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Prophylactic percutaneous endoscopic gastrostomy tube feeding to prevent weight loss in head and neck cancer patients- a retrospective cohort study

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SUMMARY

Significant weight loss occurs in head and neck cancer patients who receive concurrent chemo radiation. Prophylactic use of Percutaneous Endoscopic Gastrostomy (PEG) tube has not been well explored. This study aimed to compare the weight loss in head and neck cancer patients treated with concurrent chemo radiotherapy with or without a PEG tube Methods: This was a retrospective cohort study that included patients with head and neck cancers treated with concurrent chemo radiation with or without PEG feeding. All patients, irrespective of their feeding status, were on a regular diet. Bodyweight during treatment was compared between patients without PEG feeding and PEG feeding. Chi-square test and Mann Whitney U test were used to compare the groups. Mixed method analysis of variance (ANOVA) was used to model the difference in the outcome variables across different time points. Results: A total of 80 patients were studied, of whom 29 received PEG feeding prophylactically, and 51 did not. The median weight of all patients had a decreasing trend from the beginning until the completion of treatment. The difference between the two groups reached statistical significance by week four and maintained the significant difference at week five and week six, P=.04, P=.39, P=.05, respectively. Pairwise comparison of weight across the two groups without taking into consideration the effects of time showed a statistically significant difference (P<.001). However, there was no statistically significant difference between the two groups when the observations were modelled with mixed-method ANOVA (F=3.7 and P= .052). Conclusions: Weight loss occurs in head and neck cancer patients during concurrent chemo radiation even after prophylactic PEG feeding. There was no evidence to state that nutritional intervention with PEG will result in reduced weight loss.

Key words: head and neck cancer, percutaneous endoscopic gastrostomy (PEG) feeding, weight loss, chemo radiation

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INTRODUCTION

The incidence of squamous cell carcinoma of head and neck is very high, and most patients present at a very advanced stage [1]. Intensive treatment to achieve a complete response in the form of a combination of radiotherapy and chemotherapy (i.e., concurrent chemo radiation) is required in most cases. Concurrent chemo radiation with three weekly or weekly cisplatin chemotherapy is an acceptable treatment with comparable efficacy and tolerance [2]. Accompanying this treatment is oral mucositis, a well-known complication that interferes with treatment leading to poor tolerance, decreased food intake, and weight loss. Enteral nutrition using a feeding tube is required if Grade 3 mucositis develops during treatment [3]. Dysphagia is another common issue seen in head and neck cancer patients, especially hypo pharyngeal cancers, due to the broader field of radiation, coexisting factors like an advanced stage, and advanced age [4, 5]. Patients with head and neck cancers are at high risk of malnutrition due to various risk factors, and nutritional intervention performed before concurrent chemo radiation improves patient tolerance [6]. During treatment, there are multiple factors like nausea, vomiting, dysphagia, mucositis, dry mouth, and altered taste sensation, which require nutritional intervention [7]. Weight loss occurs early during treatment; nutritional intervention is required before starting the treatment and should be continued during follow-up [8]. Nutritional support in the form of Percutaneous Endoscopic Gastrostomy (PEG) tube is required in patients receiving concurrent chemo radiation [9]. Limited studies are available on the nutritional status of patients undergoing chemo radiation. The primary objectives of this study were to assess the nutrition status by measuring changes in body weight during concurrent chemo radiation and to analyse the difference in body weight in patients without PEG feeding and with PEG feeding.

MATERIALS AND METHODS

This was a retrospective cohort study on head and neck cancer patients treated with concurrent chemo radiation with or without PEG feeding conducted in south India. The study was approved by the institutional ethics committee. There was no change in the study design or outcome measurement after

starting the study.

Patients and study setting

Patients with squamous cell carcinoma of head and neck were eligible for the study if they had received concurrent chemo radiation with curative intent. Some of the head and neck cancer patients received enteric feeding prior to initiation of treatment if they were at high risk of developing nutritional problems as decided by the physician. We have included patients who were histologically confirmed squamous cell carcinoma, non-metastatic disease Stage II, Stage III, Stage IV, with Karnofsky performance status ≥ 80, and creatinine clearance >50 ml/minute. Patients received concurrent chemo radiation without any nutritional intervention or with nutritional intervention by PEG feeding. We included PEG feeding patients if their PEG tubes were inserted before starting the treatment. Recurrent and metastatic disease patients were excluded. We also excluded patients who received prior chemotherapy or radiation treatment to the head and neck region, synchronous malignancy, age >70 years, and pregnant women. They were clinically staged with comprehensive head and neck examination, endoscopies, and radiologically using computed tomography scanning or magnetic resonance imaging of the head and neck. A chest x-ray was also taken for all patients. The American Joint Committee on Cancer staging was used to stage the primary tumour and involved lymph nodes.

