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IMPACT OF PROPHYLACTIC NASOGASTRIC TUBE FEEDING IN HEAD AND NECK CANCER PATIENTS DURING CONCURRENT CHEMORADIOTHERAPY

Dr. Mohammad Rahmat Ullah Bhuiyan[1*], Prof. Dr. Qazi Mushtaq Hussain[2], Prof. Dr. Golam Mohiuddin Faruque[3], Dr. Mamun OR Rashid[4], Dr. Golam Zel Asmaul Hosna[5], Dr. Sharifuddin Hasnat[6], Dr. Noor Esrate[7], Dr. Altaf Hossain Riad[8], Dr. Mohammad Arifur Rahman[9]

[1]Emergency Medical Officer, 250 Beded General Hospital, Brahmanbaria, Bangladesh.
[2]Senior Consultant, Lab aid Cancer Hospital and Super Specialty Care, Ex-Director, National Institute of Cancer Research & Hospital, Mohakhali, Dhaka, Bangladesh.
[3]Project Director, Bangladesh Cancer Society, Ex- Head of Dept., Dhaka Medical College, Dhaka, Bangladesh
[4]Associate Professor, Dept of Clinical and Radiation Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
[5]MBBS, MD (Radiation Oncology, Resident, Phase B), National Institute of Cancer Research & Hospital, Mohakhali, Dhaka, Bangladesh.
[6]MBBS, MPH, Surveillance Coordinator, Institute of Epidemiology, Disease Control and Research, Dhaka, Bangladesh
[7]MBBS, MD (Medical Oncology, Resident, Phase B) National Institute of Cancer Research & Hospital, Mohakhali, Dhaka, Bangladesh.
[8]MBBS, MD (Radiation Oncology), Indoor medical Officer, Khulna Medical College Hospital, Bangladesh.
[9]MBBS, MD (Radiation Oncology), Medical Officer, National Institute of Cancer Research & Hospital, Mohakhali, Dhaka, Bangladesh.

***Corresponding Author: Dr. Mohammad Rahmat Ullah Bhuiyan**

Emergency Medical Officer, 250 Beded General Hospital, Brahmanbaria, Bangladesh.

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ABSTRACT

Background: Worldwide, head and neck cancer (HNC) was the 6th most common cancer in 2020 in all ages and both sexes. In Bangladesh, lip and oral cavity cancer was the 2nd most common cancer in 2020. Up to 60% of HNC patients presents with locally advanced disease. Concurrent chemoradiotherapy (CCRT) is the standard of care in locally advanced stage disease but it increases toxicity and worsens nutritional status of the patients. HNC patients are frequently malnourished at presentation prior to treatment due to feeding difficulty which deteriorates later because of CCRT. Maintaining proper nutrition and completing treatment become a challenge for these patients. **Aim and Objective:** To determine the impact of prophylactic nasogastric tube feeding in head and neck cancer patients during concurrent chemoradiotherapy. **Materials and Method**: A quasi-experimental study was performed in Radiation Oncology Department of National Institute of Cancer Research & Hospital from 1st January 2020 to 31st December 2020. A total number of 68 Patients (34 patients in each arm) was included in this study according to inclusion and exclusion criteria by purposive Sampling technique. All patients in Arm A and Arm B were planned for total 66 Gray in 33 daily fractions, 2 Gray per fraction, 1 fraction per day, 5 fractions per week over 6½ weeks and inj. Cisplatin 40mg/m² was given intravenously 2 hours before radiotherapy on 1st day and then weekly. Arm A received prophylactic nasogastric tube prior to CCRT and Arm B did not receive any prophylactic tube but nasogastric tube was introduced during treatment whenever needed. Patients were evaluated from the beginning of CCRT up to 24 weeks of end of CCRT. All the information's were recorded in a pre-tested and semi-structured questionnaire. The analysis was done by using independent sample t test for continuous variables and chi-square test for categorical variables and data were presented in tables and graphs. **Results:** In this study, mean age was 52.5 ± 8.5 years and male: female ratio was 4.2: 1 among all patients. Pretreatment baseline characteristics and anthropometric measurements were almost similar in both arms; differences were not statistically significant ($p > 0.05$). Patients in Arm A lost significantly less weight during CCRT compared to Arm B (mean weight loss at the end of CCRT was -2.9 ± 1.3 in Arm A and -5.3 ± 1.3 in arm B of pre-treatment weight, $p < 0.05$). Mean BMI decreased between diagnosis and treatment completion in both arms, after that moderately increased in Arm A (18.74) and slightly decreased in Arm B (17.12), ($p < 0.05$ between two arms). There were no significant differences in treatment response and toxicities between the two groups. **Conclusion:** Prophylactic nasogastric tube feeding at the beginning of CCRT in head and cancer patients is beneficial in terms of minimizing weight loss.

KEYWORDS: Head and neck cancer, Prophylactic Nasogastric Tube, Chemoradiotherapy, impact.

