EFFECTS OF FEEDING TUBE PLACEMENT ON NUTRITIONAL OUTCOMES IN HEAD AND NECK CANCER PATIENTS

By

Jessica M. Hummel

A THESIS

Presented to the Graduate Programs in Human Nutrition
and the Oregon Health & Science University
School of Medicine
in partial fulfillment of
the requirements for the degree of

Master of Science in Human Nutrition

May 2018

School of Medicine

Oregon Health & Science University

CERTIFICATE OF APPROVAL

This is to certify that the Master's thesis of

Jessica M. Hummel

has been approved

Mentor: Julie McGuire, MS, RDN, LD

Member: Daniel Clayburgh, MD, PhD

Member: John Holland, MD

TABLE OF CONTENTS

Acknowledgments

First and foremost, I would like to express my sincere gratitude to my thesis mentor and program advisor, Julie McGuire, MS, RDN, LD, for her continuous support, motivation, and guidance during my thesis project. I was extremely lucky to have a mentor whose door was always open and who pushed me to exceed my own expectations.

Second, I would like to thank my committee members, Dr. Daniel Clayburgh and Dr. John Holland, for their time and commitment to this project. My thesis is stronger because of your clinical expertise and insightful feedback during my research.

I would also like to thank Marcy Stooksbury, RDN, and Dr. Melanie Gillingham for their assistance shaping my thesis.

Finally, I must express my profound gratitude to my husband and biggest cheerleader, Ben. His endless encouragement and support throughout my years of study helped me through the ups and downs of both undergraduate and graduate school. I know his love and support are with me in whatever I pursue.

This accomplishment would not have been possible without them. Thank you!

Abstract

The ideal timing of feeding tube placement for head and neck cancer patients is debated and no standard protocol has been established. The study aim was to determine if prophylactic gastrostomy tube (g-tube) placement prior to treatment for head and neck cancer patients improves their nutritional, clinical, and long-term quality of life outcomes. Using existing clinical head and neck cancer patient data from the VA Portland Health Care System and OHSU, a retrospective chart review of 230 patients was conducted to compare outcomes following a prophylactic versus reactive approach. We hypothesized head and neck cancer patients who received prophylactically placed feeding tubes would have improved nutritional, clinical, and long-term quality of life outcomes compared to patients who received reactively placed feeding tubes. The prophylactic g-tube group lost statistically significant more weight than the reactive group during the pretreatment period (-2.22% vs -0.82%; P=0.0052), however, they lost statistically significant less weight than the reactive group during the treatment period (-7.54% vs -10.56%; P<0.001). No other significant differences in weight loss between the groups were observed during the follow-up or three-month post-treatment time periods or in overall total weight change. Prophylactic g-tube placement did not result in long-term feeding tube dependence and no differences between the groups were observed with unplanned hospital admission rates or long-term quality of life scores. While this study indicates prophylactic placement may be beneficial, it is still uncertain which patients would benefit the most from prophylactic g-tube placements.

Further research is needed to better identify indicators for the use of a prophylactic approach in head and neck cancer patients.

Introduction

Specific Aims

Changes in nutritional status are commonly observed in head and neck cancer patients undergoing chemoradiation treatment. Due to the location of the cancer, patients often develop oral treatment-related symptoms, such as xerostomia, dysphagia, mucositis, and mouth sores. These symptoms can significantly impact their dietary intake, resulting in substantial weight loss, signs of lean body mass wasting, and dehydration. Enteral nutrition support for head and neck cancer patients is indicated when undernutrition already exists or if it is anticipated that nutritional needs cannot be met through volitional intake, however, the ideal timing of the gastrostomy tube (g-tube) placement, prophylactically versus reactively, is debated and no standard protocol has been established.

Individualized dietary counseling has been shown to have beneficial effects on the nutritional status of head and neck cancer patients,[1] however, the consensus on whether prophylactic versus reactive feeding tube placement improves nutritional outcomes remains unclear. Weight loss among patients who received prophylactic feeding tube placements ranges from significantly less overall weight loss[2-9] to no difference[10] or even a higher amount of overall weight loss than a reactive approach.[11] Similarly, differences in the number of hospital admissions varies from up to 19% fewer admissions with a prophylactic placement[12] to no significant differences between the two approaches.[13,14] Patients with prophylactic feeding tubes have also been shown to use their

feeding tubes for enteral nutrition longer than patients with reactively placed feeding tubes,[11,15,16] however, it is unclear whether long-term feeding tube use can negatively impact swallowing function and quality of life over time.[7,16,17]

The overall goal of this project was to determine if prophylactic placement of a feeding tube prior to treatment for head and neck cancer patients improves nutritional, clinical, and long-term quality of life outcomes during and after treatment. Using existing clinical head and neck cancer patient data from the VA Portland Health Care System and OHSU, a retrospective chart review was conducted to compare outcomes following a prophylactic versus reactive approach. We hypothesized head and neck cancer patients who received prophylactically placed feeding tubes would have improved nutritional, clinical, and long-term quality of life outcomes compared to patients who received reactively placed feeding tubes. The specific aims of this project were:

Specific Aim 1: To determine whether prophylactically placing a feeding tube influences nutritional and clinical outcomes, including weight loss, time to return to oral feeding, and unplanned hospital admissions, in head and neck cancer patients.

Hypothesis: Prophylactic tube placement would improve nutritional and clinical outcomes in head and neck cancer patients.

Specific Aim 2: To determine whether prophylactically placing a feeding tube influences long-term quality of life measurements in head and neck cancer patients.

Hypothesis: Long-term quality of life would be improved in head and neck cancer patients who received a prophylactically placed feeding tube.

Identifying the differences in outcomes between a prophylactic versus reactive approach will help inform future clinical practice about the optimal timing for g-tube placement, which may improve the nutritional status and overall health outcomes of head and neck cancer patients undergoing treatment.

Background & Review of Literature

Enteral Feeding in Head and Neck Cancer Patients

Head and neck cancer involves cancer of the oral cavity, pharynx (including the nasopharynx, oropharynx, and hypopharynx), larynx, paranasal sinuses and nasal cavity, and salivary glands.[18] The American Cancer Society estimates 51,540 new cases of head and neck cancer will be diagnosed in the United States in 2018.[19] Due to the location of the cancer, head and neck cancer patients are at risk for developing malnutrition. Patients may experience swallowing dysfunction related to pain or obstruction from their tumor prior to treatment and/or dysphagia, odynophagia, xerostomia, dysgeusia, oral mucositis, nausea, and vomiting as a result of treatment.[20] These symptoms can result in dehydration and weight loss, leading to a worsening of malnutrition with the potential for a prolonged treatment time and poorer clinical outcomes. The nutrition assessment of head and neck cancer patients should occur throughout their entire continuum of care to identify any changes in their nutritional status and nutrition interventions, like initiating enteral nutrition.

Head and neck cancer patients should undergo a nutrition screening to identify patients who are at risk for or who currently have malnutrition. Enteral nutrition support is indicated for patients who are malnourished and/or who are anticipated to have an inadequate food intake for a prolonged period of time (at least 7-14 days).[21,22] The aim of enteral nutrition support in head and neck cancer is to improve the quality of life for the patient and potentially improve the outcomes of their treatment.[22] Enteral nutrition support is commonly delivered

using a nasogastric tube or g-tube, the latter of which is frequently used for patients with swallowing disorders and/or who are expected to require prolonged nutritional support (longer than four weeks[22]).[20]

Prophylactic Versus Reactive Feeding Approach

While the indication for initiating enteral nutrition is known, the optimal time for when to place the feeding tube is not as clear. Two approaches used for the placement of feeding tubes are either using a prophylactic approach or a reactive approach. A prophylactic approach involves having the feeding tube proactively placed prior to the treatment start, while a reactive approach involves placing the feeding tube after the start of treatment when there is an immediate need for nutrition support. The Royal Brisbane and Women's Hospital developed the "Swallowing and Nutrition Management Guidelines for Patients with Head and Neck Cancer" in 2006 to assist in identifying patients who may benefit from proactively placed feeding tubes due to dysphagia or malnutrition.[23] Their guidelines help identify high nutritional risk patients versus lower risk patients and use pathways for appropriate nutritional management recommendations.[24] The National Comprehensive Cancer Network (NCCN) releases guidelines giving recommendations for prophylactic tube placements and they do not recommend a prophylactic placement of a feeding tube if the patient is low-risk (e.g. no significant pretreatment weight loss or severe dysphagia), however, they suggest monitoring these patients closely for weight loss since they could require a feeding tube in the future.[25] The NCCN does recommend considering the placement of prophylactic feeding tubes for high-risk patients (e.g. severe weight

loss prior to treatment, ongoing dehydration or dysphagia, significant comorbidities, severe aspiration, and/or predictive long-term swallowing dysfunction).[25] While there are guidelines and recommendations being utilized for the use of a prophylactic versus reactive approach, there is currently conflicting data regarding which approach leads to better patient outcomes from a nutritional and clinical standpoint, like weight loss, unplanned hospital admissions, and time to return to oral feeding, or from a long-term functional standpoint, like quality of life.

