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Original Research Article

Reactive versus prophylactic percutaneous gastrostomy: outcomes in a cohort of advanced oropharyngeal carcinoma patients

Nuno Medeiros*, Paulo Pina, João Larangeiro, Pedro Oliveira

Department of Otorhinolaryngology, Centro Hospitalar Vila Nova de Gaia, Portugal

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***Correspondence:**
Dr. Nuno Medeiros,
E-mail: nuno.medeiros.oliveira@chvng.min-saude.pt

ABSTRACT

Background: Dysphagia is a common complaint in patients with oropharyngeal tumors, both due to limitations of the underlying disease and the adverse effects of medical or surgical treatments. Percutaneous gastrostomy is used to prevent malnutrition, but there is currently no consensus on the best timing for its placement (prophylactic - pPEG or reactive - rPEG). The objective of this study was to analyze differences in nutritional and survival outcomes between patients who used pPEG and rPEG.
Methods: Retrospective analysis of a cohort of patients with advanced-stage oropharyngeal neoplasm undergoing chemoradiotherapy between January 2013 and December 2020. PEG placement was performed before (prophylactic - pPEG) or after (reactive - rPEG) initiation of treatment. Relevant demographic and clinical variables were analyzed.
Results: 49 patients received PEG during the studied period (age 57.6±8.2 years; 89.8% male). Of these, 32 (65.3%) received pPEG, while 17 (34.7%) placed rPEG. Device length of stay was significantly longer in patients with the pPEG strategy (205.5 vs 159.2 days; r=0.40; p=0.03). There was no difference in weight percentage at 3 (p=0.82) and 6 (p=0.08) months. Kaplan-Meyer analysis showed no difference in survival between the two strategies (log-rank p=0.49).
Conclusions: Nutritional and survival outcomes were not statistically different between the two analyzed subgroups. PEG dependence seems to be influenced by PEG timing strategy.

Keywords: Percutaneous gastrostomy, Head and neck cancer, Nutrition, Survival

INTRODUCTION

Head and neck cancer (HNC) patients are at risk of malnourishment, both from disease burden, and as a result of combined treatment modalities.[1] Malnutrition effects on wound healing may prolong recovery following treatment and increase the risk of morbidity for those undergoing subsequent salvage treatments.[2,3]

Percutaneous gastrostomy (PEG) is one of the most commonly used enteral feeding methods in HNC patients.[4] This is a safe procedure with a low complication rate5. It might be used as the sole way of feeding, or it might be used in conjunction with oral intake, to optimize it.

Optimal timing for PEG placement is still up to much debate, leading to inconsistencies in practice between centers. Prophylactic placement (pPEG) might prevent further weight loss in HNC patients that is expected with the beginning of chemoradiotherapy with/without surgery. On the other hand, prophylactic enteral feeding might hinder swallowing outcomes, prolonging the dependency on PEG. Reactive PEG placement (rPEG) is defined as placement after treatment initiation. Although there is compelling evidence showing increased difficulty on regaining weight during on-going cancer therapy,

most studies could not prove a difference in disease outcomes with both strategies.

The primary goal of our study was to analyze differences in nutritional and survival outcomes between patients who used pPEG and rPEG in our institution.

METHODS

This retrospective cohort study included oropharyngeal cancer patients treated in Centro Hospitalar Vila Nova de Gaia / Espinho center, between January 2013 and December 2020. Adult patients with advanced oropharyngeal cancer were included. These patients received chemoradiotherapy ±surgery. Patients were excluded if they presented other synchronous tumors and/or early stage tumors.

Before the beginning of treatment, all patients were referred to a multidisciplinary consultation, where decision between reactive or prophylactic PEG was made, according to clinical and patient preferences. Similarly to other studies, we classified pPEG if performed before the beginning of radiotherapy and rPEG if performed after.

Demographics characteristics (sex, age) and clinical characteristics (staging, treatment, percentage of weight loss pre-treatment) were collected at baseline from medical records. Clinical stage was categorized into four groups: stage III, IVa, IVb and IVc.

Both nutritional and survival outcomes were measured. Nutritional outcomes included days until PEG removal, and weight variation at 3 and 6 months. Considering survival outcomes, we measured overall survival as the primary outcome. Survival time was defined as the time between the first day of the radiotherapy treatment until the date of death or censored to last day of data updating on death.

