

PROPHYLACTIC PERCUTANEOUS ENDOSCOPIC GASTRIC  
TUBES FOR HEAD AND  
NECK CANCER: ARE THEY WORTH THEIR WEIGHT?

by

Kathy D. Martin

A Major Paper Submitted in Partial Fulfillment

of the Requirements for the Degree of

Master of Science in Nursing

in

The School of Nursing

Rhode Island College

2021

## **Abstract**

It is estimated that 54,000 new cases of Head and Neck Cancer will be diagnosed in the United States in 2021 (Cancer Facts and Figures, 2021). Head and Neck cancers represent those that originate from sites which include the nasopharynx, oropharynx, oral cavity and hypo-pharynx. In advanced cases, treatment modalities are combined to include surgery, radiation and chemotherapy. Expected side effects of treatment can include mucositis, dysgeusia, dysphagia, odynophagia, nausea, vomiting and xerostomia. These toxicities can contribute to dehydration, weight loss and malnutrition. This paper examines the current state of evidence as it pertains to nutritional outcomes for Head and Neck cancer patients receiving concurrent chemotherapy and radiation when prophylactic percutaneous endoscopic gastrostomy (PEG) tubes versus reactive tubes were used. A retrospective chart review was conducted to examine the following research question: Does prophylactic percutaneous gastrostomy tube placement improve nutritional outcomes in patients receiving concurrent chemotherapy and radiation for Head and Neck Cancer patients when compared to those patients with reactive PEG tubes placed. The results of this study identified that despite timing of tube placement, patients in both groups lost weight and showed signs of worsening nutritional outcomes as evidenced by decreased body mass index, total protein, and albumin levels. Advanced practice nurses are in a unique position to develop innovative approaches to enhance nutrition in this patient population. Risk assessment tools, interdisciplinary collaboration and the development of a Head and Neck cancer pre-habilitation clinic may improve nutritional outcomes in the Head and Neck cancer patient receiving cancer treatment.

## **Acknowledgements**

This major paper is dedicated to my boss and friend Karen Messier. Karen has provided me the opportunity to pursue my academic goals. She has guided and mentored me which has been instrumental in my professional career and my academic success. She has been a role model to me and has made a huge impact on my professional career. Her support has been endless and I am truly fortunate to know her. Thank-you Karen.

## Table of Contents

Background/Statement of the Problem .....	1
Literature Review.....	4
Theoretical Framework .....	20
Method .....	24
Results .....	26
Summary and Conclusions .....	30
Recommendations and Implications for Advanced Nursing Practice .....	35
References .....	38

## Prophylactic Percutaneous Endoscopic Gastric Tubes for Head and Neck Cancer: Are They Worth Their Weight?

### **Background/Statement of the Problem**

Head and Neck cancer refers to malignancies that include the lip, oral cavity, pharynx, larynx and para nasal sinuses. In the United States, it is estimated that over 54,000 new cases of Head and Neck cancer will be diagnosed in 2021 (Cancer Facts and Figures, 2021) and greater than ninety percent of these patients are determined to have squamous cell pathology. Tobacco and alcohol have been identified as the most common causative agents which contribute to the development of this complex disease. Patients with Head and Neck cancer are also at an increased risk for secondary primary cancers of the Head and Neck as well as cancers of the aero digestive tract.

Treatment modalities for these cancers include surgery, chemotherapy, immunotherapy and radiation alone or in combination. Treatment is complicated and guided by site of disease, stage and pathological findings. A multitude of physical and functional impairments result from treatment related toxicities, disease itself and health behaviors. Nutritional complications are often present before treatment is initiated if the tumor is present in the oral cavity or throat (Lees, 1999). Pain, xerostomia, mucositis, and impaired swallow function negatively affects the patient's ability to maintain adequate nutrition and hydration. Malnutrition has been associated with hospitalizations, treatment interruptions, decreased treatment efficacy and diminished quality of life.