While there is an expected need for enteral nutrition when prophylactic feeding tubes are placed, the actual use of the feeding tubes is not consistent among head and neck cancer patients. Several studies reported the majority of prophylactically placed feeding tubes were being used at some point during treatment, with up to a 95% usage rate.[4,26-28] Even though there are high usage rates reported, additional studies documented there are patients with prophylactically placed feeding tubes who never use the feeding tube after it was placed[27-29] or used it for less than two weeks during their treatment.[27] Additionally, Brown et al.[4] reported that 43% of patients who received a reactively placed feeding tube could have benefited from a prophylactically placed feeding tube based on their eventual need for a feeding tube or having experienced weight loss of ≥10% of their body weight during treatment. These findings demonstrate a more sensitive system is needed to identify patients that could truly benefit from a prophylactically placed feeding tube.

A prophylactic versus reactive approach also plays a role in the start and duration of enteral nutrition throughout treatment. Patients with a prophylactically placed feeding tube have been shown to start enteral nutrition within a month into treatment[14,26,30] or within several days of starting treatment if they already had an impaired swallowing function prior to treatment.[30] After the initiation of enteral nutrition, patients with prophylactic feeding tubes used their feeding tubes for enteral nutrition longer than patients with reactively placed feeding tubes.[11,15,16] The mean days of duration ranged from 71-235 days with a prophylactically placed feeding tube[11,26,28-30] and 53-139 days with a reactively placed feeding tube.[11,16] A significant difference was also seen in the duration of feeding tube use after treatment, with prophylactically placed feeding tubes being used for a median of 181 days and reactively placed feeding tubes being used for a median of 64 days.[14] Even though there is a varying duration of feeding tube usage, one study reported the mean time to the removal of feeding tubes after the completion of treatment was not affected by when the feeding tube was placed.[9] Additionally, about 72% of head and neck cancer patients with a feeding tube have been able to be tube free at 12 months post-treatment.[7] This may indicate patients are able to rely less on their feeding tubes as a source of nutrition once treatment ends.

Nutritional Outcomes

Head and neck cancer patients often lose weight while they are undergoing treatment.[2-11,13,14,29-34] The timing of the feeding tube insertion, however, may have an impact on the severity of weight loss during and after

treatment. Many studies have shown prophylactically placing a feeding tube prior to treatment results in significantly less overall weight loss post-treatment compared to a reactive feeding tube placement or no tube placement at all.[2-9] Other similar studies also reported less weight loss with a prophylactically placed feeding tube, however, the differences in weight loss between a prophylactic versus a reactive approach were not significant.[13,35] Conversely, other findings have shown a prophylactic feeding tube placement can result in either no significant difference in weight loss[10] or a higher amount of overall weight loss than a reactive approach.[11] A summary of the data from these studies can be found in Table 1. Of these 12 published studies that looked at feeding tube placement timing and weight loss, 10 found prophylactically placed feeding tubes decreased overall weight loss, one found no difference, and one found an increase in weight loss. One and two-year follow-ups after the completion of treatment do not show a significant difference in overall weight loss between prophylactic or reactive feeding tube placements.[34] Declines in body mass index (BMI) have also been significantly related to the feeding tube insertion time, with a greater decline in BMI when a feeding tube was placed after the start of treatment.[7,31] Additionally, patients experiencing a weight loss of ≥10% of their baseline body weight have been found in both the prophylactic and reactive approach groups, with up to 22% of patients in the prophylactic group and up to 21% in the reactive group losing ≥10% of their baseline body weight.[4,29,30] A weight loss of ≥10% puts head and neck cancer patients at risk for increased infections, delayed wound healing, muscle weakness, poorer quality of life,

Table 1: Studies investigating the effect of prophylactic vs. reactive feeding tube placements on weight loss during treatment in head and neck cancer patients

Author (year)	*n*	Outcomes
Assenat (2011)	139	Median Weight Loss: 1.0 kg with prophylactic g-tube vs. 5.0 kg with reactive g-tube (*P*<0.001) at the end of treatment
Beaver (2001)	249	Severe Weight Loss During Treatment: 14% of patients with prophylactic feeding tube vs. 60% with reactive feeding tube (*P*<0.05) experienced severe weight loss (>10% of usual body weight (UBW) lost in six months, 5% of UBW lost in one month, 2% of UBW lost in one week, or >7% of body mass index lost in six months)
Brown (2016)	130	Mean % Weight Loss: 7.0% with prophylactic g-tube vs. 9.0% with reactive g-tube (*P*=0.048) at end of treatment
Chen (2010)	120	Mean Weight Loss: 19 lbs with prophylactic feeding tube vs. 43 lbs with reactive feeding tube (*P*<0.001) at end of treatment
Lewis (2014)	109	Mean % Weight Change: -2.4% with prophylactically placed feeding tube vs. -10.4% with reactively placed feeding tube (*P*=0.012) at end of treatment
Morton (2009)	33	% Weight Loss: Significantly lower % weight loss with g-tube insertion within 1 month of treatment start (*P*=0.049)
Romesser (2012)	400	Mean Absolute Weight Loss: 6.80 kg with prophylactically placed g-tube vs. 8.38 kg with reactively placed g-tube (*P*=0.007) at end of treatment Mean % Weight Loss: 7.53% with prophylactically placed g-tube vs. 9.37% with reactively placed g-tube (*P*=0.002) at end of treatment
Rutter (2011)	111	Mean Weight Loss: 14.8 lbs with proactively placed feeding tube vs. 26.2 lbs with reactively placed feeding tube (*P*=0.003) six weeks post-treatment
Nugent (2013)	196	Mean Range % Weight Loss: Prophylactically placed g-tube (-4.6% to 1.4%) vs. reactively placed g-tube (-9.4% to -4.3%) at the end of treatment
Chang (2009)	71	Median Absolute Weight Loss: 1.6 kg with prophylactically placed feeding tube vs. 4.4 kg with reactively placed feeding tube (*P*=0.10)
Langmore (2012)	59	% Weight Change: Adjusted mean difference = -2.19% at end of treatment between prophylactically placed g-tube and reactively placed g-tube (*P*=0.19)
Kramer (2014)	86	Mean % Weight Change: -18.1% with prophylactically placed g-tube vs. -16.6% with reactively placed g-tube (*P*=0.63) six months post-treatment

increased complications, reduced responses to treatment, and increased mortality rates.[22] As treatment cycles progressed, however, the percentage of patients with a prophylactic feeding tube placement who lost ≥10% of their baseline body weight significantly declined when compared to patients with a reactive feeding tube placement.[33] Furthermore, weight loss has been correlated with a decline in health-related quality of life measurements, like lower speech and swallow functioning.[7] While a substantial amount of head and neck cancer patients lose weight after a feeding tube placement, up to 24% of patients have been shown to either be able to maintain or gain weight during treatment.[29,30] Even though it is assumed weight loss will occur during treatment, potential efforts may be available to help minimize overall losses.

Individuals undergoing treatment for head and neck cancer are at an increased risk for malnutrition due to common treatment side effects, like mucositis, xerostomia, and taste alterations, that can negatively impact their volitional intake. Studies have reported fewer patients with prophylactically placed feeding tubes were diagnosed with malnutrition during their treatment, but there was not a significant difference when comparing the results to patients with reactively placed feeding tubes.[31,34] A two-year follow-up after treatment additionally showed no significant difference in malnutrition diagnoses between a prophylactic versus reactive approach.[34] It is worth noting that individuals with a prophylactic feeding tube have been shown to have 29% fewer malnutrition diagnoses at the end of treatment,[31] illustrating the potential need for early nutrition support throughout the entire duration of treatment.

