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Response Analysis of Hypo-Fractionated Radiotherapy in the Treatment of Locally Advanced Inoperable Head and Neck Cancer

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Abstract
Introduction: *Locally advanced head and neck carcinomas constitute a substantial proportion of cancer patients in Bangladesh. The common practice is to treat the condition by conventional fractionation (2 gray/fraction, total dose 66 gray). Hypo-fractionated radiotherapy (2.75 gray/fraction, total 55 gray) might be able to produce a similar response in a shorter time.*
Aim of the study: *The aim of the study was to determine tumor response and toxicities in hypo-fractionated radiotherapy.*
Methods: *This Quasi-Experimental study was conducted at the Department of Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, and the Department of Radiation Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh. The study duration was 1.5 years, from July 2018 to December 2019. During this period, a total of 74 patients with inoperable locally advanced squamous cell carcinoma of the head and neck, and equally distributed in two groups, Arm-A and Arm-B. Arm-A received conventionally fractionated chemo-radiotherapy and Arm-B received hypo-fractionated radiotherapy*
Result: *The mean age of Arm-A and B patients were 53.27 (±11.23) & 51.03 (±9.48) years, respectively. Among 74 patients, 46 patients were smokers. 33.68 % of patients were in stage III and 66.22% of patients were in stage IV. In Arm-A 10 patients (27.03%) showed a complete response and in Arm-B, a complete response was observed in 7 patients (18.93%). Partial response was 19 (51.35%) and 18 (48.64%) in Arm-A and B, respectively. There were 4 (10.81%) progressive disease cases in Arm-A and 5 (13.51%) in Arm-B. Significant differences in frequencies of acute grade 2 skin toxicity, mucositis, were found, with higher frequencies. Grade 2 oral mucositis was seen in 26 (70.27%) and 14 (37.83%) patients of Arm-A and B, respectively which was statistically significant. Other toxicities had no significant differences between Arm-A and B. in Arm-B.*
Conclusion: *Hypo-fractionated radiotherapy can achieve a similar tumor response to conventionally fractionated radiotherapy in HNSCC, although with some increase of manageable toxicity.*
Keywords: *Chemotherapy, Carcinoma, Radiotherapy, Fractionated, Hypo-Fractionated*

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I. Introduction

Cancer incidence and mortality are rapidly increasing worldwide. It is the leading cause of death globally, approximately causing 1 in 6 deaths.[1] There were an estimated 18.1 million new cancer cases and 9.6 million cancer deaths in 2018 globally. Just in Bangladesh, over 1.5 lakhs of new cases and 1.08 lakhs of cancer-related deaths were recorded in the year 2020.[2] Head and neck cancers are the names given to a variety of malignant tumors that develop in the head and neck region. Among them, the vast majority arise from the surface epithelium and squamous cell carcinoma (about 90%), or one of its variants is common histology.[3] In Bangladesh, the estimated new cases of head and neck cancers in 2018 was more than 30,000. Among them, the number of new cases of lip and oral cavity cancers was 13,401, hypopharynx cancers were 7099, larynx cancers were 4996, oropharynx cancers were 3667, salivary gland cancers were 849 and nasopharynx cancers were 845.[4] The epidemiology of head and neck cancer strongly reflects exposure to certain environmental agents, particularly tobacco and alcohol. There is a strong causal relationship between smoking and cancer of the oral cavity. Smoking is identified as an independent risk factor in 80% to 90% of oral cancer patients.[5],[6] The combined use of alcohol and tobacco may have a synergistic effect on carcinogenesis.[7] Management of head and neck cancer represents a significant treatment challenge because the disease is within such an anatomic environment that contains several critical structures, such as the salivary glands, mandible, nerves, major blood vessels, spinal cord, the organs of taste & speech, organs of swallowing and hearing. If surgical removal of the cancerous portion is possible with minimal risk, it is often preferred, but minimal risk can rarely be guaranteed. Among the non-surgical treatment method, radiation and chemotherapy are considered the most common. The basic principle of radiotherapy is to cure patients with minimum functional and structural involvement. Radiotherapy involves the exposure of a defined area of the body by ionizing and non-ionizing radiation to treat the tumor. Nearly 60% of all patients with head and neck cancers visit the oncology department in the advanced stages of cancer, which may be due to ignorance, poverty, lack of a proper referral system, illiteracy, and some traditional beliefs.[8] Some Randomized controlled trials have demonstrated major improvements in loco-regional tumor control from hypo-fractionated radiotherapy. Hypo-fractionated radiotherapy utilizes a small number of fractions with a large dose per fraction while shortening the overall treatment time. Altering fractionation or adding chemotherapy to conventional External beam radiation therapy (EBRT) gives similar improvements in local control and overall survival with increased acute toxicity and little to no evidence of worsening late toxicity.[9] Reducing the overall treatment time by increasing the dose per fraction while maintaining the biological equivalent dose results in comparable tumor control in patients with head and neck squamous cell carcinomas. Hypo-fractionated schedules seek to improve the therapeutic ratio between tumor cell killing and normal tissue damage by exploiting the dissociation between acute and late radiation effects. The number of fully functioning radiotherapy machines is inadequate compared to the high cancer load in Bangladesh.[10] The reduction in the number of fractions and overall treatment time can allow for more efficient use of machines, which in turn can help avoid long waiting times to get treatment. Therefore, this study may help to treat more inoperable locally advanced head and neck cancer patients for better locoregional control.

