes	1.91 (9.36-3.91)			
Mucositis				
▪ Gr 1, 2	Reference			
▪ Gr 3, 4	2.10 (0.8-3.54)	0.071		
Investigation				
▪ NLR	**1.55 (1.02-2.34)**	**0.037**		
▪ PLR	**1.10 (1.01-1.02)**	**<0.001**	**1.10 (1.01-1.20)**	**0.010**
▪ PNR	**1.10 (1.01-1.02)**	**0.016**		
Response				
▪ CR	Reference		Reference	
▪ PR/SD/PD	**7.19 (3.40-15.19)**	**<0.001**	**6.32 (2.29-17.44)**	**<0.001**

Cox regression analysis, HR: hazard ratio, 95% CI: 95% confidence interval.

DISCUSSION

Head and neck cancers present unique therapeutic challenges, and the choice of radiotherapy fractionation plays a crucial role in balancing tumor control with the preservation of normal tissues**.** Conventional fractionation schemes have long been used in clinical practice due to their favorable balance between tumor control and normal tissue preservation. However, over the past few decades, modifications to radiotherapy schedules—particularly accelerated radiotherapy—have been explored as potential strategies to enhance locoregional control and survival outcomes [15].

Accelerated fractionated radiation therapy has become the standard of care for managing head and neck cancers in countries such as Denmark [15]. This approach not only reduces treatment duration but also alleviates the burden on radiation departments, which is especially important in low- to medium-income regions or resource-limited countries [20]. The Meta-Analysis of Radiotherapy in Carcinomas of the Head and Neck (MARCH), conducted by **Bourhis *et al.*** [21], pooled data from numerous randomized controlled trials and demonstrated that altered fractionation schedules, including accelerated regimens, resulted in significant improvements in tumor control and overall survival compared to conventional radiotherapy. Among the altered schedules, hyperfractionated regimens provided the greatest survival benefit; however, accelerated regimens, even without an increased dose, still conferred a notable advantage in locoregional control.

From a biological perspective, accelerated RT operates through several fundamental mechanisms. It limits tumor cell repopulation, promotes reoxygenation of hypoxic tumor regions, thereby increasing radiosensitivity, and allows better redistribution of cancer cells into more radiosensitive phases of the cell cycle [22].

Our retrospective study has compared outcomes of patients with head and neck SCC who received radical radiotherapy as the main component of their treatment either by conventional standard fractionation or by accelerated fractionated radiotherapy. Median age was 53.12 years with male predominance, majority of cases were laryngeal followed by oral cavity cancer, T3 only in 21.7% versus 18% in accelerated and conventional arms respectively and more cases were node negative with no effect of these parameters on response, OS, DFS and LR.

Although each day prolongation of treatment time was associated with reduced tumor control probability and the rate of interruption was lower in accelerated than conventional significantly, no significant difference was found in acute toxicities in accelerated compared to conventional and both had nearly the same rate of CR. **Narvaez *et al.*** [23] documented that 19.3% of cases in the accelerated arm had interruptions of more than 7 days, with no impact on OS or toxicity grading. Similarly, our study showed no significant difference in locoregional recurrence rate and toxicity between the two groups.

Narvaez *et al.* [23] reported a median OS of 44 months, while **Tripathy *et al.*** [12] documented a median OS of 37.63 months. In contrast, our study found a median OS of 48 months, with statistical significance favoring the accelerated arm. This could be attributed to the earlier stages represented in our study, as most cases were T2 and N0.

In our study, there was no significant difference in acute and late toxicities between the two arms, which aligns with the findings of **Tripathy *et al.*** [12] **and Narvaez *et al.*** [23]. However, our results differ from those of **Arora *et al.*** [13] **and Rades *et al.*** [24] who reported higher acute and late toxicity grading in the accelerated arm compared to conventional, with no difference in OS and DFS.

DFS was better in patients received accelerated fractionation and affected by PS, PLR, response with no effect of stage, tumor site, age and sex. **Das *et al.*** [11] also documented that the type of radiotherapy given affect DFS with median DFS was 39 months and LR 44.7% and statistically differ between the 2 arms, this LR was more than the documented LR in our study as it was 28.3% in conventional and 14% in accelerated arm with no statistically significant difference. In **Das *et al.*** [11] study the high LR rate and lower DFS may be attributed to the more advanced stages of cases as most cases had T3-T4 and N positive.

Matuschek *et al.* [25] documented no improvement of OS, local control, PFS and late side effects of Accelerated radiotherapy over conventional Radiotherapy. However, acute mucositis occurred with significant higher frequency with accelerated radiotherapy. Also, in GORTEC-99002 phase 3 trial comparing concomitant conventional chemoradiation, concomitant accelerated chemoradiation and accelerated radiotherapy alone for stage III-IV non metastatic head and neck cancer did not show benefit in OS between the 3 groups [21]. We documented statistically higher levels of NLR, PLR, and PNR in patients with OS less than 48 months and in patients with shorter DFS. PLR showed the best accuracy and discriminatory ability for predicting OS and DFS, which is consistent with a meta-analysis conducted by Yukinori Takenaka et al. [26].

CONCLUSION

The findings of this study suggest that accelerated radiotherapy offers a potential advantage in improving survival outcomes, with comparable toxicity profiles to conventional treatment, and could be considered in clinical practice, especially in regions with limited resources.