Due to the location of the site of treatment, head and neck cancer patients are at risk for developing acute and chronic swallowing difficulties. One study showed 66% of patients with a prophylactically placed feeding tube required a texture modified diet when their tube feeding was first initiated.[26] During treatment, several studies demonstrated there was not a significant difference between patients with prophylactic feeding tubes and reactive feeding tubes who developed acute toxicities of dysphagia, mucositis, and xerostomia.[5,8] Conversely, a study by Langmore et al.[10] showed patients who had a prophylactically placed feeding tube had significantly worse swallowing-related outcomes during treatment than patients who received a reactive feeding tube placement or no feeding tube placement at all. An additional study reported up to 85% of their patients who received a prophylactic feeding tube developed Grade 3-4 mucositis,[32] where patients either have oral ulcers and are only able to take liquids or they are unable to consume anything by mouth.[36] Post-treatment, several studies showed prophylactically placed feeding tubes led to significantly worse swallowing abilities compared to a reactively placed feeding tube at three, six, and 12-month follow-ups,[5,10] while one study reported there were no differences in the swallowing outcomes between the two groups at the same time points.[14] Two studies looked at the esophageal stricture rates between a prophylactic versus reactive tube placement. One study reported patients with a prophylactic feeding tube had significantly more strictures after treatment,[5] while the other study showed patients with a reactive feeding tube had significantly more strictures post-treatment.[12] A potential contributing factor for the

development of strictures, regardless of when the feeding tube was placed, may be whether a patient is able to continue swallowing throughout the duration of treatment to maintain their upper esophageal/hypopharyngeal musculature activity.[37] The varying degrees of short and long-term swallowing difficulties between the two groups needs to be better understood to help reduce potential delays in the ability of the patient to return to oral feeding.

Clinical Outcomes

Head and neck cancer patients may experience unplanned hospital admissions. Common reasons for admissions include nausea and vomiting, mucositis, dehydration, dysphagia, odynophagia, malnutrition, and/or maintenance or issues with their feeding tube.[4,6,12] Several studies have shown individuals who have received a prophylactically placed feeding tube have significantly less hospital admissions compared to individuals who received a reactively placed feeding tube,[4,6,9,12,15] with up to 19% fewer admissions in the prophylactic group.[12] Other studies, however, showed no significant difference in the number of unplanned admissions between a prophylactic versus reactive approach.[13,14] Average length of stay during an admission ranged from 4-26 days for individuals with a prophylactically placed feeding tube to 6.2-25 days for individuals with a reactively placed feeding tube.[4,15,34] Hospital stay length has been shown to be influenced by weight loss, with a reduced odds of length of stay greater than seven days with less overall weight loss.[4] Individuals with a prophylactically placed feeding tube have also had significantly fewer admissions related to feeding and dysphagia.[14] Baschnagel et al.[12] reported the average cost

related to hospitalizations (including the initial tube placement) was $8,089 for a reactive approach versus $6,233 for a prophylactic approach. With a better understanding of the overall impact of each approach, it may be possible to help reduce the number, length of time, and even costs of hospitalizations for head and neck cancer patients.

Another long-term outcome measured between a prophylactic versus reactive approach is the difference in overall survival and disease-free survival in head and neck cancer patients. One study showed a significant difference between the two groups with disease-free survival rates at 12 months post-treatment, with 100% of patients with a reactively placed feeding tube disease-free compared to 80% of patients with a prophylactically placed feeding tube.[11] No significant differences in overall survival and disease-free survival rates between the two approaches have been reported at two year and three year follow-ups.[5,9,14] One study only looked at patients who received a prophylactically placed feeding tube and showed a 40% survival rate five years post-treatment.[30] Further investigation is needed to identify if there truly is a difference in mortality rates between a prophylactic versus reactive approach.

Quality of Life Outcomes

Prophylactic versus reactive feeding tube placement may have the potential to impact long-term functional outcomes, specifically the overall quality of life for a patient. Common issues of concern for head and neck cancer patients are saliva production, swallowing ability, chewing ability, and taste.[7] An inverse relationship was found between the duration a feeding tube was used and long-

term functional and behavioral outcomes, like eating in public, speech, diet, and swallowing function.[7] Questionnaires are commonly used to measure different aspects of quality of life in head and neck cancer patients. The MD Anderson Dysphagia Inventory (MDADI) questionnaire is used to measure swallowing-related quality of life in head and neck cancer patients. The MDADI consists of 20 questions subdivided into scales measuring emotion, function, physical, and global scores, with higher scores (from 0-100) representing better functioning.[38] Oozeer et al.[17] reported patients who received a prophylactically placed feeding tube had significantly poorer long-term quality of life MDADI scores related to swallowing ability compared to patients with a reactively placed feeding tube. Conversely, Prestwich et al.[16] reported patients with a prophylactic tube placement had equal to or higher MDADI scores related to long-term swallowing ability than patients with a reactive tube placement. Other questionnaires that have been used to measure quality of life in head and neck cancer patients include the 36-Item Short Form Health Survey (SF-36) and the European Organization for Research and Treatment of Cancer Quality of Life (EORTC QLQ C-30 and EORTC QLQ-H&N35) assessments. The SF-36 measures quality of life through different health concepts, like limitations in physical activities, social activities, and/or usual role activities, bodily pain, general mental health, vitality, and general health perceptions.[39] The EORTC QLQ C-30 questionnaire measures quality of life in cancer patients using functional scales (physical, role, emotional, social, and cognitive), symptom scales (fatigue, nausea, vomiting, and pain), global health and quality of life scales, and single items (dyspnea,

insomnia, appetite loss, constipation, diarrhea, and financial difficulties).[40] EORTC QLQ-H&N35 is the head and neck cancer module questionnaire used in conjunction with the EORTC QLQ C-30 questionnaire. A study using the EORTC QLQ C-30 and EORTC QLQ-H&N35 questionnaires reported patients with a prophylactically placed feeding tube had significantly better scores in role and social functioning, appetite loss, constipation, and diarrhea compared to patients receiving reactive nutrition support at three months after the start of treatment.[34] At six months after the start of treatment, the prophylactic group scored significantly better in global, physical, cognitive, social, and role functioning scores and better scores with ability to open the mouth wide and sticky saliva after two years. Another study utilized the SF-36 and EORTC QLQ C-30 questionnaires and reported significantly better physical, mental, and global health status scores for patients with a prophylactically placed feeding tube six months after the completion of their treatment.[41] A prophylactic approach may be beneficial in improving overall quality of life in head and neck cancer patients, but it's important to note the tube duration could have a negative influence on their scores.

The overall goal of this project was to determine if prophylactic placement of a feeding tube prior to treatment for head and neck cancer patients improves nutritional, clinical, and long-term quality of life outcomes during and after treatment.

Methods

Study Population

A retrospective chart review was conducted of oropharyngeal (T1, T2, and T3) head and neck cancer patients treated with radiation +/- chemotherapy from January 1, 2010 to June 30, 2017 at the VA Portland Health Care System and OHSU in Portland, Oregon. Patients were identified using electronic medical records and divided into two groups based on their feeding tube status: prophylactic g-tube and reactive/no g-tube. The prophylactic g-tube group included patients who underwent a feeding tube placement prior to the start of treatment, while the reactive/no g-tube group included patients who either underwent a reactive feeding tube placement after the start of treatment or who never had a feeding tube placed. The sample size was based on eligible patients during the study time period. Approval from the OHSU Institutional Review Board and VA Portland Health Care System was obtained prior to data collection. The medical records of potential subjects were reviewed to determine if they met the following eligibility criteria:

Inclusion Criteria:

- Diagnosis of oropharyngeal (T1, T2, and T3) cancer
- Treatment with radiation +/- chemotherapy at OHSU and/or VA Portland Health Care System between January 1, 2010 and June 30, 2017
- Prophylactic, reactive, or no g-tube placement
- Age ≥ 18 years old
- Received curative intent treatment

Exclusion Criteria:

- Ineligible cancer locations (e.g. esophagus, skin)
- Required therapeutic enteral feeding before start of treatment
- Patients unable to have g-tube placement due to medical contraindications to the procedure
- Incomplete data at baseline (e.g. missing patient weight on treatment start date)

Study Protocol

All data was obtained from the OHSU electronic medical record system EPIC and the Department of Veterans Affairs Computerized Patient Record System (CPRS). Baseline data collected at the start of treatment included age, gender, race, location and stage of cancer, P16 status, treatment type, Charlson Comorbidity Index, smoking status, alcohol use, weight (kg), and body mass index (BMI) (kg/m^2). Date of feeding tube placement was used to determine whether a feeding tube was prophylactically or reactively placed in relation to the treatment start date. Outcome measurements included weight loss, time to return to oral feeding, unplanned hospital admissions, and quality of life measurements.