II. Objective

General Objective

- To observe the clinical response status of inoperable head and neck cancer after hypo-fractionated radiotherapy.

Specific Objectives

- To compare the clinical response status of inoperable head and neck cancer after conventional radiotherapy vs hypo-fractionated radiotherapy
- To observe the post-operative toxicity levels of conventional vs hypo-fractionated radiotherapy in the treatment of inoperable head and neck cancer

III. Methods

This Quasi-Experimental study was conducted at the Department of Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh, and the Department of Radiation Oncology, National Institute of Cancer Research & Hospital, Dhaka, Bangladesh. The study duration was 1.5 years, from July 2018 to December 2019. During this period, a total of 74 patients with inoperable locally advanced squamous cell carcinoma of the head and neck (oral cavity, oropharynx, hypopharynx, larynx) who met the inclusion and exclusion criteria were selected from both study places for this study. A convenient and purposive sampling technique was used for the selection of the participants. Informed consent was obtained from all participants, and ethical approval was also obtained from the ethical committee of both study places. Patients were divided into two equal groups of 37 patients, "Arm-A" and "Arm-B" based on their treatment method. Arm-A patients were treated with Conventional fractionation of radiotherapy along with concurrent low-dose weekly inj.

Cisplatin (40 mg/m2), while Arm-B patients were treated with hypo-fractionated radiotherapy, 2.75 Gy per fraction, a total of 55 Gy in 4 weeks. Hypo-fractionated radiotherapy consisted of a dose given over a shorter period of time than standard radiotherapy and typically larger doses. The ECOG scale of Performance Status was used to measure and describe a patient's level of functioning in terms of their ability to care for them-self, daily activity, and physical ability. Patients were assessed weekly during treatment, and the patient's tumor response was evaluated according to the WHO guideline for responses.

Inclusion Criteria

- Inoperable cases of locally advanced squamous cell carcinoma of head and neck origin.
- Patients aged 18 years or older
- Only Stage III and Stage IV carcinoma cases without distant metastasis.
- Patients who had given consent to participate in the study.

Exclusion Criteria

- squamous cell carcinoma of other sub-sites
- Patients over 70 years of age
- ECOG Performance status >2
- Initial surgery (excluding diagnostic biopsy of the primary site)
- Patients with a life expectancy of fewer than 6 months
- Patients with double primaries
- Non-squamous histology
- Unable to answer the criteria question.
- Exclude those affected with other chronic diseases.