All patients received concurrent cisplatin chemotherapy with external beam radiation. All patients received dental prophylaxis and an audiology evaluation before starting treatment. The external beam radiation dose used was 66 Gy with 2 Gy per fraction with five days per week treatment. All treatment was delivered using parallel opposed beams to the head and neck area and a low anterior neck field. The field size was reduced after 44 Gy to shield the spinal cord. After field size reduction, additional treatment sparing the spinal cord was chosen to treat the involved nodes and site if deemed necessary to a total dose of 66 Gy. The high-risk nodal areas received a dose of 50 Gy. The lower neck supraclavicular field was matched to the inferior border of the opposing field of head and neck and treated prophylactically to a dose of 50 Gy. The chemotherapy regimen received, along with external beam radiation, was single-agent cisplatin to achieve a target dose of cisplatin ≥ 200 mg/m.

Nutritional support

All patients received counselling as per routine departmental protocol by the radiation oncologist before the initiation of chemo radiation, about the acute toxicities of radiation, including mucositis and dysphagia occurring during the treatment and possible development of nutritional deficiency and weight loss. Patients were offered enteral feeding support in the form of PEG before starting the treatment. Patients who accepted the PEG feeding as a modality of nutritional support were referred to the surgeon for PEG feeding tube placement. All patients were admitted one day before the procedure, and consent was taken before the procedure. Following PEG tube insertion, they were referred to the radiation oncology department for the initiation of concurrent chemo radiation.

All patients who had nutritional support with PEG feeding had their insertion done before beginning the treatment. The indication for PEG placement was inadequate oral intake resulting in a calorie deficit and anticipated weight loss of more than 10% of body weight during the treatment or expected treatment-related toxicity resulting in severe dysphagia. PEG feeding was initiated without delay before starting the treatment. Oral feeding was encouraged in all patients. The PEG feeding was in addition to the oral feeding they were having, and all recorded their intake through PEG in a diary. PEG patients received advice regarding PEG care from the treating radiation oncologist and nursing staff. PEG-related complications, if any, were also searched in the case records. Major complications required hospital admission and treatment. Minor complications, like desquamation of skin, fluid leakage, or redness, were looked for in the clinical assessment charts. Following the completion of treatment, if there was no swallowing difficulty and if they could maintain a regular diet, they were weaned from PEG feeding, and it was later removed. Treatment delays, if any, or any PEG related complications and unplanned admissions were recorded.

All patients, irrespective of the feeding status, were advised to maintain a regular diet. No other feeding formulas or dietary supplements were prescribed. All patients were routinely monitored every week for clinical response assessment and recording of their body weight and other vital parameters, including complete blood counts, renal function tests, and body weight. After completion of treatment, patients were followed up monthly for one year, every two months from the second year and every three months interval until the fifth year.

All the demographic data and variables, including the site of the tumour, Tumour-Node-Metastasis (TNM) status, histopathological type, baseline body weight, and weekly body weight records, until the completion of treatment, were obtained from case records. Patient response at the end of treatment was assessed clinically and documented in the file. A complete response was documented when there was no clinical evidence of disease, and partial response was documented if there was least a 50% reduction in the size of the lesion when measured.

Data collection

Case records of patients were reviewed to collect the data on chemotherapy and radiation. Chemotherapy details included the chemotherapy drug used and its dosage and frequency. Radiotherapy details collected included the fields used, description of the local area treated, dose and fractionation of radiation. Demographic variables including age and sex, tumour characteristics including the site of the tumour, histopathological type, tumour differentiation, tumour status, nodal status, metastasis status, and composite stage were also noted from the case file. Details of PEG feeding tube insertion, including the date of insertion and any complications, were recorded. Weekly clinical assessment data were available in the case record from which the weekly body weight recordings of patients were obtained. Clinical response after radiation treatment was obtained from the case record.

Statistical analysis

Basic demographic data were summarized with median and interquartile range and categorical variables in percentages. Chi-square test and Mann Whitney U test were used to compare the groups. Mixed method analysis of variance (ANOVA) was used to model the difference in the outcome variables across different time points in the groups. All statistical analysis was done using R statistical software.