Comparisons between groups were conducted using Chisquare test and exact Fisher test for categorical variables, and student t-test and Mann–Whitney test for continuous variables. We used Kaplan–Meier procedure to estimate the distribution of time to death and log-rank tests for the difference in survival time. Control for confounders was performed by using a hierarchical multiple regression analysis. Significance level was set at $p<0.05$. Data was analyzed using Statistical package for social sciences (SPSS) version 26.0.

RESULTS

This cohort consisted of 49 advanced oropharyngeal cancer patients, subdivided in two groups: rPEG (n=17) and pPEG (n=32).

Table 1: Demographic and clinical characteristics of studied sample.

Baseline characteristics	Reactive (n=17)		Prophylactic (n=32)		
	N	%	N	%	P value
Sex					
Male	15	30.6	29	59.2	0.574
Female	2	4.1	3	6.1	
Overall cancer stage					
III	6	12.2	0	0	0.002*
IVa	9	18.4	21	42.9	
IVb	2	4.1	9	18.4	
IVc	0	0	1	2.0	
Treatment modality					
Platinum-based QT + RT	14	28.6	31	65.3	0.114
Cetuximab QT + RT	3	6.1	1	2.0	
Karnofsky					
70	2	4.1	2	4.1	0.461
80	7	14.3	20	40.8	
90	8	16.3	10	20.4	
BMI					
Underweight	2	4.1	14	28.6	0.070
Normal	10	20.4	13	26.5	
Overweight	5	10.2	5	10.2	
Initial malnourishment					
Yes	7	14.3	17	34.7	0.353
No	11	22.4	14	28.6	

* $p<0.05$. BMI – body mass index; QT – chemotherapy; RT – Radiotherapy.

Mean of age was not statistically different between rPEG (59.9±9.2 y.o.) and pPEG (56.5±7.4 y.o.), p=0.23. Other demographic and clinical variables are summarized in Table 1. There was a statistically significant difference between both groups regarding overall staging, with rPEG being comprised of patients with lower advanced stages. Other variables were not statistically different between groups.

Table 2: Nutritional and survival outcomes for each PEG strategy.

Outcomes	Reactive (n=17)	Prophylactic (n=32)	P value
Weight loss (%)	-5.5	-4.8	0.824
3 months	-10.3	-3.2	0.082
6 months			
PEG (days)	159.5	205.5	0.032*
Survival (days)	458.0	566.0	0.210

*p<0.05

Prophylactic PEG patients had a median of 205.5 days of PEG placement, compared with 159.5 days for rPEG. On multivariate analysis, after controlling for confounders (age, stage, initial weight), PEG dependence was significantly associated with PEG strategy (r=0.41; p=0.03).

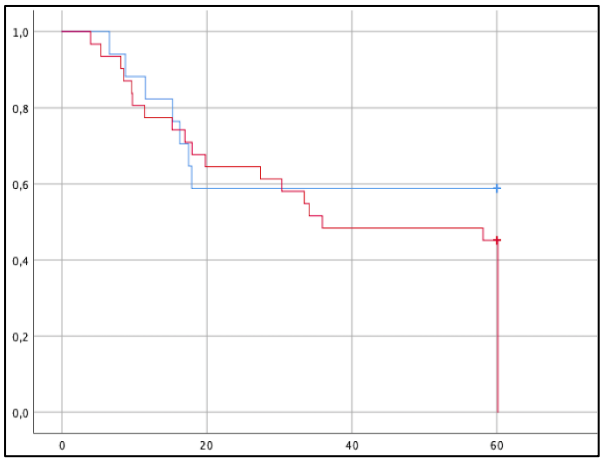

Figure 1: Kaplan-Meyer curves for overall survival between the two groups (red – rPEG; blue – pPEG). Max-follow-up: 60 months; x-axis: survival (months); y-axis: percentage. Log-rank test (p=0.49).

After controlling for confounders, this variable was the only one related to timing of PEG. No difference on percentage of weight loss was apparent at 3 months between both groups (p=0.824). Despite a trend for less weight loss at 6 months is apparent, this value did not achieve statistical significance (p=0.08).