IV. Results

Table 1: Distribution of both group participants by socio-demographic characteristics (n=74)

Variables	Arm-A (n=37)		Arm-B (n=37)	
	n	%	n	%
Age Range				
31-40	1	2.70%	0	0.00%
51-50	6	16.22%	5	13.51%
51-60	28	75.68%	31	83.78%
51-70	2	5.41%	1	2.70%
Mean ± SD	53.27 ± 11.23		51.03 ± 9.48	
Gender				
Male	24	64.86%	22	59.46%
Female	13	35.14%	15	40.54%
Economic Condition				
Lower Class	13	35.14%	11	29.73%
Middle Class	21	56.76%	21	56.76%
Upper Class	3	8.11%	5	13.51%

Among the participants of both groups, the highest prevalence was observed in patients aged 51-60 years, with 75.68% prevalence in Arm-A and 83.78% prevalence in Arm-B. The mean age of the participants was 53.27 ± 11.23 in Arm-A and 51.03 ± 9.48 in Arm-B. Overall male prevalence was observed in the study, with 64.86% male prevalence in Arm-A and 59.46% male prevalence in Arm-B. 56.76% of participants from both groups had been from the middle class, with only 8.11% upper-class participants from Arm-A and 13.51% upper-class participants from Arm-B.

Table 2: Distribution of participants by the origin of tumor (n=74)

Origin of Tumor	Arm-A (n=37)		Arm-B (n=37)	
	n	%	n	%
Oral Cavity	10	27.02%	13	35.13%
Tongue Base	6	16.22%	5	13.51%

Buccal Mucosa	6	16.22%	8	21.62%
Tonsil	3	8.11%	2	5.41%
Pyriform Fossa	4	10.81%	2	5.41%
Larynx	14	37.84%	15	40.54%

The primary site of the tumor for the majority of the patients was the larynx (37.84% in Arm-A and 40.54% in Arm-B) and oral cavity (27.02% in Arm-A and 35.13% in Arm-B). Tonsil was observed in only 8.11% of Arm-A and 5.41% of Arm-B participants, while Pyriform fossa had the second lowest prevalence, 10.81% in Arm-A and 5.41% in Arm-B.

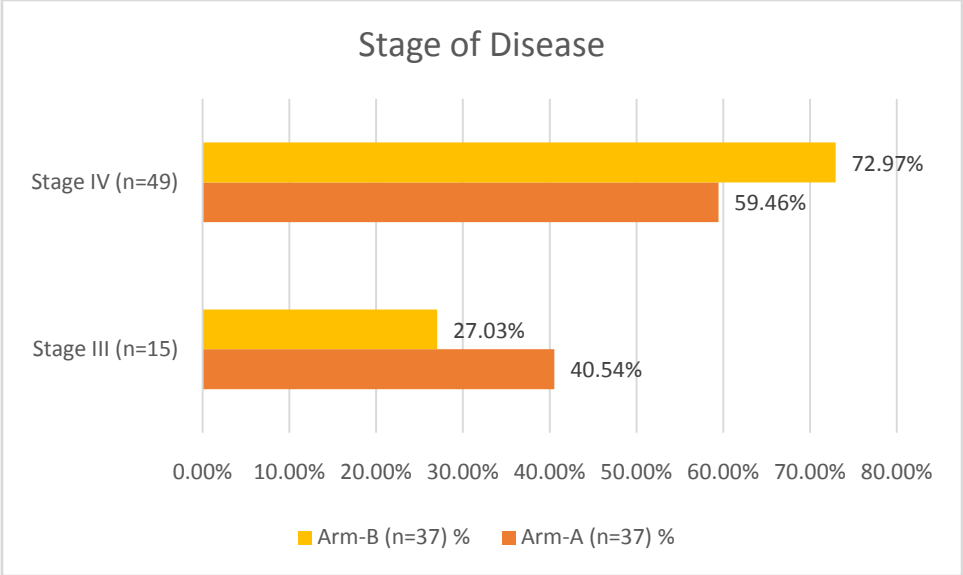

Figure 1: Distribution of participants by Staging of the disease (n=74)

In total, 15 patients had Stage III carcinoma, while 49 had stage IV carcinoma. It was observed that 40.54% of Arm-A patients had Stage III carcinoma, while 72.97% of Arm-B had Stage IV carcinoma.