Weight Loss

Patient weights (kg) were collected at their initial radiation oncology consult visit, treatment start, treatment end, follow-up (two to four weeks post-treatment), and three months post-treatment. Absolute weight loss (kg) was calculated for the following time periods: pretreatment (weight change from

consult to treatment start), treatment (weight change from first to last day of treatment), follow-up (weight change from treatment end to two to four weeks post-treatment), three months post-treatment (weight change from treatment end to three months post-treatment), and total weight change (weight change from consult to three months post-treatment). Percent weight loss was calculated for the following time periods: pretreatment (percent weight change from consult to treatment start), treatment (percent weight change from first to last day of treatment), follow-up (percent weight change from treatment end to two to four weeks post-treatment), three months post-treatment (percent weight change from treatment end to three months post-treatment), and total weight change (percent weight change from consult to three months post-treatment).

Unplanned Hospital Admissions

The number of patients admitted, number of total admissions, reasons for unplanned hospital admissions, and length of stay were collected from the start date of treatment to one-month post-treatment. Unplanned hospital admissions included but were not limited to dehydration, nausea, vomiting, diarrhea, constipation, odynophagia, mucositis, dysphagia, feeding tube complications, and other medical reasons. Admissions for elective reasons (e.g. chemotherapy administration, feeding tube placement) were not included.

Time to Return to Oral Feeding

The documented date of the feeding tube removal was used to determine the length of time it took a subject to return to oral feeding after the treatment end date, indicating the subject was shown to have adequate oral intake and no

longer required a feeding tube as a source of nutrition. Subjects who never used their feeding tube for enteral feedings after it was placed were not included in the analysis.

Quality of Life

Existing subject responses using the Eating Assessment Tool (EAT-10) questionnaire and University of Michigan Head and Neck Specific Quality of Life Instrument (HNQoL) questionnaire were used to measure quality of life measurements in the subjects. The EAT-10 survey is a 10-item validated self-administered survey measuring dysphagia severity.[42] Individuals can score different swallowing scenarios from 0 (no problem) to 4 (severe problem) for each of the 10 items and a total EAT-10 score of three or greater is considered to be abnormal. The HNQoL questionnaire is a validated head and neck cancer-specific quality of life questionnaire consisting of four domains: communication (four items), pain (four items), eating (six items), and emotion (six items).[43] Each question under the different domains is rated using a five-choice, Likert-scale and a score of zero (worst score) to 100 (best score) is generated for each domain, with a higher score reflecting better quality of life. Patient scores two to five years post-treatment from the EAT-10 and HNQoL questionnaires were collected for analysis.

Statistical Analysis

Descriptive statistics were used to characterize the sample to determine whether there were any baseline differences between the prophylactic g-tube versus reactive/no g-tube groups. Categorical variables, including gender, race,

location and stage of cancer, P16 status, treatment type, smoking status, and alcohol use, were summarized as frequency (counts) and percentages and compared using chi-squared analysis for significance. Continuous variables, including age, weight (kg), BMI (kg/m^2), and Charlson Comorbidity Index, were summarized as mean ± standard deviation and compared using two-sample unpaired *t*-tests for significance. $P<0.05$ was considered statistically significant.

Specific Aim 1: A two-sample unpaired *t*-test was used to compare differences between the two groups for weight loss and length of stay for unplanned hospital admissions. A chi-squared analysis was used to compare the unplanned hospital admissions outcomes of number of patients admitted, number of total admissions, and reasons for unplanned hospital admissions between the two subject groups. A Kaplan-Meier analysis was used to compare time to return to oral feeding between the two groups and differences were calculated with a log-rank test. $P<0.05$ was considered statistically significant.

Specific Aim 2: A two-sample unpaired *t*-test was used to compare the EAT-10 questionnaire and HNQoL questionnaire scores between the two subject groups. $P<0.05$ was considered statistically significant.

Results

Patient Characteristics

Eight hundred ten (810) oropharyngeal cancer patients from OHSU and the VA Portland Health Care System were identified during the study period. Three hundred five (305) patients had primary tumor stage classifications of T1, T2, or T3 and received radiation +/- chemotherapy and were included in the study. Seventy-five (75) patients were excluded from the study because of missing data or use of their g-tube prior to the treatment start. The final total number of patients eligible for inclusion was 230 (Figure 1).

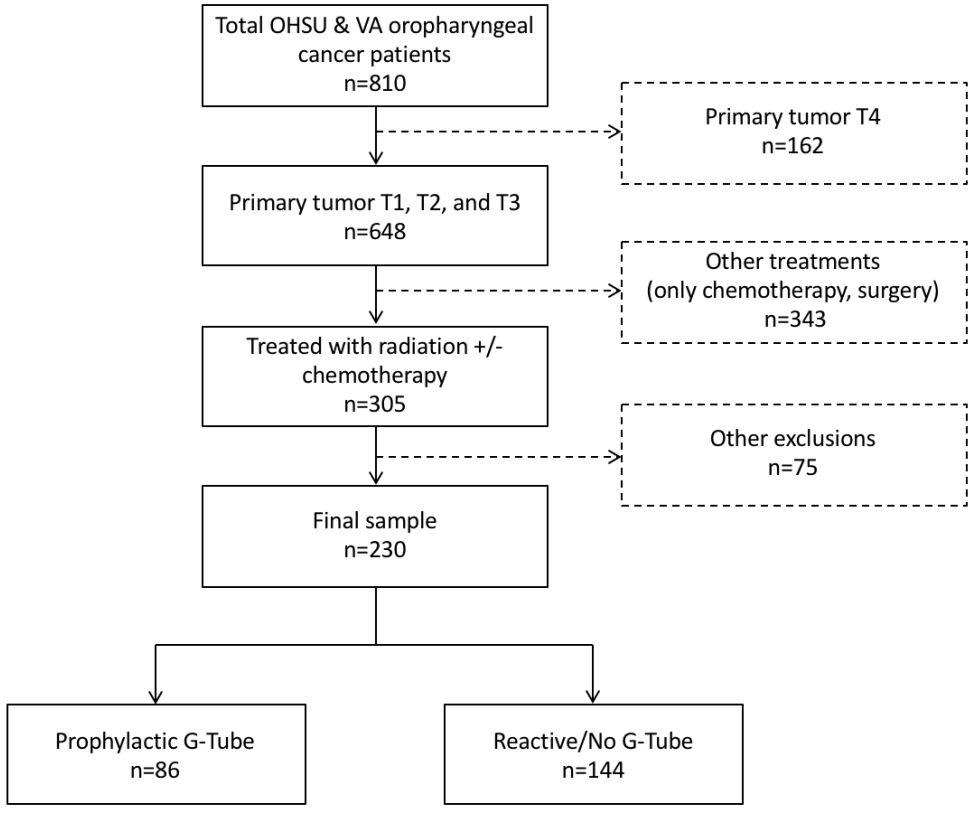

Figure 1. Flow diagram of the approach used for patient selection

Eighty-six (86) patients received a prophylactic g-tube placement and 144 patients either received a reactive g-tube placement or no feeding tube placement. There were no significant differences between the prophylactic g-tube and reactive/no g-tube groups with regards to age, BMI, Charlson Comorbidity Index, sex, race, primary tumor site, primary tumor stage, or smoking status (Table 2). The treatment start weight of the prophylactic g-tube group was significantly lower than the reactive/no g-tube group (87.19±19.33 kg vs 92.85±18.30 kg; P=0.03). Statistically significant differences in treatment type (P<0.001), P16 status (P=0.02), and alcohol use (P=0.01) were also observed between the two groups.