RESULTS

Data from 80 patients who received concurrent chemo radiation were included in the study, of whom, 29 received PEG feeding before the start of concurrent chemo radiation. A total of 51 patients who did not receive PEG feeding were on oral feeding alone. In our study, the mean age of patients was 50 years (range, 45 to 60 years). The majority were men (77.5%). Of all the sites, tongue cancer was the most common (41.2%). The least common subsite was the Sino nasal and soft palate malignancy. When the histopathological type was considered, well-differentiated squamous cell carcinoma and moderately differentiated squamous carcinoma constituted the majority. The least common histopathological type was undifferentiated Sino nasal squamous cell cancer, which contributed only 1%. Regarding T status, T3 and T4 tumours comprise the majority. Regarding the N status, N3 patients constituted the fewest. Overall complete response at the end of treatment was 93.8%.

Without PEG feeding, the median age was 51 years (range, 45 to 62 years), whereas, for those with PEG feeding, the median age was 48 years (range, 43 to 50 years). The distribution of men and women was uniform in both sets of patients. The distribution is also uniform across subsite. T2, T3, and T4 tumours constituted the majority in both groups of patients. There were no T1 tumours in this study. Regarding N status, N0, N1, and N2 distribution constituted the majority in both groups of patients. Only one patient in both groups had N3 status. Stage III and Stage IV constituted most of the cases in both groups. Well-differentiated and moderately differentiated squamous cell carcinoma constituted the major histopathological type in both groups (Table 1).

Complete response at the end of treatment in the group without PEG was 98% and 2% in the group with PEG feeding; this difference was not statistically significant (Table 2).

Tab. 1. Patient characteristics summary descriptive by groups of percutaneous endoscopic gastrostomy details

	All; N=80	PEG No; N=51	PEG Yes; N=21	*P* overall
AGE:	50.0 (45.0;60.0)	51.0 (45.0;62.0)	48.0 (43.0;50.0)	.023
SITE:				.065
Buccal mucosa	11 (13.8%)	7 (13.7%)	4 (13.8%)	
Larynx	9 (11.2%)	8 (15.7%)	1 (3.45%)	
Post cricoid	7 (8.75%)	7 (13.7%)	0 (0.00%)	
Posterior pharyngeal wall	4 (5.00%)	3 (5.88%)	1 (3.45%)	
Pyriform fossa	4 (5.00%)	3 (5.88%)	1 (3.45%)	
Retromolar trigone	5 (6.25%)	2 (3.92%)	3 (10.3%)	
Sinonasal	2 (2.50%)	2 (3.92%)	0 (0.00%)	
Soft palate	2 (2.50%)	0 (0.00%)	2 (6.90%)	
Tongue	33 (41.2%)	18 (35.3%)	15 (51.7%)	
Tonsil	3 (3.75%)	1 (1.96%)	2 (6.90%)	
T STATUS:				.293
2	22 (27.5%)	17 (33.3%)	5 (17.2%)	
3	30 (37.5%)	18 (35.3%)	12 (41.4%)	
4	28 (35.0%)	16 (31.4%)	12 (41.4%)	
N STATUS:				.126
0	21 (26.2%)	14 (27.5%)	7 (24.1%)	
1	27 (33.8%)	21 (41.2%)	6 (20.7%)	
2	30 (37.5%)	15 (29.4%)	15 (51.7%)	
3	2 (2.50%)	1 (1.96%)	1 (3.45%)	
M STATUS: 0	80 (100%)	51 (100) %	29 (100%)	
STAGE:				.184
2	8 (10.0%)	6 (11.8%)	2 (6.90%)	
3	22 (27.5%)	17 (33.3%)	5 (17.2%)	
4	50 (62.5%)	28 (54.9%)	22 (75.9%)	
HISTOPATHOLOGY				.572
Moderately differentiated squamous cell carcinoma	34 (42.5%)	20 (39.2%)	14 (48.3%)	
Poorly differentiated squamous cell carcinoma	7 (8.75%)	6 (11.8%)	1 (3.45%)	
Undifferentiated Sinonasal squamous cell carcinoma	1 (1.25%)	1 (1.96%)	0 (0.00%)	
Well differentiated squamous cell carcinoma	38 (47.5%)	24 (47.1%)	14 (48.3%)	

Abbreviation: PEG, percutaneous endoscopic gastrostomy.

The median weight of all patients had a decreasing trend from the beginning of treatment until completion at six weeks (Figure 1).

This trend was noted in both groups of patients irrespective of their nutritional intervention with PEG feeding. The difference between the two groups reached statistical significance by week four and maintained the significant difference at week five and week six, P = .04, P = .39, P = .05, respectively (Table 3). Tab.3. Change in body weight across groups.