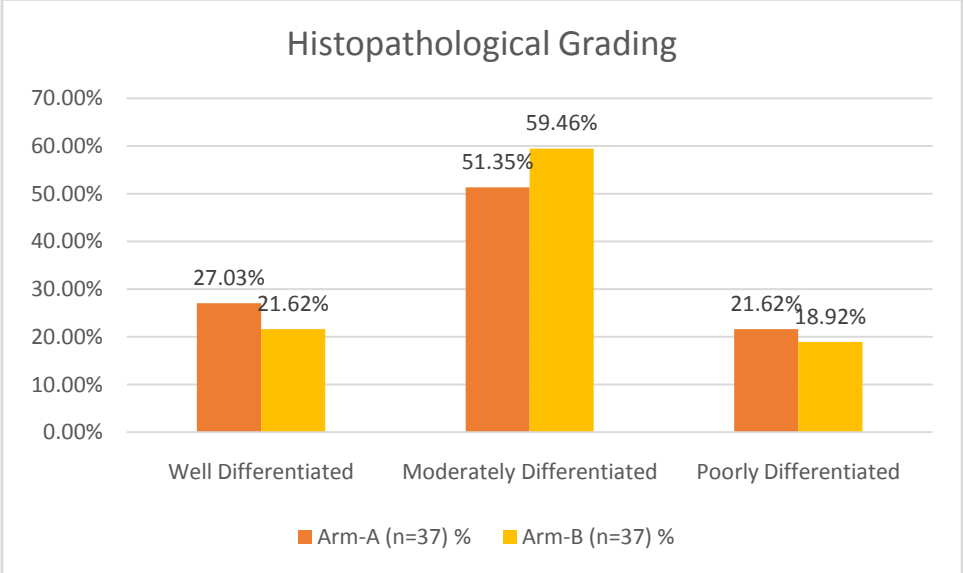

Figure 2: Distribution of participants by the histopathological grading of the disease (n=74)

It was observed that among the Arm-A participants, 27.03% had well differentiated carcinoma, 51.35% had moderately differentiated carcinoma, and 21.62% had poorly differentiated carcinoma. Among the Arm-B participants, 21.62% had well differentiated carcinoma, 59.46% had moderately differentiated carcinoma, and 18.92% had poorly differentiated carcinoma.

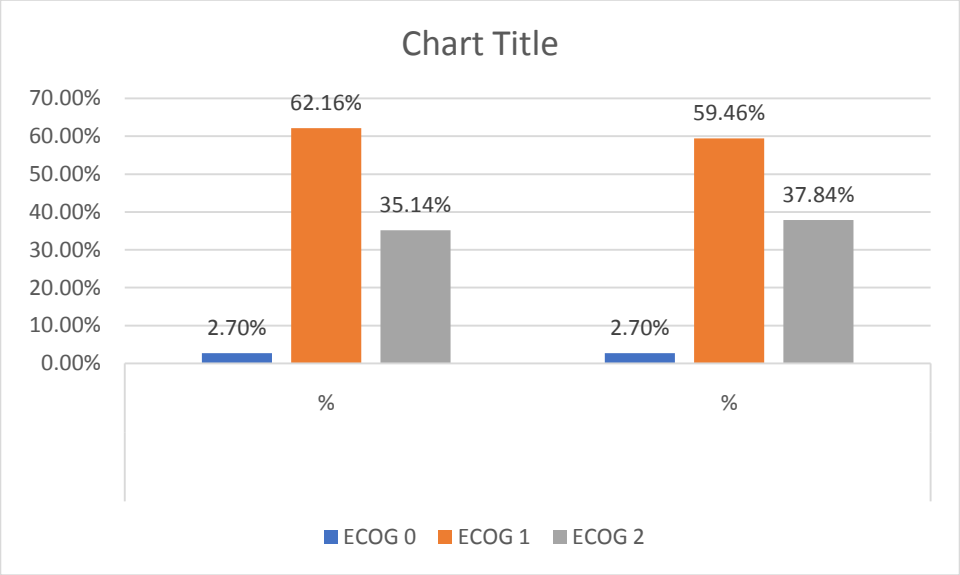

Figure 3: Distribution of the participants by ECOG stage grading (n=74)

Among the 37 Arm-A participants, 2.70% had been of ECOG grade 0, 62.16% had been from ECOG stage grade 1, and the remaining 35.14% had been of ECOG grade 2. Among Arm-B participants, 2.70% were ECOG grade 0, 59.46% were ECOG grade 1 and 37.84% were ECOG grade 2