Table 2. Patient Characteristics

Characteristics	All patients (n=230)	Prophylactic G-Tube (n=86)	Reactive/No G-Tube (n=144)	*P* value[a]
		Mean±SD		
Age, year	63.03±8.29	61.77±7.37	63.78±8.73	0.07
Weight, treatment start, kg	90.73±18.85	87.19±19.33	92.85±18.30	0.03
BMI, kg/m^2	28.82±5.26	28.03±5.72	29.29±4.94	0.08
Charlson Comorbidity Index	4.32±1.37	4.12±1.11	4.44±1.49	0.09
		n (%)		
Sex				0.80
Male	221 (96)	83 (97)	138 (96)	
Female	9 (4)	3 (3)	6 (4)	
Race				0.74
White, not Hispanic or Latino	192 (83)	72 (84)	120 (84)	
Black	1 (1)	0 (0)	1 (1)	
American Indian or Alaska Native	3 (1)	1 (1)	2 (1)	
Asian Indian or Pakistani	2 (1)	0 (0)	2 (1)	
Unknown	32 (14)	13 (15)	19 (13)	
Primary Tumor Site				0.62
Base of Tongue	100 (43)	38 (45)	62 (43)	
Tonsil	117 (51)	44 (51)	73 (51)	
Oropharynx	5 (2)	1 (1)	4 (3)	
Soft Palate	5 (2)	2 (2)	3 (2)	
Vallecula	1 (1)	1 (1)	0 (0)	
Epiglottis	2 (1)	0 (0)	2 (1)	
Primary Tumor Stage				0.73
T1	63 (27)	21 (24)	42 (29)	
T2	107 (47)	42 (49)	65 (45)	
T3	60 (26)	23 (27)	37 (26)	
Treatment Type				<0.001
Chemoradiotherapy	190 (83)	82 (95)	108 (75)	
Radiotherapy	40 (17)	4 (5)	36 (25)	
P16 Status				0.02
Positive	193 (84)	66 (76)	127 (88)	
Negative	23 (10)	10 (12)	13 (9)	
Unknown	14 (6)	10 (12)	4 (3)	
Smoking Status				0.73
Current	43 (19)	18 (21)	25 (18)	
Former	134 (58)	50 (58)	84 (58)	
Never/Unknown	53 (23)	18 (21)	35 (24)	
Alcohol Use				0.01
Current	107 (47)	47 (55)	60 (42)	
Former	42 (18)	19 (22)	23 (16)	
Never/Unknown	81 (35)	20 (23)	61 (42)	

Abbreviations: G-Tube, Gastrostomy tube; SD, Standard deviation; kg, Kilograms; BMI, Body mass index

[a]Continuous variables analyzed using two-sample *t*-tests and categorical variables analyzed using chi-squared analysis with statistical significance set at $P<0.05$

Weight Loss

The mean weight of both groups declined from their initial consult through three months post-treatment and the mean weight of the prophylactic g-tube group remained less than reactive/no g-tube group over time (Figure 2). The only mean weight of the prophylactic g-tube group that was statistically less than the reactive/no g-tube group was at the treatment start date (87.19±19.33 kg vs 92.85±18.30 kg; *P*=0.03).

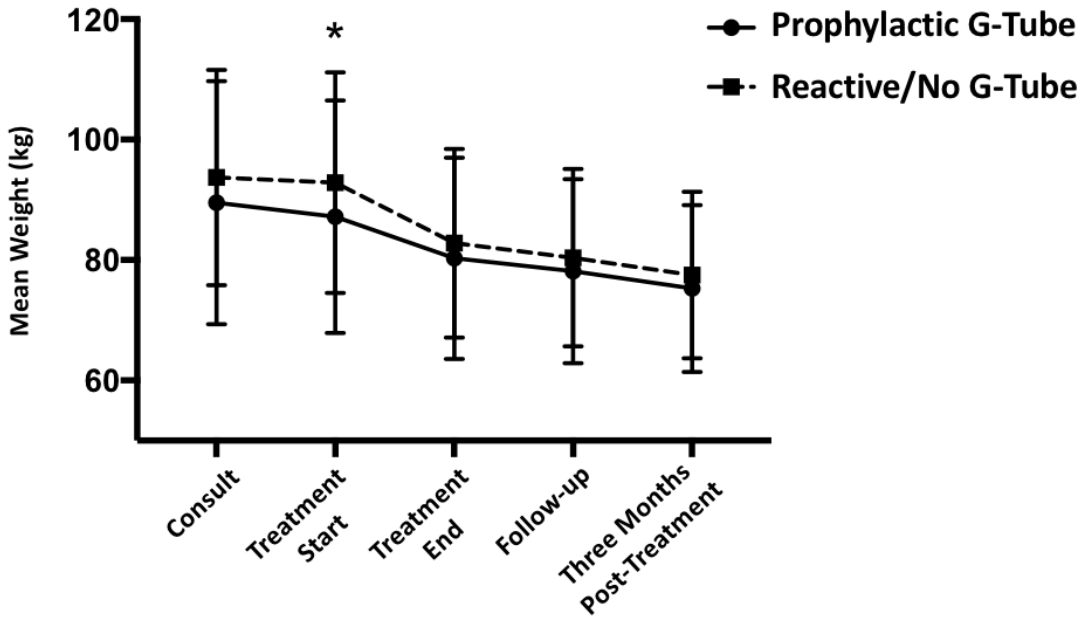

Figure 2. Patient weight change over time. Mean patient weight (kg) for the prophylactic g-tube vs reactive/no g-tube groups at different time points during their treatment. The asterisk (*) indicates a statistically significant mean weight difference between the prophylactic g-tube and reactive/no g-tube group (87.19±19.33 kg vs 92.85±18.30 kg; *P*=0.03; Two-sample *t*-test analysis).

The prophylactic g-tube group lost significantly more weight during the pretreatment period than the reactive/no g-tube group (-2.02±3.08 kg vs -0.78±3.42 kg; *P*=0.008) (Table 3). The mean duration of the pretreatment time period was 34.18 days, with no significant differences in duration during this time

period between the prophylactic g-tube and reactive/no g-tube groups (31.79±20.22 days vs 35.61±29.06 days; *P*=0.28). During the treatment period, the reactive/no g-tube group lost significantly more weight than the prophylactic g-tube group (-10.05±4.57 kg vs -6.89±4.87 kg; *P*<0.001). The mean duration of the treatment time period was 50.03 days, with no significant differences in duration during this time period between the prophylactic g-tube and reactive/no g-tube groups (48.36±6.85 days vs 51.03±13.48 days; *P*=0.09). The prophylactic g-tube group continued to lose less weight through the follow-up and three-month post-treatment periods compared to the reactive/no g-tube group, however, none of the differences were statistically significant. Total weight change from the initial consult date to three months post-treatment was also not found to be statistically significant between the two groups (*P*=0.10).

Table 3. Absolute weight loss (kg) for each time period by feeding tube status

Time Period	Prophylactic G-Tube	Reactive/No G-Tube	*P* value[a]
	Mean±SD		
Pretreatment[b]	-2.02±3.08	-0.78±3.42	0.008
Treatment[c]	-6.89±4.87	-10.05±4.57	<0.001
Follow-up[d]	-2.60±3.34	-2.72±3.06	0.79
Three months[e]	-5.03±5.96	-5.22±5.07	0.81
Total weight change[f]	-14.14±9.17	-16.23±7.89	0.10

Abbreviations: G-Tube, Gastrostomy tube; kg, Kilogram; SD, Standard deviation
[a]Two-sample *t*-test analysis with statistical significance set at *P*<0.05
[b]Pretreatment: weight change from consult to treatment start (n=217)
[c]Treatment: weight change from first to last day of treatment (n=230)
[d]Follow-up: weight change from treatment end to two to four weeks post-treatment (n=219)
[e]Three months: weight change from three months post-treatment (n=203)
[f]Total weight change: weight change from consult to three months post-treatment (n=195)

Similar to absolute weight loss, the percent weight change during the pretreatment period was significantly higher in the prophylactic g-tube group

compared to the reactive/no g-tube group (-2.22±3.42% vs -0.82±3.60%; *P*=0.005) (Table 4). The reactive/no g-tube group had a significantly higher percent weight change during the treatment period than the prophylactic g-tube group (-10.56±4.12% vs -7.54±4.87%; *P*<0.001). While the percent weight change for the prophylactic g-tube group continued to be lower than the reactive/no g-tube group through the follow-up and three-month post-treatment periods, the differences between the groups were not statistically significant. Total percent weight change from the initial consult to three months post-treatment was less in the prophylactic g-tube group compared to the reactive/no g-tube group (-14.89±7.69% vs -16.78±6.54%), however, the difference was not statistically significant (*P*=0.07).