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REFERENCES

1. **Ferlay J, Ervik M, Lam F *et al.* (2020):** Estimating the global cancer incidence and mortality in 2020: GLOBOCAN sources and methods. CA Cancer J Clin., 71(3):209-249.
2. **Ferlay J, Colombet M, Soerjomataram I *et al.* (2021):** Cancer statistics for the year 2020: An overview. Int J Cancer, 76: 717. https://doi.org/10.3322/caac.21660
3. **Windon M, D'Souza G, Rettig E *et al.* (2018):** Increasing prevalence of human papillomavirus positive oropharyngeal cancers among older adults. Cancer, 124(14):2993-2999.
4. **Fung S, Lam J, Chan K (2016):** Clinical utility of circulating Epstein Barr virus DNA analysis for the management of nasopharyngeal carcinoma. Chin Clin Oncol., 5(2):18. doi: 10.21037/cco.2016.03.07.
5. **Gupta B, Johnson N, Kumar N (2016):** Global epidemiology of head and neck cancers: a continuing challenge. Oncology, 91:13-23.
6. **Lee Y, Hashibe M (2014):** Tobacco, alcohol, and cancer in low and high income countries. Ann Glob Health, 80(5):378-383.
7. **Gillison M, Koch W, Capone R *et al.* (2000):** Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst., 92(9):709-720.
8. **Ang K, Harris J, Wheeler R *et al.* (2010):** Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med., 363(1):24-35.
9. **Pignon J, le Maître A, Maillard E *et al.* (2009):** Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients. Radiother Oncol., 92(1):4-14.
10. **Adelstein D, Li Y, Adams G *et al.* (2003):** An intergroup phase III comparison of standard radiation therapy and two schedules of concurrent chemoradiotherapy in patients with unresectable squamous cell head and neck cancer. J Clin Oncol., 21(1):92-98.
11. **Das S, Roy N, Singh D *et al.* (2023):** A comparative prospective study between conventional chemo-radiotherapy and pure accelerated radiotherapy with concurrent chemotherapy for the treatment of locally advanced head and neck cancer. Cureus, 15(7):e42206. doi:10.7759/cureus.42206.
12. **Tripathy A, Muzumder S, Srikantia N *et al.* (2023):** A comparison of conventional and accelerated hypofractionated radiotherapy in definitive chemoradiation for locally advanced head and neck carcinoma: a retrospective cohort study. Radiat Oncol J., 41(4):248-257.
13. **Arora C, Sharma N, Kapoor A *et al.* (2024):** A comparative study of the treatment outcome of moderately accelerated radiation fractionation (with concurrent chemotherapy in daily dosing) to conventional chemo-radiotherapy in locally advanced head and neck cancers: Supportive in a resource-constrained environment. Indian J Cancer, 61:262-272.
14. **Fu K, Pajak T, Trotti A *et al.* (2000):** A Radiation Therapy Oncology Group (RTOG) phase III randomized study to compare hyperfractionation and two variants of accelerated fractionation to standard fractionation radiotherapy for head and neck squamous cell carcinomas: first report of RTOG 9003. Int J Radiat Oncol Biol Phys., 48:7-16.
15. **Overgaard J, Hansen H, Specht L *et al.* (2003):** Five compared with six fractions per week of conventional radiotherapy of squamous cell carcinoma of head and neck: DAHANCA 6 and 7 randomized controlled trial. Lancet, 362:933-940.
16. **Nguyen L, Ang K (2002):** Radiotherapy for cancer of the head and neck: altered fractionation regimens. Lancet Oncol., 3:693-701.
17. **Bernier J, Bentzen S (2003):** Altered fractionation and combined radio-chemotherapy approaches: pioneering new opportunities in head and neck oncology. Eur J Cancer, 39:560-571.
18. **Mireștean C, Stan M, Iancu R *et al.* (2023):** The prognostic value of platelet–lymphocyte ratio, neutrophil–lymphocyte ratio, and monocyte–lymphocyte ratio in head and neck squamous cell carcinoma (HNSCC)—a retrospective single center study and a literature review. Diagnostics, 13(22):3396. doi:10.3390/diagnostics13223396.
19. **Amin M, Greene F, Edge S *et al.* (2017):** The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin., 67(2):93-99.
20. **Overgaard J, Mohanti B, Begum N *et al.* (2010):** Five versus six fractions of radiotherapy per week for squamous-cell carcinoma of the head and neck (IAEA-ACC study): A randomised, multicentre trial. Lancet Oncol., 11:553-560.
21. **Bourhis J, Overgaard J, Audry H *et al.* (2006):** Hyperfractionated or accelerated radiotherapy in head and neck cancer: A meta-analysis. Lancet, 368:843-854.
22. **Boustani J, Grapin M, Laurent P *et al.* (2019):** The 6th R of Radiobiology: Reactivation of anti-tumor immune response. Cancers (Basel), 11(6):860. doi:10.3390/cancers11060860.
23. **Narvaez C, Schild S, Janssen S *et al.* (2021):** Accelerated fractionation with concomitant boost vs. conventional radio-chemotherapy for definitive treatment of locally advanced squamous cell carcinoma of the head-and-neck (SCCHN). Anticancer Res., 41:477-484.
24. **Rades D, Narvaez C, Janssen S *et al.* (2021):** Accelerated fractionation plus chemotherapy versus conventionally fractionated radiochemotherapy for unresectable head-and-neck cancer. Anticancer Res., 41(2):877-884.
25. **Matuschek C, Haussmann J, Bölke E *et al.* (2018):** Accelerated vs. conventionally fractionated adjuvant radiotherapy in high-risk head and neck cancer: A meta-analysis. Radiat Oncol., 13(1): 1133. doi:10.1186/s13014-018-1133-8.
26. **Takenaka Y, Oya R, Kitamiura T *et al.* (2018):** Platelet count and platelet-lymphocyte ratio as prognostic markers for head and neck squamous cell carcinoma: Meta-analysis. Head Neck, 40(10):2229-2239.