INTRODUCTION

The term "Head and Neck Cancer" (HNC) refers to cancers of the upper aero digestive tract including the lips, oral cavity, oropharynx, sino nasal cavities, larynx, hypopharynx and salivary glands.[1] As per Globocan (2020), worldwide the incidence of head and neck cancer in 2020 was about 9, 31, 931; which was the 6th most common cancer in both sexes and all ages.[2] Number of HNC death was 4, 67,125 that was about 4.71% of all cancer deaths in both sexes.

In Bangladesh no reliable data is available on cancer statistic. Some international organizations, journals and local institutes provide discrete data. Globocan (2020) showed that in Bangladesh total 1, 56, 775 patients were diagnosed as cancer; among them 88, 075 were male and 68, 700 were female.[2] The 5-years prevalence of cancer cases was 2, 70, 866 in both sexes; 1, 39, 147 in male and 1, 31, 719 in female. The Number of cancer deaths in 2020 was 1, 08, 990 in both sexes; 62, 520 in male and 45, 617 in female.

Nearly 60% of head and neck cancer patients presents with locally advanced but non-metastatic disease.[3] Current treatment of locally advanced HNC requires multimodality treatment. Surgery, radiotherapy, and concurrent chemotherapy and radiotherapy (CCRT) have become the standard of care.[4] Combined modality therapy is generally recommended for approximately 60% of patients with locally or regionally advanced disease at diagnosis (National Comprehensive Cancer Network NCCN guidelines Version 1.2021). CCRT improves the loco-regional control of advanced stage disease but with increased toxicity that often has negative impact on nutritional status.[5] HNC patients are frequently malnourished at presentation and prior to the beginning of treatment.[6] Adding to the insult, CCRT causes or exacerbates the symptoms, such as alteration or loss of taste, mucositis, xerostomia, fatigue, nausea and vomiting, which consequently worsen the nutritional status.[7] Nutritional management is very important in HNC patients to improve outcomes and to minimize significant or permanent treatment related complications eg, severe weight loss (NCCN guidelines Version 1.2021). Weight loss of 5% or more during treatment has been associated with worse survival outcomes.[8] To maintain good nutritional status during treatment enteral nutrition (EN) is required which can be delivered either via a nasogastric tube (NGT) or via percutaneous endoscopic gastrostomy (PEG).[9] Both NGT and PEG are equally effective in maintaining body weight, and data to recommend one application method over the other is insufficient.[10] For patients with diagnosis of head and neck cancer receiving radiotherapy and/or chemoradiotherapy there is no conclusive evidence on which to base recommendations for the optimal method of enteral feeding during treatment and in the post-treatment period.[11] For HNC patients, NGT placement is often preferred due to a low complication rate, less invasiveness, and lower costs compared to PEG. Prophylactic feeding tubes (PFTs) are placed prior treatment in a prediction of significant oral toxicity, whereas reactive feeding tubes (RFTs) are placed later during treatment because of actual toxicity.[12] In case of RFT, Patients' oral intake should frequently be monitored to identify timely who is requiring a feeding tube to lower the risk of weight loss, dehydration and treatment interruption. On the other hand, prophylactic feeding tube placement may prevent this. Prophylactic feeding tube placement may prevent the risk of weight loss, dehydration.

The purpose of this study was to compare weight loss due to nutrition related complications in two feeding tube status groups, one is PFT and another is without PFT in National Institute of Cancer Research & Hospital. This was the first study regarding a PFT intervention prior to treatment in National Institute of Cancer Research & Hospital.

OBJECTIVE

General Objective

To study the impact of prophylactic nasogastric tube feeding in head and neck cancer patients during concurrent chemoradiotherapy.

Specific objectives

1. To find out the demographic characteristics of the patients.
2. To measure the effect on body weight with prophylactic nasogastric feeding tube (PFT).

METHODOLOGY

Type of study: Quasi-experimental study.

Place of study: Department of Radiation Oncology, National Institute of Cancer Research & Hospital (NICRH), Mohakhali, Dhaka.

Period of study: 1st January 2020 to 31st December 2020 (1 year).

Study population: Patients with histopathologically diagnosed head & neck cancers and selected for concurrent chemoradiotherapy in Radiation Oncology Department, NICRH in between 1st January 2020 to 31st December 2020.

Sampling method: Purposive sampling technique.

Sample size: Total of 68 patients were included in this study and were distributed in two arms (A and B), 34 patients in each arm. Arm A received prophylactic nasogastric tube prior to concurrent chemoradiotherapy and Arm B did not receive any prophylactic tube but nasogastric tube was introduced during treatment whenever needed.

Selection Criteria

Inclusion Criteria

- Histopathologically proven head and neck cancer.
- Squamous cell carcinoma histology.
- Stage III, IVA and IVB.
- Patients selected for CCRT.