Table 3: Distribution of the participants by habitual risk factors (n=74)

Habitual Risk Factors	Arm-A (n=37)		Arm-B (n=37)	
	n	%	n	%
Smoking	24	64.86%	22	59.46%
Betel leaf	9	24.32%	11	29.73%
Jarda/tobacco leaf	4	10.81%	5	13.51%
Gul	3	8.11%	2	5.41%
Multiple	18	48.65%	19	51.35%
None	7	18.92%	9	24.32%

Smoking was the most prevalent habitual risk factor among the participants, with 64.86% prevalence in Arm-A and 59.46% prevalence in Arm-B. Almost half the participants (48.65% in Arm-A, 61.35% in Arm-B) had multiple risk factors. The less prevalent risk factors were Gul and tobacco leaf use, while 18.92% of Arm-A and 24.32% of Arm-B patients did not have any habitual risk factors.

Table 4: Distribution of the participants by major presenting complaints (n=74)

Major Complaints	Arm-A (n=37)		Arm-B (n=37)	
	n	%	n	%
Hoarseness of voice	13	35.14%	10	27.03%
Pain in the throat and/or oral cavity	19	51.35%	25	67.57%
Difficulty in deglutition	11	29.73%	14	37.84%
Difficulty in taking food	21	56.76%	23	62.16%
Neck node	37	100.00%	37	100.00%
weight loss	10	27.03%	14	37.84%
Oral ulcer	15	40.54%	19	51.35%

Neck node was a common complaint of all 74 patients. Among the Arm-A patients, difficulty in ingesting food had the next highest prevalence, at 56.76%, while 51.35% had an oral cavity, 40.54% had an oral ulcer, 35.14% had a hoarse voice, 29.73% had difficulty in deglutition, and 27.03% had weight loss as major complaints. Among the Arm-B patients, 67.57% had an oral cavity, 62.16% had difficulty ingesting food, 51.35% had an oral ulcer,27.03% had hoarseness of voice, and weight loss and difficulty in deglutition were each observed in 37.84% of patients.

Table 5: Distribution of the participant's post-treatment response by stage of cancer (n=74)

TNM Stage	Response Status	Arm-A (n=37)		Arm-B (n=37)		P value
		n	%	n	%	
Stage III	Complete response (CR)	10	27.03%	7	18.92%	0.437
	Partial response (PR)	4	10.81%	3	8.11%	
	Stable Disease (SD)	1	2.70%	0	0.00%	
	Progressive disease (PD)	0	0.00%	0	0.00%	
Stage IV	Complete response (CR)	0	0.00%	0	0.00%	0.16
	Partial response (PR)	15	40.54%	15	40.54%	
	Stable Disease (SD)	3	8.11%	7	18.92%	
	Progressive disease (PD)	4	10.81%	5	13.51%	

After completion of treatment, in stage III disease, both the Arm-A and Arm-B patients showed complete response in 27.03% and 18.92% of patients respectively. Partial responses (PR) were developed in 04 (10.81%) and 03 (8.10%) patients of both arms, respectively. Statistically, a non-significant result was found between the two groups ($p>0.05$). in stage IV disease, both the Arm-A and Arm-B patients showedPR in 15 (40.54%) patients, respectively. None of the patients developed CR in either group. Statistically, a non-significant result was found between the two groups ($p>0.05$).

Table 6: Distribution of the participant's post-treatment response according to subgroup analysis (n=74)

Site of Cancer	Response Status	Arm-A (n=37)		Arm-B (n=37)		P value
		n	%	n	%	
Oral Cavity	Complete response (CR)	1	2.70%	0	0.00%	0.62
	Partial response (PR)	6	16.22%	7	18.92%	
	Stable Disease (SD)	2	5.41%	3	8.11%	
	Progressive disease (PD)	1	2.70%	3	8.11%	
Larynx	Complete response (CR)	7	18.92%	5	13.51%	0.56
	Partial response (PR)	4	10.81%	6	16.22%	
	Stable Disease (SD)	1	2.70%	3	8.11%	
	Progressive disease (PD)	2	5.41%	1	2.70%	
Hypopharynx	Complete response (CR)	1	2.70%	1	2.70%	0.54
	Partial response (PR)	3	8.11%	1	2.70%	
	Stable Disease (SD)	0	0.00%	0	0.00%	
	Progressive disease (PD)	0	0.00%	0	0.00%	
Oropharynx	Complete response (CR)	1	2.70%	1	2.70%	0.98
	Partial response (PR)	6	16.22%	4	10.81%	
	Stable Disease (SD)	1	2.70%	1	2.70%	
	Progressive disease (PD)	1	2.70%	1	2.70%	