Table 4. Percent weight loss for each time period by feeding tube status

Time Period	Prophylactic G-Tube	Reactive/No G-Tube	*P* value[a]
	Mean±SD		
Pretreatment[b]	-2.22±3.42	-0.82±3.60	0.005
Treatment[c]	-7.54±4.87	-10.56±4.12	<0.001
Follow-up[d]	-2.94±4.26	-3.12±3.55	0.73
Three months[e]	-5.68±6.94	-5.95±5.65	0.76
Total weight change[f]	-14.89±7.69	-16.78±6.54	0.07

Abbreviations: G-Tube, Gastrostomy tube; kg, Kilogram; SD, Standard deviation
[a]Two-sample *t*-test analysis with statistical significance set at *P*<0.05
[b]Pretreatment: % weight change from consult to treatment start (n=217)
[c]Treatment: % weight change from first to last day of treatment (n=230)
[d]Follow-up: % weight change from treatment end to two to four weeks post-treatment (n=219)
[e]Three months: % weight change three months post-treatment (n=203)
[f]Total weight change: % weight change from consult to three months post-treatment (n=195)

Unplanned Hospital Admissions

A total of 40 patients had unplanned hospital admissions from the start of their treatment to one-month post-treatment, with 14 patients (16%) in the

prophylactic g-tube group versus 26 patients (18%) in the reactive/no g-tube group (*P*=0.73) (Table 5). The prophylactic g-tube group had 19 unplanned hospital admissions and the reactive/no g-tube group had 31 unplanned hospital admissions (*P*=0.92). The prophylactic g-tube group had significantly more unplanned hospital admissions compared to the reactive/no g-tube group for mucositis (3 admissions vs 0 admissions; *P*=0.02) and other medical reasons (neutropenia, acute renal injury, and fever) (15 admissions vs 4 admissions; *P*<0.001). Unplanned hospital admissions for gastrointestinal disturbances (nausea, vomiting, and diarrhea), dysphagia, odynophagia, and other nutrition reasons (dehydration and poor intake) were not significantly different between the two groups (Table 5). No significant differences were found in regards to length of stay during each hospital admission between the prophylactic g-tube and reactive/no g-tube groups (4.00±1.71 days vs 3.37±2.20 days; *P*=0.30).

Table 5. Unplanned hospital admissions by feeding tube status

	Prophylactic G-Tube (n=86)	**Reactive/No G-Tube** (n=144)	***P* value**[a]
	n (%)		
No. of patients admitted	14 (16)	26 (18)	0.73
No. of admissions	19	31	0.92
Reasons for admission			
Gastrointestinal disturbances[b]	4	14	0.17
Mucositis	3	0	0.02
Dysphagia	0	3	0.18
Odynophagia	1	2	0.88
Other nutrition[c]	2	9	0.18
G-Tube complications	2	0	0.07
Other medical[d]	15	4	<0.001

Abbreviations: G-Tube, Gastrostomy tube
[a]Chi-squared analysis with statistical significance set at *P*<0.05
[b]Gastrointestinal disturbances: nausea, vomiting, diarrhea
[c]Other nutrition: dehydration, poor intake
[d]Other medical: neutropenia, acute renal injury, fever

Time to Return to Oral Feeding

One hundred thirty-eight (138) patients had g-tubes placed during their treatment. There was a total of 86 prophylactic placements and 52 reactive placements, indicating 36% of patients in the reactive/no g-tube group required a reactively placed feeding tube. A Kaplan-Meier analysis was used to compare the rates of feeding tube removals post-treatment due to unknown dates of feeding tube removals for 28 patients lost to follow-up. There was no significant difference found between the prophylactic g-tube and reactive/no g-tube groups for the time of feeding tube removal post-treatment (*P*=0.29) (Figure 3).

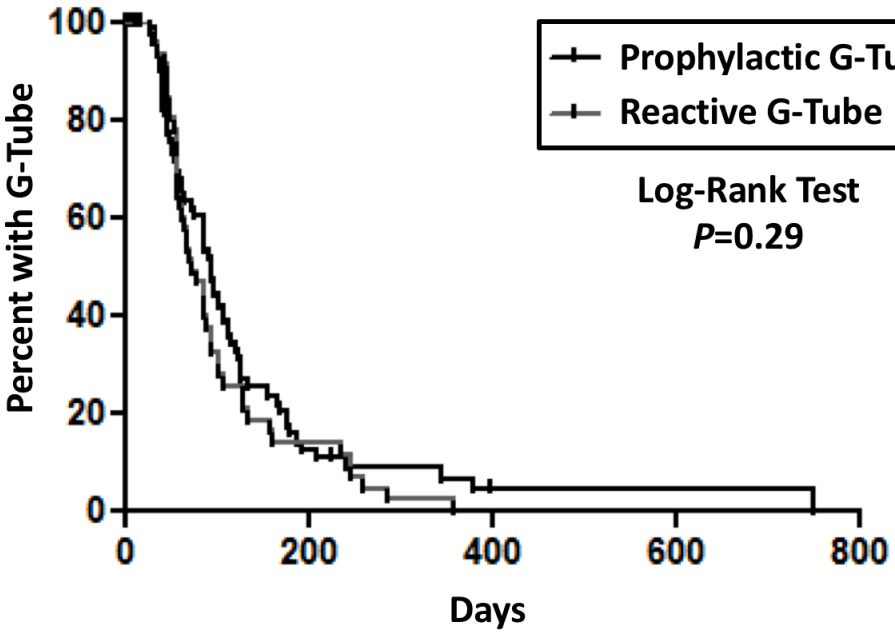

Figure 3. Comparison of time to g-tube removal post-treatment between prophylactic and reactive placements

Quality of Life

A total of 36 patients completed HNQoL and EAT-10 quality of life questionnaires two to five years post-treatment. No statistically significant

differences in the quality of life scores for either questionnaire were found between the prophylactic g-tube and reactive/no g-tube groups during this time period (Table 6).

Table 6. Quality of life scores two to five years post-treatment by feeding tube status

	Prophylactic G-Tube (n=16)	**Reactive/No G-Tube** (n=20)	***P* value[a]**
	Mean±SD		
HNQoL			
Communication	74.61±26.37	84.69±20.02	0.20
Pain	70.83±23.77	64.58±25.49	0.46
Eating	66.15±17.00	69.79±22.17	0.59
Emotion	83.07±19.03	81.04±26.64	0.80
Overall	74.45±16.36	75.44±20.94	0.88
EAT-10	12.56±10.25	11.32±9.52	0.71

Abbreviations: G-Tube, Gastrostomy tube
[a]Two-sample *t*-test analysis with statistical significance set at $P<0.05$

Discussion

Head and neck cancer patients are vulnerable to changes in their nutritional status throughout their treatment due to the location of the cancer. The decision to place a g-tube before the start of treatment is often based on current symptoms the patient is experiencing (e.g. unplanned weight loss or difficulty swallowing) or future predicted treatment-related symptoms the patient may encounter during treatment. Health care providers and patients may also opt out of proactive g-tube placements since there may not be an immediate need or the future need for one is unknown. Due to the lack of standard protocol for g-tube placements in head and neck cancer patients, we evaluated the nutritional, clinical, and long-term quality of life outcome effects of prophylactic versus reactive feeding tube placements to asses which method may be more beneficial.

In line with the findings of this study, weight loss is commonly observed in head and neck cancer patients undergoing treatment, regardless of the time of g-tube placement.[2-6,8,9,11,13,14,30-32,34,35] Our study showed the prophylactic g-tube group lost significantly more weight in the pretreatment period than the reactive/no g-tube group. Assenat et al.[2] reported similar findings in a retrospective study comparing the nutritional status of 139 head and neck cancer patients who did or did not receive prophylactic g-tubes. They observed the median pretreatment weight loss of the prophylactic g-tube group was significantly more than the group without prophylactic g-tube placements (-5.0 kg vs -2.0 kg; $P<0.001$). These results may indicate patients chosen for prophylactic

feeding tube placements may already be experiencing difficulty maintaining adequate oral intake prior to their treatment start, which likely influences the decision for a prophylactic placement.

While both groups continued to lose weight throughout treatment, the reactive/no g-tube group in our study lost significantly more weight than the prophylactic g-tube group during treatment. This is most likely due to the declining volitional intake in patients without access to a feeding tube for supplemental nutrition. These results are reflected in a recent study by Brown et al.[4] comparing outcomes between a prophylactic or reactive approach to feeding tube placement in 130 head and neck cancer patients. The prophylactic g-tube group in their study lost significantly less weight compared to the reactive group (-7.0% vs -9.0%; *P*=0.048). Romesser et al.[8] reported similar observations in their study examining the clinical benefit of prophylactic g-tubes in 400 oropharyngeal cancer patients undergoing treatment. They found patients who received prophylactic g-tube placements had a significant lower absolute weight loss at the end of treatment compared to patients who received a reactive g-tube placement or no placement at all (-7.53% vs -9.37%; *P*=0.002). Our results further support these findings that prophylactic g-tube placement is associated with decreased weight loss during treatment.