Exclusion Criteria

- Carcinoma unknown primary, salivary gland tumor and nasopharyngeal carcinoma were excluded.
- Age less than 18 years or >70 years.
- If diagnosed as severely or moderately malnourished patient who need total parenteral nutrition.
- Patients Eastern Co-operative Oncology Group (ECOG) performance status score >2.
- History of prior chemotherapy or radiotherapy or surgery to the head and neck region.
- Serious uncontrolled concomitant medical illness including heart disease, diabetes mellitus, hypertension or renal disease etc.
- Laboratory criteria for exclusion

Study Procedure

A total 78 patients were selected in NICRH from 1st January 2020 to 31st December 2020. After assessment of eligibility, 10 patients were excluded and a total number of 68 patients were included in the study according to the selection criteria. After selecting the patients, informed written consent (Appendix-III) was taken from each patient before his/her participation in the study. Then history taking, Clinical examination and necessary investigations were done and documented in questionnaire.

Data Collection

Appropriate data were collected by using a preformed questionnaire (appendix II). Following introducing and informing the study purpose and objectives, an informed written consent was sought from the patient to take part in this study. Data were collected by face to face interview ensuring privacy and confidentiality of the patients. All others required data were collected from available relevant papers.

Data processing, analysis and interpretation

- Data were checked and verified.
- Then it was tabulated in a master sheet.
- Data were entered into computer and coded.
- Data categorization and summarization were done.
- Continuous data were expressed as mean ± standard deviation (SD), whereas, categorical data were expressed with rate, ratio and proportion.
- Data were presented in tables and graphs.
- Statistical analysis was done according to the objective of the study by using IBM SPSS (Statistical Package for Social Science) software version 25.0 for windows and graphs by MS Excel 2010.
- The analysis was done by using independent sample t test for continuous variables and chi-square test for categorical variables. All reported *p*-values were two sided and value less than 0.05 was taken significant.

RESULTS

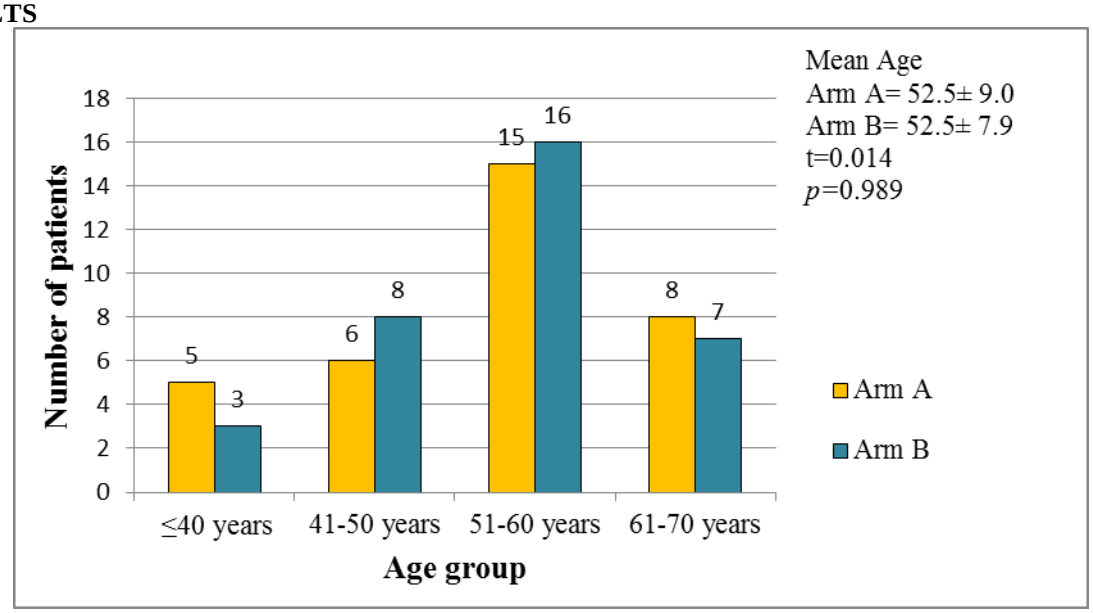
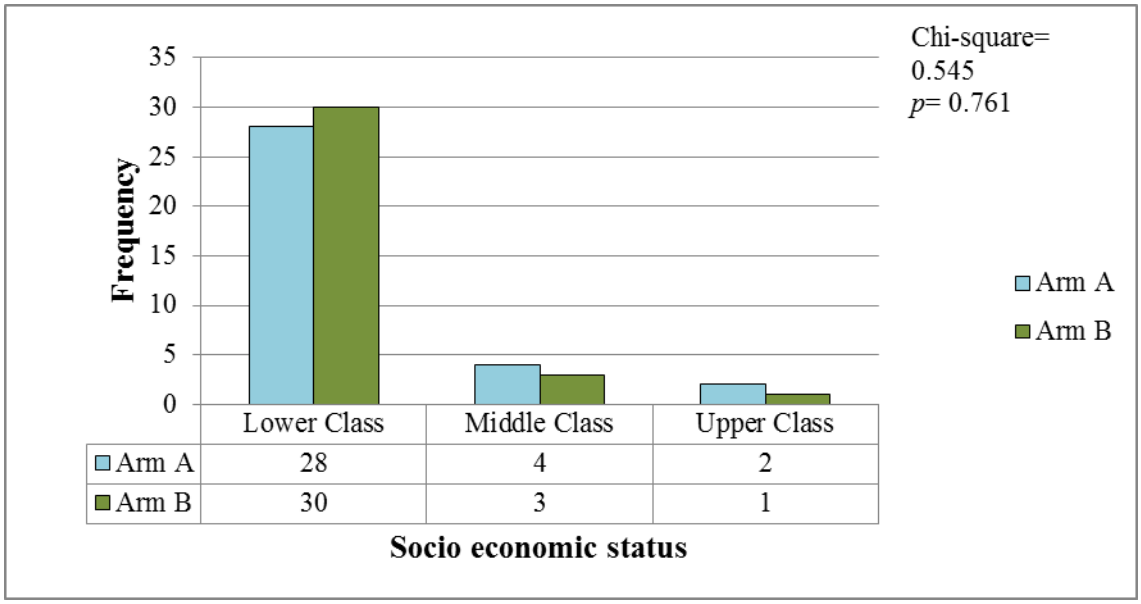