Percutaneous endoscopic gastrostomy (PEG) tubes for enteral feeding in patients with Head and Neck cancer, undergoing multimodal therapy, is often utilized to provide nutritional support in this at-risk population (Kasozi et al., 2018). Percutaneous

endoscopic gastric (PEG) tubes may be placed prophylactically in anticipation of patient needs prior to beginning treatment or reactively, during or after treatment, when the patient can no longer meet their nutritional requirements. Prophylactic PEG tube placement is a common practice despite the lack of research to support the procedure. Although PEG tube placement timing is discussed frequently in the literature, there is no consensus on whether prophylactic versus reactive placement for Head and Neck cancer patients is preferable (Locher et al., 2011).

The National Comprehensive Cancer Network (NCCN) does not recommend the placement of prophylactic PEG tubes in patients with very good performance status or for patients without significant pre-treatment weight loss, significant airway obstruction or severe dysphagia. However, the NCCN guidelines state that PEG tubes should be strongly considered if patients have severe weight loss prior to treatment. Percutaneous endoscopic gastric tubes should also be considered if patients experience ongoing dehydration, dysphagia, anorexia or pain which prohibits the ability to eat or drink. Aspiration risk, comorbidities, radiation field and impaired swallow function are other factors that influence prophylactic tube placement in the Head and Neck cancer patient.

The purpose of the Cochrane Systematic Review was to compare the effectiveness of different enteral feeding methods (PEG vs. nasogastric) used in the nutritional management of patients with Head and Neck cancer receiving radiotherapy or chemo radiotherapy using clinical outcomes, nutritional status, quality of life and rates of complications (Nugent et al., 2011). There was insufficient evidence to make a determination on the optimal method of enteral feeding. Timing of tube placements were not studied. Although PEG tube placement is considered relatively safe, complications

can occur. Infection, tube obstruction, migration and dislodgement are common occurrences. More serious complications such as peritonitis, abscess or fistula development are rare (Riera, 2002). Long term negative outcomes with PEG tube placements include tube dependency, loss of swallow function, and metastasis or seeding at the PEG tube site. Furthermore, some prophylactic PEG tubes placed may never be used. It is important to assess each patient and weigh the risks and benefits of prophylactic versus reactive tube placement while considering the potential effects on quality of life. Because the decision to place a PEG tube often relies on patient values and clinician preferences, additional research is needed to understand the use of prophylactic feeding tube placement in this compromised patient population and provide evidence based guidelines that can be followed by care teams. The purpose of this study is to describe nutritional outcomes in the Head and Neck cancer population receiving concurrent chemotherapy/radiation in those patients with prophylactic endoscopic gastric tubes versus those with reactive ones.

## **Literature Review**

A literature review was conducted using the Cumulative Index of Nursing and Allied Health Literature (CINAHL) and PUB MED databases. Keywords used included combinations of head and neck cancer, neoplasm, prophylactic PEG tube, PEG, nutrition and malnutrition. Literature was searched between 2011 and 2019. Study indexes included English language and full-text. Thirteen research articles retrieved and six were selected for literature review.

### **Percutaneous Endoscopic Gastric Tube Placement**

Most patients with Head and Neck cancer lose weight and are nutritionally compromised as a result of their disease, health behaviors and treatment-related toxicities making nutritional management important (NCCN, 2020). Feedings through percutaneous endoscopic gastric (PEG) tubes, whether placed prophylactically or reactively, has become a relatively common practice in this population (Langius et al., 2013). Although PEG tube placement is considered relatively safe and has a low rate of significant associated complications, it brings both risks and benefits. Currently, criteria for patient selection regarding PEG tube placements are not standardized and there are no published criteria or national guidelines on the optimum method of enteral tube feeding in this patient group (Nugent et al., 2010). More research is needed to inform and guide provider decisions in regards to PEG tube placement and timing.

A 2011 comprehensive review conducted by Locher et al., (2011) sought to describe the prevalence of PEG tube placement in patients undergoing treatment for Head and Neck cancer, describe factors associated with PEG tube placement at any time and to describe the reported and potential benefits and risks associated with PEG tube placement. Seven hundred thirty-nine articles were identified for review and the authors



identified multiple benefits for prophylactic feeding tube placement. Benefits included decreased weight loss, hospitalizations and treatment interruptions. For example, one study included in this review was a prospective randomized trial by Salas et al., (2009). Researchers assigned Head and Neck cancer patients without nutritional deficits (prior to chemotherapy/radiation) to either receive prophylactic PEG tube or no PEG tube placement. At six months, quality of life scores were higher in the prophylactic PEG placement arm. Despite a small sample size, these findings suggest that further studies on PEG placement timing and quality of life may be of clinical interest.