Our study demonstrated the prophylactic g-tube group continued to lose less weight than the reactive/no g-tube group post-treatment, however, the differences between the groups were not significant. Similar to our study, Romesser et al.[8] also looked at weight loss in the post-treatment period and

found patients with a prophylactic g-tube placement continued to lose less weight than patients following a reactive approach at one-month (-2.39% vs -3.16%) and three months post-treatment (-4.48% vs -4.97%). The results from our study and the Romesser et al. study may illustrate a protective benefit of prophylactically placed feeding tubes in decreasing weight loss in head and neck cancer patients post-treatment.

In the current study, there were no significant differences in the unplanned hospital admission rates and length of stay between the prophylactic g-tube and reactive/no g-tube groups. In a retrospective study by Baschnagel et al,[12] the hospitalization rate up to two months post-treatment of a prophylactic approach was significantly lower than a reactive approach in 193 head and neck cancer patients (33% vs 52%; *P*=0.02). Their reasons for hospitalizations included dehydration, malnutrition, dysphagia, g-tube placement, or g-tube-related problems. We did not include hospitalizations for g-tube placements, so the insignificance of our unplanned hospital admission rates could have potentially been influenced by these findings. We also found the prophylactic g-tube group had significantly more admissions for other medical reasons, including neutropenia, acute renal failure, and fever. This begs the question of whether prophylactic feeding tube placements could potentially increase the likelihood of a patient requiring a hospital admission for non-nutrition related reasons or if patients receiving prophylactic feeding tubes are already at a lower health status putting them at risk for admissions related to other medical reasons.

There is concern that patients who receive prophylactic g-tube placements are at a greater risk of developing dysphagia and long-term feeding tube dependence, however, a recent review concluded the impact of prophylactic g-tubes use on swallowing-related outcomes is unclear.[44] We observed there were no significant differences in the feeding tube removal times post-treatment between the prophylactic g-tube and reactive/no g-tube groups. Rutter et al.[9] retrospectively examined a similar outcome among 90 head and neck cancer patients undergoing treatment. Their Kaplan-Meier analysis showed having a g-tube placed before or after the start of treatment did not impact the time it took to remove the g-tube post-treatment ($P>0.05$). While these results may indicate prophylactic g-tube placement does not impact feeding tube dependence, there is research showing continuing some degree of oral intake with g-tube use can decrease the degree of adverse swallowing-related outcomes post-treatment.[10] Our study did not collect data regarding the oral intake of the patients using g-tubes, but patients were encouraged to continue some sort of oral intake for as long as tolerated.

Using existing responses from the EAT-10 and HNQoL questionnaire, we did not find any significant differences in the quality of life scores between the prophylactic g-tube and reactive/no g-tube groups at two to five years post-treatment. To our knowledge, this is the first study using these specific questionnaires to compare quality of life scores between a prophylactic versus reactive approach in head and neck cancer patients. Silander et al.[34] examined whether prophylactic g-tube placements could improve health-related quality of

life in a randomized study of 134 head and neck cancer patients. The two validated questionnaires they used for their quality of life assessments were the EORTC QLQ C-30 and EORTC QLQ-H&N35. At two years after the start of treatment, they found no significant differences in the EORTC QLQ C-30 scores looking at functioning and symptoms between the prophylactic and reactive g-tube groups. The EORTC QLQ-H&N35 identified significant differences between the two groups in two out of the 13 measures, with a higher function in the ability to open mouth wide and decreased sticky saliva in the prophylactic group verses the reactive group. They did note the most significant differences in the quality of life scores between the two groups was at their six-month follow-up after the start of treatment, which indicates any effect the g-tube placement approach may have had on the quality of life scores was no longer existent two years after the start of treatment. This may be the reason we observed no significant differences in the quality of life scores in our study. It is important to note the EAT-10 scores in both of our groups were above three, which is considered an abnormal score and may indicate the patients were still experiencing some degree of swallowing difficulties two to five years post-treatment.

Several limitations are observed in our study, mainly due to its retrospective nature. We were limited by the data available to us in the electronic medical record and had to rely on the data entered as being accurate. Patients were found to have missing data and some were lost to follow-up, decreasing our available sample size for several outcomes (e.g. quality of life and time to return to oral feeding) and potentially influencing our findings. The professional

judgement of the health care providers and the personal preference of the patients could have also influenced the timing of the g-tube placement, as some providers or patients may have waited longer than others to place a feeding tube as oral intake started to decline. Patient weight may have also influenced when or if a feeding tube was placed, as patients with an underweight BMI classification may have been more likely to have a prophylactic g-tube placed and a reactive approach may have been followed more for patients with an overweight or obese BMI classification. Another limitation is that we used the feeding tube removal date as a surrogate date for when the patients returned to oral feeding post-treatment. While the feeding tube removal date indicates the patient no longer relied on the feeding tube for nutrition, the patients were likely not using the feeding tube and meeting all of their nutritional needs orally for a short period of time prior to its removal. This could indicate our results are an overestimate of the time it took patients to return to oral feeding in both groups.

Despite these limitations, this study demonstrated the placement of a prophylactic g-tube helped to reduce patient weight loss during treatment and did not contribute to long-term feeding tube dependence compared to a reactive g-tube placement. Further research is needed to help identify early predictors of g-tube need in head and neck cancer patients, like tumor characteristics and/or treatment type. Additionally, investigation into whether the degree of oral intake during feeding tube use for either approach is needed to determine its influence on patient outcomes. Creating standardized protocols that also include baseline

and ongoing evaluations of a patient's nutritional status could further help detect patients at risk for needing enteral nutrition support.

Conclusion

Prophylactic g-tube placement was associated with a significant decrease in weight loss during treatment compared to a reactive approach, however, the difference was not observed during the pretreatment, follow-up, and three-month post-treatment time periods or in overall total weight change. Prophylactic g-tube placement did not result in long-term feeding tube dependence and no differences between the groups were observed with unplanned hospital admission rates or long-term quality of life scores. While this study indicates prophylactic placement may be beneficial, it is still uncertain which patients would benefit the most from prophylactic g-tube placements. Further studies are needed to better identify indicators for the use of a prophylactic approach in head and neck cancer patients.

References

1. Langius JA, Zandbergen MC, Eerenstein SE, et al. Effect of nutritional interventions on nutritional status, quality of life and mortality in patients with head and neck cancer receiving (chemo)radiotherapy: a systematic review. *Clin Nutr.* 2013;32(5):671-678.
2. Assenat E, Thezenas S, Flori N, et al. Prophylactic percutaneous endoscopic gastrostomy in patients with advanced head and neck tumors treated by combined chemoradiotherapy. *J Pain Symptom Manage.* 2011;42(4):548-556.
3. Beaver ME, Matheny KE, Roberts DB, Myers JN. Predictors of weight loss during radiation therapy. *Otolaryngol Head Neck Surg.* 2001;125(6):645-648.
4. Brown TE, Banks MD, Hughes BG, Lin CY, Kenny LM, Bauer JD. Comparison of Nutritional and Clinical Outcomes in Patients with Head and Neck Cancer Undergoing Chemoradiotherapy Utilizing Prophylactic versus Reactive Nutrition Support Approaches. *J Acad Nutr Diet.* 2016.
5. Chen AM, Li BQ, Lau DH, et al. Evaluating the role of prophylactic gastrostomy tube placement prior to definitive chemoradiotherapy for head and neck cancer. *Int J Radiat Oncol Biol Phys.* 2010;78(4):1026-1032.
6. Lewis SL, Brody R, Touger-Decker R, Parrott JS, Epstein J. Feeding tube use in patients with head and neck cancer. *Head Neck.* 2014;36(12):1789-1795.
7. Morton RP, Crowder VL, Mawdsley R, Ong E, Izzard M. Elective gastrostomy, nutritional status and quality of life in advanced head and neck cancer patients receiving chemoradiotherapy. *ANZ J Surg.* 2009;79(10):713-718.
8. Romesser PB, Romanyshyn JC, Schupak KD, et al. Percutaneous endoscopic gastrostomy in oropharyngeal cancer patients treated with intensity-modulated radiotherapy with concurrent chemotherapy. *Cancer.* 2012;118(24):6072-6078.
9. Rutter CE, Yovino S, Taylor R, et al. Impact of early percutaneous endoscopic gastrostomy tube placement on nutritional status and hospitalization in patients with head and neck cancer receiving definitive chemoradiation therapy. *Head Neck.* 2011;33(10):1441-1447.
10. Langmore S, Krisciunas GP, Miloro KV, Evans SR, Cheng DM. Does PEG use cause dysphagia in head and neck cancer patients? *Dysphagia.* 2012;27(2):251-259.
11. Kramer S, Newcomb M, Hessler J, Siddiqui F. Prophylactic versus reactive PEG tube placement in head and neck cancer. *Otolaryngol Head Neck Surg.* 2014;150(3):407-412.
12. Baschnagel AM, Yadav S, Marina O, et al. Toxicities and costs of placing prophylactic and reactive percutaneous gastrostomy tubes in patients with locally advanced head and neck cancers treated with chemoradiotherapy. *Head Neck.* 2014;36(8):1155-1161.