Figure I: Distribution of the study patients by age (n = 68).

This figure shows that most of the patients belonged to age group 51-60 years. The mean age was 52.5 ± 9.0 in arm A and 52.5 ± 7.9 in arm B. Minimum age was 33 years in Arm A and 36 years in Arm B. Maximum age was in Arm A 66 years and in Arm B 67 years.

The difference was not statistically significant ($p > 0.05$) between two arms.



(According to the report of Household Income and Expenditure Survey- 2010, Statistics and Information Division, Bangladesh Bureau of Statistics, Ministry of Planning, March, 2011)

Figure II: Distribution of patients according to socio-economic status (n = 68).

Figure II shows that most of the patients in this study were from lower socioeconomic class. In Arm A 28 (82.4%) and in arm B 30 (88.2%) patients were from lower socioeconomic class. The difference was not statistically significant ($p > 0.05$) between two arms.

Table I: Distribution of patients according to risk factors (n = 68).

Risk factors	Arm A		Arm B		χ^2 value	*p*-value
	n	%	n	%		
Tobacco smoking	27	79.4	26	76.5	0.086	0.770
Betel nut chewing	26	76.5	28	82.4	0.360	0.549
Smokeless tobacco	16	47.1	12	35.3	0.971	0.324

(Multiple responses considered)

This table shows that various risk factors were identified among the patients of arm A and arm B. The most common risk factor was smoking. There was no statistically significant difference between the populations of two arms (p value > 0.05).

Table II: Baseline characteristics of pretreatment weight, height, BMI and mid upper arm circumference (n = 68).

Trait	Arm A		Arm B		t value	*p*-value
	Mean	Standard deviation	Mean	Standard deviation		
Pretreatment weight (kg)	50.6	±6.0	51.6	±6.7	-0.666	0.508
Pretreatment height (meter)	1.6	±0.1	1.6	±0.1	-1.063	0.292
Pretreatment BMI (kg/m²)	19.3	±1.3	19.4	±1.8	-0.167	0.868
Pretreatment MUAC (cm)	25.1	±1.6	25.8	±1.9	-1.567	0.122

(BMI= Body Mass Index, MUAC= Mid Upper Arm Circumference)

This table shows that Baseline characteristics of two arms are not statistically different (p value > 0.05). Pretreatment mean BMI was 19.309 ± 1.332 in Arm A and 19.372 ± 1.773 in Arm B, which was the lower border of normal BMI level.