On subgroup analysis, Arm-A patients had CR in the larynx for 18.92% for the hypopharynx it was 2.70%, same for the oropharynx, and oral cavity. On the other hand, Arm-B patients had CR in the larynx in 13.51%, for the oral cavity it was 0%, and for both the hypopharynx and oropharynx, a complete response was observed in 2.70% of participants. PR had the highest frequency overall, as in Arm-A, 16.22% were from oral cavity cases and oropharynx cases each. 10.81% were from larynx cases, and 8.11% were from hypopharynx. In Arm-B, PR was observed in 18.92% with the oral cavity, 16.22% with the larynx, 2.70% with the hypopharynx, and 10.81% with the oropharynx. None of the subgroup distributions of response had any significant association between Arm-A and Arm-B.

Table 7: Distribution of participants by response status at different follow-ups (n=74)

Follow-up Week	Response Status	Arm-A (n=37)		Arm-B (n=37)		P value
		n	%	n	%	
Week 6	Complete response (CR)	10	27.03%	7	18.92%	0.693
	Partial response (PR)	26	70.27%	29	78.38%	
	Stable Disease (SD)	0	0.00%	0	0.00%	

	Progressive disease (PD)	1	2.70%	1	2.70%	
Week 12	Complete response (CR)	10	27.03%	7	18.92%	0.693
	Partial response (PR)	26	70.27%	29	78.38%	
	Stable Disease (SD)	0	0.00%	0	0.00%	
	Progressive disease (PD)	1	2.70%	1	2.70%	
Week 24	Complete response (CR)	10	27.03%	7	18.92%	0.68
	Partial response (PR)	19	51.35%	18	48.65%	
	Stable Disease (SD)	4	10.81%	7	18.92%	
	Progressive disease (PD)	4	10.81%	5	13.51%	

The response status of the participants at different follow-up weeks did not have any significant difference between the two groups. At week 6, the majority of both groups (70.27% of Arm-A, 78.38% of Arm-B) had PR, while CR was observed in 27.03% of Arm-A and 18.92% of Arm-B participants. 1 patient from each group had progressive disease (PD). The situation did not change at the 12-week follow-up, but at the 24th week of follow-up, PD had a 10.81% prevalence in Arm-A and 13.51% prevalence in Arm-B patients, while another 10.81% of Arm-A and 18.92% of Arm-B had stable disease. Although the prevalence of stable disease was higher among Arm-B patients, while the prevalence of CR was higher among Arm-A patients (27.03% vs 18.92%), the difference was not statistically significant.

Table 8: Distribution of participants by presenting toxicity grades (n=74)

Toxicity	**Grade**	**Arm-A (n=37)**		**Arm-B (n=37)**		**P value**
		n	**%**	**n**	**%**	
Oral mucositis	Grade 1	21	56.76%	8	21.62%	<**0.01**
	Grade 2	14	37.84%	26	70.27%	
	Grade 3	2	5.41%	3	8.11%	
Skin Toxicity	Grade 1	20	54.05%	5	13.51%	<**0.01**
	Grade 2	11	29.73%	24	64.86%	
	Grade 3	6	16.22%	8	21.62%	
Dysphagia	Grade 1	26	70.27%	19	51.35%	0.25
	Grade 2	10	27.03%	16	43.24%	
	Grade 3	1	2.70%	2	5.41%	
Xerostomia	Grade 1	35	94.59%	32	86.49%	0.23
	Grade 2	2	5.41%	5	13.51%	
	Grade 3	0	0.00%	0	0.00%	
Laryngeal Edema	Grade 1	10	27.03%	9	24.32%	0.652
	Grade 2	7	18.92%	12	32.43%	
	Grade 3	1	2.70%	1	2.70%	