13. Chang JH, Gosling T, Larsen J, Powell S, Scanlon R, Chander S. Prophylactic gastrostomy tubes for patients receiving radical radiotherapy for head and neck cancers: a retrospective review. *J Med Imaging Radiat Oncol.* 2009;53(5):494-499.
14. Williams GF, Teo MT, Sen M, Dyker KE, Coyle C, Prestwich RJ. Enteral feeding outcomes after chemoradiotherapy for oropharynx cancer: a role for a prophylactic gastrostomy? *Oral Oncol.* 2012;48(5):434-440.
15. Hughes BG, Jain VK, Brown T, et al. Decreased hospital stay and significant cost savings after routine use of prophylactic gastrostomy for high-risk patients with head and neck cancer receiving chemoradiotherapy at a tertiary cancer institution. *Head Neck.* 2013;35(3):436-442.
16. Prestwich RJ, Teo MT, Gilbert A, Williams G, Dyker KE, Sen M. Long-term swallow function after chemoradiotherapy for oropharyngeal cancer: the influence of a prophylactic gastrostomy or reactive nasogastric tube. *Clin Oncol (R Coll Radiol).* 2014;26(2):103-109.
17. Oozeer NB, Corsar K, Glore RJ, Penney S, Patterson J, Paleri V. The impact of enteral feeding route on patient-reported long term swallowing outcome after chemoradiation for head and neck cancer. *Oral Oncol.* 2011;47(10):980-983.
18. National Cancer Institute. Head and Neck Cancers. 2013; https://www.cancer.gov/types/head-and-neck/head-neck-fact-sheet. Accessed March 24, 2017.
19. American Cancer Society. Cancer Facts & Figures 2018. 2018; https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2018/cancer-facts-and-figures-2018.pdf. Accessed May 7, 2018.
20. Pfister DG, Ang KK, Brizel DM, et al. Head and neck cancers, version 2.2013. Featured updates to the NCCN guidelines. *J Natl Compr Canc Netw.* 2013;11(8):917-923.
21. August DA, Huhmann MB. A.S.P.E.N. clinical guidelines: nutrition support therapy during adult anticancer treatment and in hematopoietic cell transplantation. *JPEN J Parenter Enteral Nutr.* 2009;33(5):472-500.
22. Talwar B, Donnelly R, Skelly R, Donaldson M. Nutritional management in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol.* 2016;130(S2):S32-s40.
23. Brown T, Ross L, Jones L, Hughes B, Banks M. Nutrition outcomes following implementation of validated swallowing and nutrition guidelines for patients with head and neck cancer. *Support Care Cancer.* 2014;22(9):2381-2391.
24. Brown TE, Spurgin AL, Ross L, et al. Validated swallowing and nutrition guidelines for patients with head and neck cancer: identification of high-risk patients for proactive gastrostomy. *Head Neck.* 2013;35(10):1385-1391.
25. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) Head and Neck Cancers. 2017;

https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed March 24, 2017.
26. Crombie JM, Ng S, Spurgin AL, Ward EC, Brown TE, Hughes BG. Swallowing outcomes and PEG dependence in head and neck cancer patients receiving definitive or adjuvant radiotherapy +/- chemotherapy with a proactive PEG: a prospective study with long term follow up. *Oral Oncol.* 2015;51(6):622-628.
27. Madhoun MF, Blankenship MM, Blankenship DM, Krempl GA, Tierney WM. Prophylactic PEG placement in head and neck cancer: how many feeding tubes are unused (and unnecessary)? *World J Gastroenterol.* 2011;17(8):1004-1008.
28. Shinozaki T, Hayashi R, Miyazaki M, et al. Gastrostomy dependence in head and neck carcinoma patient receiving post-operative therapy. *Jpn J Clin Oncol.* 2014;44(11):1058-1062.
29. Moleiro J, Faias S, Fidalgo C, Serrano M, Pereira AD. Usefulness of Prophylactic Percutaneous Gastrostomy Placement in Patients with Head and Neck Cancer Treated with Chemoradiotherapy. *Dysphagia.* 2016;31(1):84-89.
30. Wiggenraad RG, Flierman L, Goossens A, et al. Prophylactic gastrostomy placement and early tube feeding may limit loss of weight during chemoradiotherapy for advanced head and neck cancer, a preliminary study. *Clin Otolaryngol.* 2007;32(5):384-390.
31. Beer KT, Krause KB, Zuercher T, Stanga Z. Early percutaneous endoscopic gastrostomy insertion maintains nutritional state in patients with aerodigestive tract cancer. *Nutr Cancer.* 2005;52(1):29-34.
32. Nguyen NP, North D, Smith HJ, et al. Safety and effectiveness of prophylactic gastrostomy tubes for head and neck cancer patients undergoing chemoradiation. *Surg Oncol.* 2006;15(4):199-203.
33. Peerawong T, Phungrassami T, Pruegsanusak K, Sangthong R. Comparison of treatment compliance and nutritional outcomes among patients with nasopharyngeal carcinoma with and without percutaneous endoscopic gastrostomy during chemoradiation. *Asian Pac J Cancer Prev.* 2012;13(11):5805-5809.
34. Silander E, Nyman J, Bove M, Johansson L, Larsson S, Hammerlid E. Impact of prophylactic percutaneous endoscopic gastrostomy on malnutrition and quality of life in patients with head and neck cancer: a randomized study. *Head Neck.* 2012;34(1):1-9.
35. Nugent B, Parker MJ, McIntyre IA. Nasogastric tube feeding and percutaneous endoscopic gastrostomy tube feeding in patients with head and neck cancer. *J Hum Nutr Diet.* 2010;23(3):277-284.
36. Bensinger W, Schubert M, Ang KK, et al. NCCN Task Force Report. prevention and management of mucositis in cancer care. *J Natl Compr Canc Netw.* 2008;6 Suppl 1:S1-21; quiz S22-24.
37. Lee WT, Akst LM, Adelstein DJ, et al. Risk factors for hypopharyngeal/upper esophageal stricture formation after concurrent chemoradiation. *Head Neck.* 2006;28(9):808-812.

38. Chen AY, Frankowski R, Bishop-Leone J, et al. The development and validation of a dysphagia-specific quality-of-life questionnaire for patients with head and neck cancer: the M. D. Anderson dysphagia inventory. *Arch Otolaryngol Head Neck Surg.* 2001;127(7):870-876.
39. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care.* 1992;30(6):473-483.
40. EORTC. Glossary. n.d.; http://groups.eortc.be/qol/glossary. Accessed March 23, 2017.
41. Salas S, Baumstarck-Barrau K, Alfonsi M, et al. Impact of the prophylactic gastrostomy for unresectable squamous cell head and neck carcinomas treated with radio-chemotherapy on quality of life: Prospective randomized trial. *Radiother Oncol.* 2009;93(3):503-509.
42. Belafsky PC, Mouadeb DA, Rees CJ, et al. Validity and reliability of the Eating Assessment Tool (EAT-10). *Ann Otol Rhinol Laryngol.* 2008;117(12):919-924.
43. Terrell JE, Nanavati KA, Esclamado RM, Bishop JK, Bradford CR, Wolf GT. Head and neck cancer-specific quality of life: instrument validation. *Arch Otolaryngol Head Neck Surg.* 1997;123(10):1125-1132.
44. Shaw SM, Flowers H, O'Sullivan B, Hope A, Liu LW, Martino R. The effect of prophylactic percutaneous endoscopic gastrostomy (PEG) tube placement on swallowing and swallow-related outcomes in patients undergoing radiotherapy for head and neck cancer: a systematic review. *Dysphagia.* 2015;30(2):152-175.