Pairwise comparison of weight across the two groups without taking into consideration the effects of time showed a statistically significant difference (P < .001). However, there was no statistically significant difference between the two groups when the observations were modelled with mixed-method ANOVA (F = 3.7 and P = .052; (Figure 2).

Assumption homogeneity of variance was present (Levene's test P>.05). All other assumptions, like homogeneity of covariance, were met.

No PEG-related serious complications or unplanned hospital admissions occurred in the group with PEG feeding. All patients completed treatment without interruption.

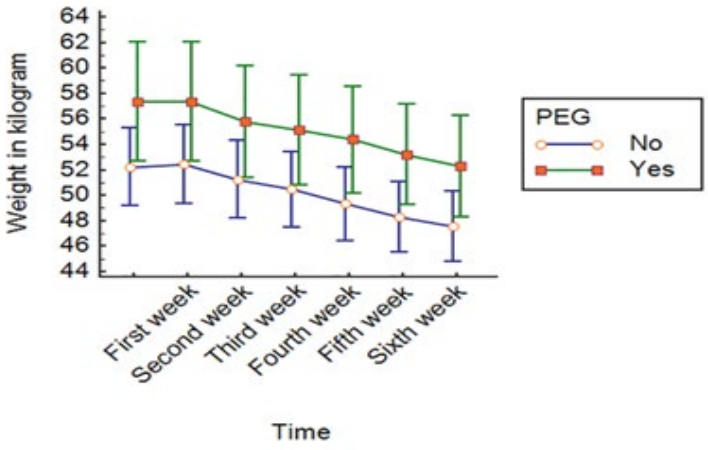

Fig. 1. Pattern of body weight loss across groups during treatment

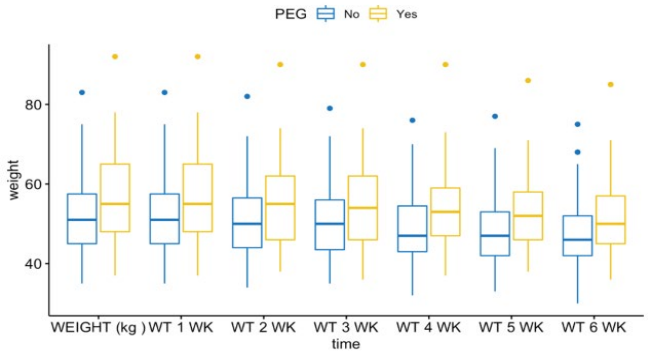

Fig. 2. Box plot showing body weight over time across groups

Tab. 2. Tumor response at the end of chemoradiation

	All; N=80	PEG No; N=51	PEG Yes; N=29	*P* overall
RESPONSE AT COMPLETION OF TREATMENT				.075
Complete response	75 (93.8%)	50 (98.0%)	25 (86.2%)	
Partial response	3 (3.75%)	1 (1.96%)	2 (6.90%)	
Not available	2 (2.50%)	0 (0.00%)	2 (6.90%)	

Abbreviation: PEG, percutaneous endoscopic gastrostomy.

Tab. 3. Change in body weight across groups

	All; N=80	PEG No; N=51	PEG Yes; N=29	*P* overall
WT.0.WK	53.0 (47.0;62.0)	51.0 (45.0;57.5)	55.0 (48.0;65.0)	.078
WT.1.WK	53.0 (47.0;62.0)	51.0 (45.0;57.5)	55.0 (48.0;65.0)	.091
WT.2.WK	52.0 (46.0;61.0)	50.0 (44.0;56.5)	55.0 (46.0;62.0)	.091
WT.3.WK	51.0 (45.0;59.2)	50.0 (43.5;56.0)	54.0 (46.0;62.0)	.080
WT.4.WK	50.0 (45.0;58.2)	47.0 (43.0;54.5)	53.0 (47.0;59.0)	.044
WT.5.WK	49.0 (44.0;55.2)	47.0 (42.0;53.0)	52.0 (46.0;58.0)	.039
WT.6.WK	48.5 (43.8;55.5)	46.0 (42.0;52.0)	50.0 (45.0;57.0)	.050

Abbreviation: PEG, percutaneous endoscopic gastrostomy; WK, week; WT, weight (Kilogram).