In terms of toxicity, grade 1 toxicity of different types was pretty common among both participants. In terms of oral mucositis, among the Arm-A patients, grade 1 oral mucositis was observed in 56.76%, grade 2 in 37.84%, and grade 3 in 5.41% of patients. Among the Arm-B patients, grade 2 oral mucositis had the highest prevalence at 70.27%, and this difference was statistically significant. In terms of skin toxicity, Grad 1 had the highest prevalence among Arm-A participants at 54.05%, while the highest prevalence of skin toxicity was observed in Grade 2 among Arm-B participants, at 64.86%. This difference was also statistically significant. Other observed toxicities were dysphagia, xerostomia, and laryngeal edema, but the difference in prevalence by grade among the 2 groups was not statistically significant in terms of these toxicities.

V. Discussion

Diagnosed patients of locally advanced (stage III and IV) head and neck squamous cell carcinoma of some sub-sites (oral cavity, oropharynx, hypopharynx, larynx) were enrolled in this study. Among 74 patients, 46 patients were male and only 28 patients were female, and male-female distribution was similar among both Arm-A and Arm-B patients. Most of the patients were diagnosed after 40 years of age. The average age of diagnosis was 53.27 years for Arm-A and 51.03 years for Arm-B. The most prevalent age group was between 51-60 years for both groups, and none of the patients were under 38 years of age. This age distribution and demographical findings were similar to the findings of multiple other studies, supporting the assumption that