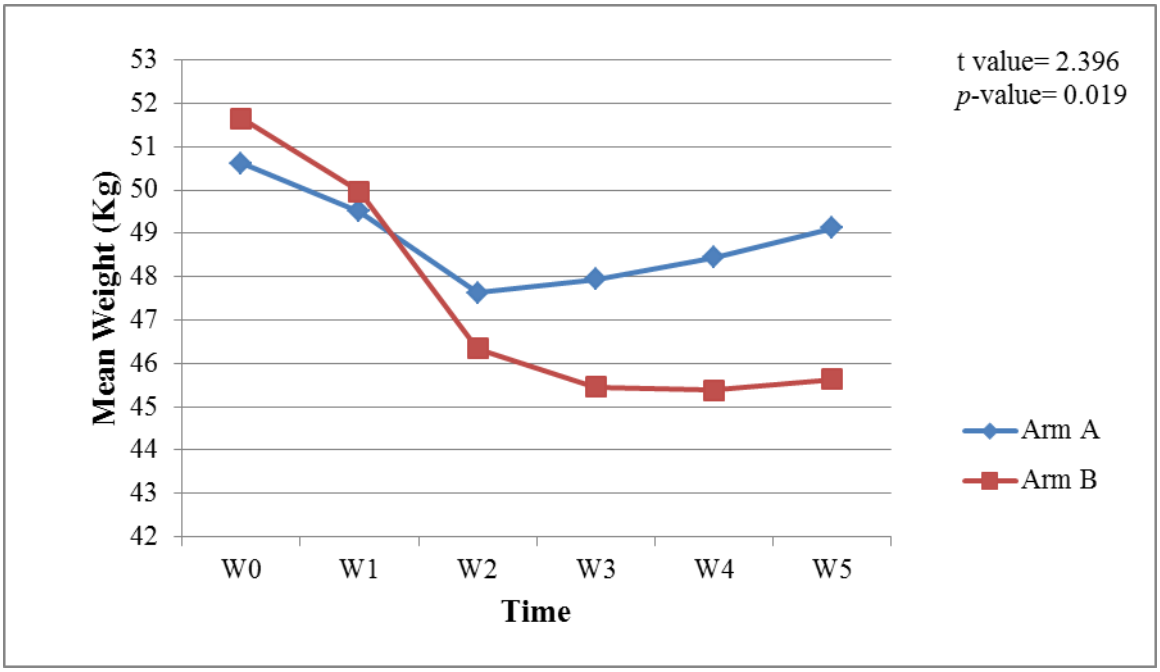


Figure III: Mean weight variation over time (n = 68).

Mean weight in different times in two groups up to 24 weeks after CCRT. (W0: pretreatment mean weight, W1: mean weight at 4 weeks of CCRT, W2: mean weight at end of CCRT, W3: mean weight at 6 weeks after completion of CCRT, W4: mean weight at 12 weeks after end of CCT, W5: mean weight at 24 weeks after the end of CCRT).

This Figure shows that the mean weight (kg) between Arm A (with PFT) and Arm B (without PFT) over period of time and up to 24 weeks after completion of CCRT. Mean weight decreased during CCRT in both arms. After CCRT mean weight increased slightly in Arm A but did not increase in Arm B.

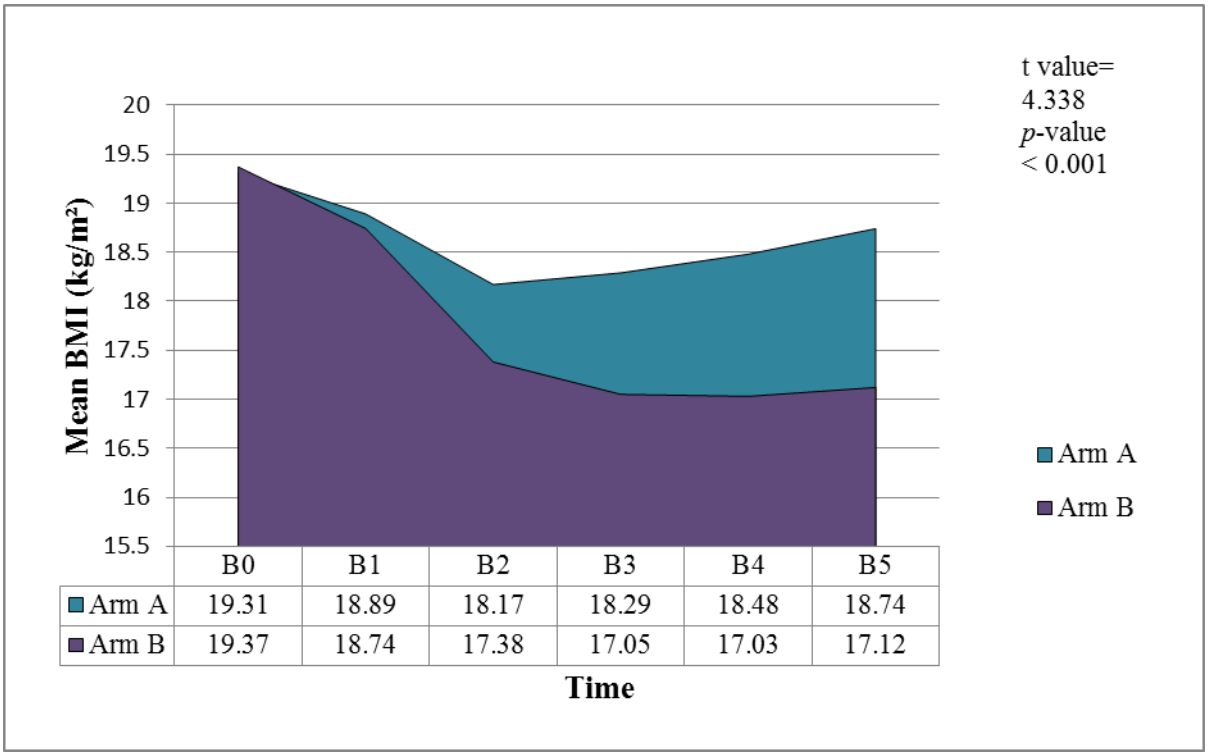
The difference was statistically significant between two groups (p-value < 0.05).