DISCUSSION

Head and neck cancer patients on treatment with concurrent chemo radiation suffer various toxicities like mucositis and dysphagia and weight loss, which cause treatment interruption and has been found to affect the treatment outcome adversely [10]. Nutritional supplementation can be achieved using nasogastric tube placement, surgical gastrostomy, or PEG tube. Our study showed that there is insufficient evidence to say nutritional supplementation by PEG resulted in weight gain, and irrespective of PEG, these patients will have a reduction in weight during chemo radiation. Most of the available literature favours the routine use of PEG in head and neck cancer patients undergoing chemo radiation. PEG insertion performed before treatment helped prevent weight loss during treatment as well as during follow-up time [11]. One study showed that very few patients require enteral feeding during treatment and early PEG insertion was unnecessary in all patients [9]. Another study that assessed the weight loss in patients who received prophylactic PEG feeding found no effect on the intervention following the completion of treatment [12].

Prophylactic PEG feeding could reduce the toxicities associated with treatment and avoid radiotherapy treatment interruption [13]. Weight loss in patients receiving concurrent chemo radiation ranges from 5.45% to 18.9%, with a mean weight loss of 10% [14]. Pre-treatment PEG feeding was required for all patients receiving concurrent chemo radiation, anticipating the need for supplementary nutrition [15]. In our study, the patients who had PEG feeding had their PEG insertion done before starting the chemo radiation protocol. Despite this, they also had a weight loss of approximately 10%, which is in line with similar studies. This effect may be due to lower calorie intake during the treatment and as it progresses. Although calorie records assessment was not done in this study, it is possible these patients had a lower calorie intake during the treatment, as illustrated in a prospective study that most weight loss occurring during treatment and early revalidation [16]. In addition, it has been found that the maximum weight loss occurs during the end of radiation treatment [17]. We also noted significant weight loss starting from the fourth week of treatment and continuing until the end of treatment.

A cheaper way to maintain nutrition in these patients is nasogastric tube insertion, as the insertion cost of a PEG tube is more expensive. Both nasogastric tube feeding and PEG feeding have their advantages and disadvantages [18]. The routine use of PEG feeding over a nasogastric tube is also controversial as the cost of placement of a PEG tube is ten times higher, and the duration of PEG use is prolonged in patients compared to a nasogastric tube, and the complications rate are not different [19]. Its use should be selective as the overall cost remains high, and quality of life assessment after treatment is not significantly different compared to nasogastric tube [20].

There is a wide variation in reporting of nutritional status and weight loss in head and neck cancer patients treated with concurrent chemo radiation with or without PEG feeding. From a previous study by Yamazaki et.al, the reported incidence of weight loss was more than 5% in 75% of patients without PEG feeding compared to 27% in patients with supportive PEG feeding [13]. Comparing PEG feeding and nasogastric tube feeding, patients with PEG feeding had the least amount of weight loss during treatment. Treatment modalities and the requirement of enteral feeding did not yield a statistically significant difference in terms of weight loss [21]. In contrast, the PEG feeding group in our study also had a significant weight loss of around 10%, and the difference between the median weight of patients without PEG and those with PEG feeding patients reached statistical significance. We are yet to ascertain which patients will receive the maximum benefit with PEG feeding. Optimal patient selection criteria, as indicated by some predictive factors for PEG tube insertion is not known clearly as of now to allow for the design of a PEG placement protocol [22]. The conflicting reports in the weight loss pattern in patients on PEG feeding may be due to the different modality of treatment used in these studies.

A weight loss of more than 20% was associated with treatment interruption and adversely affected the outcome [23]. None of the patients in this study had severe weight loss to that extent. There is also a strong association between weight loss and quality of life in head and neck cancer treated patients [24]. We did not investigate the quality of life aspect. Advice from a dietician and counselling during treatment was also shown to be beneficial for patients in preventing weight loss and maintaining nutrition status [25]. None of the patients in this study receive any form of calorie monitoring and corrective measures while on treatment. Weight loss before and after treatment is a good indicator of response to treatment and disease-specific survival [26]. In our study, the complete response at the end of treatment between the two groups was not statistically significant, which may be due to the small sample size.

Our study's low sample size may have been the reason our study failed to attain statistical significance concerning the comparison of weight across the no PEG and PEG groups.

CONCLUSION

Weight loss occurs during treatment with concurrent chemo radiation in head and neck cancer patients. Moreover, a downward trend in body weight from beginning to completion of treatment is seen in patients irrespective of feeding status. Weight loss occurs in patients even after nutritional intervention in the form of PEG feeding. However, there was no evidence to state that nutritional intervention with PEG will result in reduced weight loss.

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