Analyzing overall survival, there was no difference between both strategies (Log-rank test p=0.49) (Figure 1). After controlling for confounders, PEG placement was not significantly related to overall survival (p=0.17).

DISCUSSION

In this study, we retrospectively analyze the influence of PEG timing on nutritional and survival outcomes in a cohort of advanced-stage oropharyngeal tumors. PEG timing had an impact on PEG dependence in our cohort, with a trend of influence in weight loss at 6 months, and no impact on overall survival.

Advanced stage oropharynx tumors have variable consequences on a patient's swallowing function that are somewhat predictable, depending on the structures or treatment modality involved.[6] Combined treatment modalities like chemoradiotherapy regimens may lead to additional dysphagia and aspiration due to weakness of the base of the tongue, prolonged pharyngeal transit time, lack of coordination between the swallowing phases, reduced elevation of the larynx, reduced laryngeal closure, and epiglottic inversion.[7] PEG can provide effective long-term enteral nutrition in dysphagia patients.[8] These patients might be completely dependent on enteral nutrition, or on other hand, using it to complement oral feeding.

PEG timing is still a controversial topic in literature, with protocols differing between major centers. Prophylactic strategies are used to decrease the risk of malnourishment during treatment, as this can be associated with treatment delays as well as decreased overall survival.[9] Therefore, theoretically, this approach would favor better survival outcomes. However, most studies found no differences between groups in overall survival and/or treatment delay.[10] Some other endpoints, such as acute kidney insufficiency or increased hospital admissions were, however, correlated with a rPEG approach in some studies.[11,12]

There is, on the other hand, a high rate of unnecessary PEG placement using a pPEG approach, with approximately 50% of patients not using it during the course of treatment and in the posterior follow-up.[13] PEG placement tube carries risks such as infection, diarrhea, constipation, electrolyte abnormalities, bleeding, and/or metastatic seeding at the gastrostomy site.[14] It is also possible that decreased oral intake by prophylactic placement might further worsen pharyngeal muscle weakness, theoretically contributing to increased PEG dependence.[15,16] Published studies regarding this subject have, a high risk of bias, and this impact remains unclear.[17]

Reactive strategies are favored by some clinicians and/or patients. The downfall of this approach is a possible increased difficulty in weight recuperation during the course of the treatment.[18] It is estimated that between 11%-79% of patients will subsequently need PEG placement if a reactive approach is undertaken.[19] Some

studies tried to understand which risk factors could make PEG needs more probable in the course of the treatment. Strom et al found an association with BMI <25, accelerated irradiation fractionation, T stage of 3 or higher, and a cumulative cisplatin dose of 200 mg/m2.[20] One favored approach in most centers is to identify patients who have a higher risk of malnourishment pretreatment, and to propose pPEG to them. This should be, however, a conjoint decision between clinician and patient.

Previous studies have addressed possible outcome differences between these two subgroups of patients. Kramer et al, described similar results to ours in a cohort of head and neck cancer patients, noting mainly a difference in PEG dependence in the prophylactic subgroup, with no statistical difference in weight loss at 2, 6, or 12 months, or overall survival.[21] McClelland et al report in a systematic review (n=7) similar findings, with an apparent benefit at weight loss at 6 months, but no difference in tumor control or increased survival.[22] Quality of life (QoL) investigations performed in these two subsets of patients have found that, although QoL seems to be worse during treatment for pPEG patients, there seems to exist a difference at 6-months favoring pPEG approach.[23]

Our study is limited by its retrospective protocol and small sample. It reports the experience of a single institution. However, as most published studies take all HNC subsites as a whole in their analysis, this study is one of the few only analyzing a specific subsite for HNC. In our sample, comparability could have been hindered by the fact that HNC staging was statistically different between the two subgroups. However, after multivariate analysis, it is apparent that this difference did not have an impact in the measured outcomes.

CONCLUSION

Nutritional and survival outcomes were not statistically different between the two analyzed subgroups. However, PEG dependence seems to be influenced by PEG timing strategy. Better protocols are needed to reduce unnecessary prophylactic PEG placement while maintaining adequate nutrition during the treatment of these patients, to maximize outcomes.

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