squamous cell carcinoma of the head and neck region is a disease of the elderly aged.[8],[11] Majority of patients in this study group came from the low to middle economic class. This group jointly covered 89.5% of total patients. The reason for such a large number of low to middle-class patients was possibly due to the study place, as well as the tendency of upper-class patients to go to the private sector or abroad for treatment. As previously discussed, smoking by itself is a major risk factor for head and neck cancer globally. In this study, 64.86% of patients in Arm-A and 59.45% of patients in Arm-B were a smoker. Here smoking was defined as the inhalation of the smoke of burning tobacco encased in cigarettes, pipes, and cigars. But many of the study population took tobacco in a different form. A good percentage of the population took tobacco in form of jarda, gul, and tobacco leaf. About 24.32% of people in Arm-A and 29.72% of people in Arm-B were betel leaf users. Chewing betel nut with caustic lime and sometimes with tobacco in the form of jarda causes chronic mucosal irritation and aids as a risk factor. These findings coincided with previous studies where the majority of the study population had either smoking or tobacco addiction.[8],[12]-[15] When patients were classified according to their ECOG performance status at the time of diagnosis, most of the patients in both arms showed an ECOG score of 1 (67.56% in Arm-A and 67.40% in Arm-B). A very small portion of the participants was ECOG stage 0, and a significant percentage of patients were in ECOG score 2. Due to the selection criteria of the study, none of the patients were above ECOG stage 2. The distribution of participants according to the ECOG score was similar to the findings of Roy et al.[16] The primary site of the majority of the patients was the oral cavity and larynx. A total of 23 (31.08%) patients were suffering from carcinoma oral cavity and 29 (39.18%) patients from carcinoma of the larynx. The oropharynx and hypopharynx were the primary site of 16 (21.62%) patients and 6 (8.10%) patients respectively. Among the patients, the most common symptom was neck swelling. 100% of patients in both Arm-A and B presented with metastatic neck nodes. 2nd most common symptom was pain in the throat and difficulty in taking food. This high prevalence of pain and difficulty in swallowing pain was similar to that of other studies.[17] Considering histological differentiation, more than two-thirds of the patients were presented with grade 1 (well differentiated) and grade 2 (moderately differentiated) tumors. Grade 3 (poorly differentiated) tumors were observed in less than one-third of the patients. In this study, 40.54% of patients of Arm-A and 27.02% of patients of Arm-B were in stage III, and 59.45% of patients of Arm-A and 72.97% of patients of Arm-B were in stage IV. This distribution of participants according to their stage of cancer was similar to that of Sharma et al.[18] For evaluation of objective response, scheduled and structured follow up were given at the 6th, 12th, and 24th weeks after completion of treatment. Patients' clinical responses at different follow-up weeks were observed and recorded in 4 main stages, Complete Response (CR), Partial response (PR), Stable Disease (SD), and Progressive disease (PD). At 1st follow up Complete response was 27.03% in Arm-A and 18.93% in Arm-B. PR was 70.27% and 78.37% in Arm-A and B respectively. About 2.10% of patients in both Arm-A and B had progressive disease. In 2nd follow-up, similar responses were observed. During 3rd follow-up, CR was also similar in both arms. PR decreased to 51.35% and 48.64% in Arm-A and Arm-B respectively. SD & PD was 10.81% and 18.91%, 13.51% in Arm-A and B respectively. Statistical analysis revealed there was no significant difference. In stage III disease, CR was 10 (27.03%) in Arm-A and 7 (18.93%) in Arm-B. In stage IV disease, PR was 15 (40.54%) in both Arm-A and B, respectively. Complete response was a little bit higher in Arm-A in stage III disease, but this difference was not statistically significant. On subgroup analysis, Arm-A patients had 18.92% CR in the larynx, 2.70% in the hypopharynx, and the same in the oropharynx and oral cavity. Arm-B patients, on the other hand, had CR in the larynx in 13.51% of cases, 0% in the oral cavity, and 2.70% in both the hypopharynx and the oropharynx. PR had the highest overall frequency, as in Arm-A, 16.22% of cases were from the oral cavity and 16.22% from the oropharynx. 10.81% of the cases were from the larynx, and 8.11% were from the hypopharynx. PR was observed in 18.92% of patients with the oral cavity, 16.22% with the larynx, 2.70% with the hypopharynx, and 10.81% with the oropharynx in Arm-B. There was no significant association between Arm-A and Arm-B in any of the response subgroup distributions. These findings correlated with the response status of previous studies reinforcing the validity of the present study findings.[16],[18],[19] The most prevalent acute toxicities were skin, mucosal, dysphagia, and salivary gland related. The acute grade 2 skin toxicities were significantly higher in Arm-B than in Arm-A (64.86% vs. 29.72%; $P < 0.01$).While six patients (16.21%) in Arm-A and eight patients (21.63%) in Arm-B had grade 3 skin toxicity. Grade 2 mucositis was also higher in the hypo-fractionated Arm (70.27% in Arm-B vs. 37.83% in Arm-A; $P < 0.01$). Grade 2 dysphagia was noticed in 10 patients (27.02%) of Arm-A and 16 patients(43.24%) of Arm-B. A higher number of patients in Arm-B were given nasogastric tube insertion for feeding purposes. 18.91% of patients in Arm-A and 32.43% of patients in Arm-B showed grade 2 laryngeal toxicities. No patient developed grade 4 toxicities in either group. The acute grade 2 salivary gland toxicity was 5.40% in Arm-A and 13.51% in Arm-B. Patients were advised to take repeated sips of water, muscarinic drugs were added where needed. The significance of the difference in terms of toxicity between the two groups was similar to the findings of other studies.[16] So, after careful analysis, it was seen that hypo-fractionated radiotherapy was more effective and convenient than conventional fractionation of chemo-radiotherapy in terms of loco-regional control with manageable toxicities. As the treatment of hypo-fractionated radiotherapy finishes

two weeks earlier compared to the conventional method and has minimal and manageable toxicities, it can be a great benefit to countries like ours where machine load is a major concern.

Limitations of The Study

This study was non-randomized and only short-term outcomes were analyzed. Therefore, late toxicity, long-term loco-regional control rate, and survival rate could not be assessed.

VI. Conclusion

Hypo-fractionated radiotherapy is similarly effective as conventional chemo-radiotherapy in locoregional control of locally advanced head and neck cancer and has the additional benefit of treating more patients with the same facilities. This hypo-fractionated regimen was associated with an increased but tolerable acute morbidity pattern relative to the conventional schedule. The reduction in the number of fractions and overall treatment time allows more efficient use of resources, which can help avoid long waiting times to maximize service productivity, but the implementation of this altered fractionation schedule as a routine practice is yet to be established.

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VII. Recommendation

Further study in multiple centers in different parts of Bangladesh is necessary to better understand the situation, and further study with a larger sample size and ample time can provide definitive solutions to various related problems

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