Table III: Weight loss from baseline (n = 68).

Time	Arm A		Arm B		t value	*p*-value
	mean	Standard deviation	mean	Standard deviation		
WL1	-1.1	±0.5	-1.7	±0.5	4.615	<0.001
WL2	-2.9	±1.3	-5.3	±1.3	7.298	<0.001
WL3	-2.7	±1.5	-6.2	±1.7	9.195	<0.001
WL4	-2.2	±1.6	-6.3	±2.0	9.242	<0.001
WL5	-1.5	±1.5	-6.0	±2.1	10.308	<0.001

Weight loss (WL) from baseline, (WL1: weight loss at 4 weeks of CCRT, WL2: weight loss at completion of CCRT, WL3: weight loss at 6 weeks after CCRT, WL4: weight loss at 12 weeks after CCRT, WL5: weight loss at 24 weeks after CCRT)

This table shows that mean weight loss at various period of time from base line weight measurement. Patients in the Arm B lost significantly more weight than patients in the Arm A (p < 0.05). All patients in both arms underwent weight loss during CCRT. After CCRT patients in Arm A regained their weight, but patients in Arm B failed to regain weight.



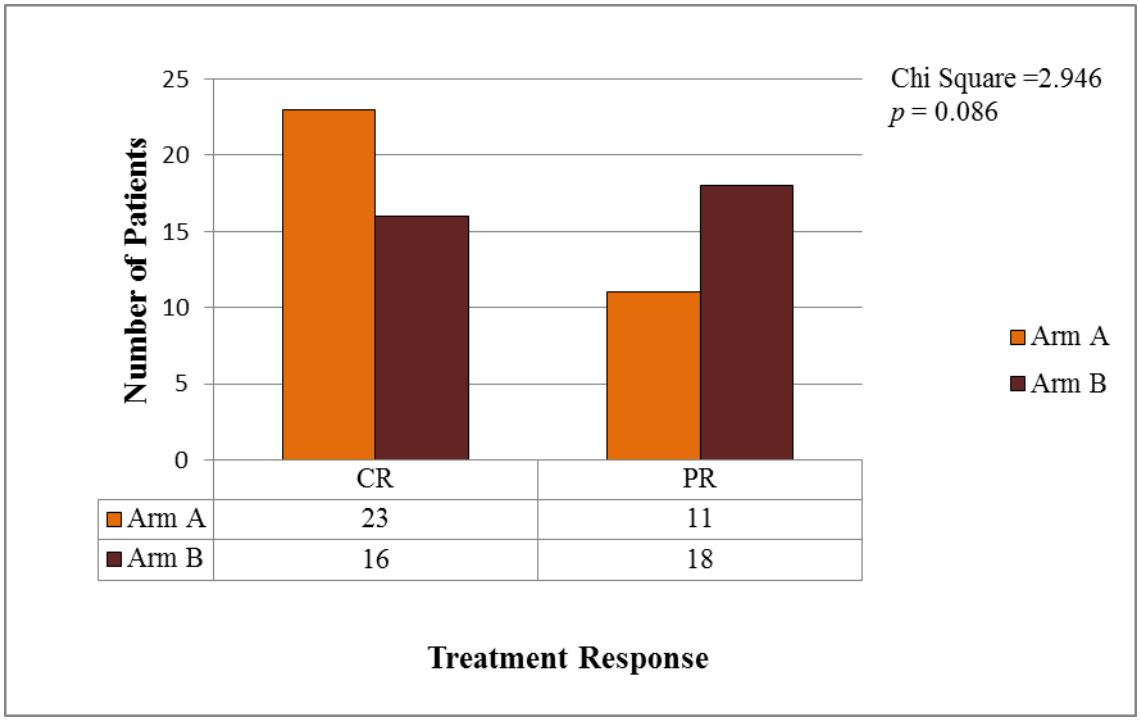
	B0	B1	B2	B3	B4	B5
Arm A	19.31	18.89	18.17	18.29	18.48	18.74
Arm B	19.37	18.74	17.38	17.05	17.03	17.12

Figure IV: Evolution of mean BMI at diagnosis, during and after CCRT (n = 68).

Mean body mass index (B) at different times (B0: pretreatment mean BMI, B1: mean BMI at 4 weeks of CCRT, B2: mean BMI at completion of CCRT, B3: mean BMI at 6 weeks after CCRT, B4: mean BMI at 12 weeks after CCRT, B5: mean BMI at 24 weeks after CCRT).

This Figure shows that mean BMI decreased between diagnosis and treatment completion in both arms, after that moderately increased in Arm A and slightly decreased in Arm B.

p-value reached from independent sample t test, which was significant ($p < 0.05$) between two arms.



	CR	PR
Arm A	23	11
Arm B	16	18

Figure V: Distribution of patients according to treatment response after 12 weeks of end of CCRT (n = 68).

This figure shows that majority of the patients in Arm A had complete response (CR) 23 (67.6%). In Arm B majority of the patients had partial response (PR) 18 (52.9%).

The difference was not statistically significant between two arms (p-value > 0.05).

Table IV: Nasogastric Tube related toxicities.

complications	Arm A		Arm B		χ^2 value	p-value
	n=34	%	n=10	%		
Dislodgement	15	44.1	4	40	0.053	1.00
Blockage	6	17.6	1	10	0.338	1.00
Cough	2	5.9	0	0	0.616	1.00

This table shows that most common nasogastric tube related complication was dislodgement and there were few incidence of blockage of tube and cough.

The difference was not statistically significant (p > 0.05) between two arms.

Table V: Duration of Nasogastric Tube feeding.

Trait	Arm A (PFT) n=34		Arm B (RFT) n=10	
	Mean	Standard deviation (SD)	Mean	Standard Deviation (SD)
Duration of NG tube feeding (days)	62.3	±5.3	14.4	±1.7

(PFT=prophylactic feeding tube, RFT= reactive feeding tube)

This table shows length of nasogastric tube feeding in both arms. In Arm A mean duration of NG feeding was 62.3 ± 5.3 days and in Arm B mean duration was 14.4 ± 1.7 days.

DISCUSSION

Multimodalities treatments are the standard care of locally advanced head and neck cancer with severe negative impact on weight and nutritional status. Minimizing weight loss during CCRT dramatically improves treatment tolerance; reduce treatment break. I performed this study to determine the impact of prophylactic nasogastric tube feeding in head and neck cancer patients during concurrent chemoradiotherapy[10].

Most of the patients in this study were belonged to age group 51 to 60years. In Arm A 15 (44.1%) and in Arm B 16 (47.1%) patients were belonged to this age group. The mean age was 52.5 ± 9.0 in Arm A and 52.5 ± 7.9 in Arm B. Among all patients male and female ratio was 4.23:1. In Arm A male and female patients were respectively 27 (79.4%) and 7 (20.6%) and ratio was 3.9:1. In Arm B male and female patients were respectively 28 (82.4%) and 6 (17.6%) and ratio was 4.7:1. Head and neck cancers are common in male and in middle and older aged people with few exceptions. Bari et al. (2018) conducted a prospective quasi-experimental study in NICRH, BSMMU and DMCH and found mean age were 54.7 ± 9.1 and 56.6 ± 7.9 in Arm A and Arm B respectively.[11] Male and female ratio in their study was 4:1. This study results nearly correlate with Hughes et al. (2013) where they found male 139 (84.24%) and female 26 (15.75%), male and female ratio was 6.346:1, with median age 58 years12. Despite non-random allocation of patients into this study demographic features were homogenous in both arms and differences were not significant (p > 0.05).

Socioeconomic status was determined according to the report of Household Income and Expenditure Survey (HIES)- 2010, Statistics and Information Division, Bangladesh Bureau of Statistics, Ministry of Planning, March, (2011). Most of the patients in this study belonged to lower socio-economic status. 28 (82.4%) patients in Arm A and 30 (88.2%) in Arm B were belonged to the lower socio-economic status[12]. Hospital Cancer Registry Report 2015-2017 from NICRH reported that in 2017 among all patients in all departments a huge number of patients (34.8%, 4883) were illiterate & about 49% patients (6868) had attained primary level education.

Multiple risk factors are responsible for head and neck cancers. Smoking is the leading cause of head and neck cancers. In this study 27 (79.4%) in Arm A and 26 (76.5%) in Arm B patients were smoker, 26 (76.5%) in Arm A and 28 (82.4%) in Arm B were habituated in betel nut chewing. Among them 16 (47.1%) in Arm A and 12 (35.3%) in Arm B were habituated in smokeless tobacco in the form of Jorda, Gul and Sadapata. Hospital Cancer Registry Report 2015-2017 from NICRH reported that in 2017 about 74.8% (5587) male cancer patients were ever smoker and only 1.3% (83) female patients were ever smoker. 56.5% males (n = 4125) were habituated with chewing tobacco and among female this percentage was 52.5% (n = 3455).

In this study, pretreatment mean weight (kg) was 50.6 ± 6.0 in Arm A and 51.6 ± 6.7 in Arm B. Mean height (meter) was 1.6 ± 0.1 in Arm A and 1.6 ± 0.1 in Arm B. Mean body mass index (BMI) (kg/m²) was 19.3 ± 1.3 in

Arm A and 19.4 ± 1.8 in Arm B. Mean mid arm circumference (MUAC) (cm) was in 25.1 ± 1.6 in Arm A and 25.8 ± 1.9 in Arm B. Espeli et al. (2018) found in their study pretreatment mean weight 68 ± 15 kg and BMI 23.7 ± 4.4.[13] Paccagnella et al. (2010) conducted similar study where pretreatment mean weight was 73.5 ± 10.8 kg in NG Arm (intervention arm) and 72.5 ± 13.3 in CG Arm (control arm) and pretreatment BMI kg/m² 26.1 ± 3.3 in NG Arm and 25.3 ± 4.0 in CG Arm[10]. Isenring et al. 2004 found mean height (meter) was 1.74 ± 7.2 in NI (nutrition intervention) and 1.71 ± 9.2 in UC (usual care). It might be due to geographical variation. In our country baseline weight, height and BMI is lower than the others.

Previous study showed that patients' receiving CCRT for head and neck cancers developed weight loss due to eating problem, malnutrition and severe toxicities. This study findings were also consistent with these findings and weight loss worsened at the end of CCRT. Mean weight in Arm A and Arm B after 4 weeks during CCRT, at the completion of CCRT, after 6 weeks of end of CCRT, 12 weeks of end of CCRT and 24 weeks of end of CCRT shows Arm A lost significantly less weight than patients in Arm B (p value < 0.05). Study results correlate with Paccagnella et al. (2010) where they found similar result.[10] Isenring et al. (2004) found both NI (nutritional intervention) and UC (usual care) lost weight between 4th and 8th week period.[14] However NI group then regained weight but UC group failed. This finding is also similar to this study result.

In this study, mean weight loss was in Arm A and arm B respectively after 4 weeks of CCRT -1.1±0.5 and -1.7 ± 0.5, after completion of CCRT -2.9 ± 1.3 and -5.3 ± 1.3, after 6 weeks of end of CCRT -2.7 ± 1.5 and -6.2 ± 1.7, after 12 weeks of completion of CCRT -2.2 ± 1.6 and -6.3 ± 2.0, after 24 weeks of end of CCRT -1.5 ± 1.5 and -6.0 ± 2.1. The difference was statistically significant (p value <0.05). These findings were found by several authors. Paccagnella et al. (2010) found statistically significant result in weight loss at various periods during and after CCRT in NG (intervention arm) and CG (control arm).[10] Espeli et al. (2018) found more weight loss in ≤ 28 days NGT arm in comparison with > 28 days NGT arm. But the difference was not significant.[13]

In this study mean BMI (kg/m²) in both arms decreased at various periods of time during chemoradiotherapy. After CCRT, patients of Arm A regained their BMI but patients of Arm B failed to regain. BMI change (kg/m²) at different period of time from baseline BMI was in Arm A and Arm B respectively after 4 weeks of CCRT -0.4 ± 0.2 and -0.6 ± 0.2, completion of CCRT -1.1 ± 0.5 and -1.9 ± 0.5, 6 weeks after end of CCRT -1.0 ± 0.6 and -2.3 ± 0.6, 12 weeks after CCRT -0.8 ± 0.6 and -2.3 ± 0.7, 24 weeks after CCRT -0.6 ± 0.6 and -2.2 ± 0.7. The difference was statistically significant (p value < 0.05). Mean mid upper arm circumference (MUAC) was initially unchanged but decreased later during chemoradiotherapy. The differences between two arms were statistically significant after 6 weeks to 24 weeks of end of CCRT. Paccagnella et al. (2010), Espeli et al. (2018) and Lewis et al. (2014) found similar results in various anthropometric measurements.[10,13,5]

Treatment response assessment by RECIST criteria after 12 weeks of end of CCRT showed in Arm A, Complete Response (CR) was 23 (67.6%) and Partial Response (PR) was 11 (32.4%) and in Arm B, CR was 16 (47.1%) and PR was 18 (52.9%). Though treatment response assessment was not one of the objectives of the study, it can be seen from data that it was clinically significant but statistically not significant (p-value 0.086). Treatment response was further analyzed to determine the association with treatment interruptions. There was significant association between treatment interruption and treatment response. From above discussion it found that treatment response is indirectly associated with prophylactic nasogastric tube feeding.

Few Complications developed due to NG tube insertion and longtime tube feeding which included dislodgement, blockage and cough. For dislodgement and blockage, tubes were changed to continue feeding. The difference was not statistically significant. Espeli et al. (2018) showed in their study, tube related complications were ablation (68%), blockage (16%) and pneumonia (11%) in prolong tube arm (> 28days).[13] Paccagnella et al. (2010) also found similar result in their retrospective study.[14]

After CCRT nasogastric tube was removed as soon as patients were able to take oral food. There were conflicting results by many authors in duration of NG tube feeding. In this study, mean length of nasogastric tube feeding was 62.3 days (range 55-74 days) in Arm A (prophylactic arm, n = 34) and 14.4 days (range 12-17 days) in Arm B (patients needed reactive feeding tube, n = 10).

CONCLUSION

In conclusion we can say that prophylactic nasogastric tube feeding at the beginning of CCRT in head and neck cancer patients is beneficial in terms of minimizing weight loss. Nutritional interventions including regular nutritious food according to diet chart and nasogastric tube management as per instructions is the prerequisite for maintaining good nutritional status.

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