Locher et al., (2011) identified that although there is no consensus in the literature to determine when PEG placement is preferable, it is an important and relevant clinical issue. A gap in the literature exists as there is a lack of research looking into the use of prophylactic PEG tube placement and outcome evaluations in the Head and Neck cancer population. In conclusion, more research is needed to guide physician practice when determining if prophylactic PEG tube placement is warranted in the treatment of Head and Neck cancer patients.

A retrospective chart review by Sachdev et al., (2015) conducted a detailed analysis of clinical and dosimetric parameters to better define factors that could predict requirements for enteral feeding. Dosimetric parameters were defined as the mean dose, maximum dose and minimum dose of radiation to head and neck structures. The investigators goal was to determine high risk patients with an objective to maximize targeted nutritional guidance, early supplementation, swallowing therapy and more aggressive symptomatic support. The second aim was to determine if the research

derived in this study could support delays or prevent placement of a feeding tube thus preventing associated long term complications (Sachdev et al., 2015).

One hundred patients with locally advanced stage III and IV Head and Neck Squamous Cell Carcinoma were chronologically selected for study at Northwestern University Medical Center between 2005 and 2010. Patients were excluded if their cancer stage was I or II, if a different treatment modality was administered and/or if a feeding tube was placed prior to treatment. All patients were retrospectively analyzed after intensity-modulated radiation therapy was completed. Ninety seven percent of patients received a combination of radiation and chemotherapy. Patients were referred for a percutaneous endoscopic gastric tube if their weight loss exceeded ten percent due to reduced oral intake. Univariate and multivariate analyses using logistic regression were used to determine clinical and dosimetric factors associated with needing enteral feeding (Sachdev et al., 2015). Fischer's exact tests and Wilcoxon rank-sum tests were also used for analysis.

Thirty-three percent of patients required placement of an enteral feeding tube. The median time to tube placement was twenty five days from start of treatment. On univariate and multivariate analysis, age remained the only statistically significant factor ( $p=0.003$ ) regardless of other clinical features and all radiation planning parameters (Sachdev et al., 2015). In conclusion, age was found to be the most significant risk factor for needing a feeding tube in this patient population. This research supported maximizing early nutritional guidance, targeted supplementation, and symptomatic support in patients older than sixty receiving concurrent chemotherapy and radiation.

Interventions may result in a delay or omission of enteral feeding theoretically reducing long term feeding tube complications such as tube dependence (Sachdev et al., 2015).

### **Risks and Benefits of Percutaneous Endoscopic Gastric Tube Placement**

Percutaneous endoscopic tubes can provide both risks and benefits in the Head and Neck cancer patients receiving concurrent chemotherapy/radiation. Percutaneous endoscopic gastric tubes have been found to be effective in maintaining body weight and preventing malnutrition in this patient population. Percutaneous endoscopic gastric tubes may decrease morbidity related to poor nutritional intake during cancer treatment and possibly prevent dehydration and unplanned hospitalizations (Bishop & Reed, 2015). Having a PEG in place may also improve treatment compliance and quality of life (Madhoun et. al., 2016). Alternatively, infection, tube malfunction/migration are all common risks associated with tube placement. Still, other data suggests even greater risks. For example, enteral feeding can induce long term tube dependence and disuse of the swallowing mechanism which has been linked to complications such as prolonged dysphagia and esophageal constriction (Sachdev et. al., 2015). Although infections and tube malfunction are more commonly seen adverse events associated with PEG tube placement, rare cases of seeding at the PEG site have also been reported (Cady, 2007).

Harm has been associated with prophylactic PEG tube placement. Various complications such as infection, tube complications, alterations in elimination, sodium and glucose alterations, gastric bleeding, peritonitis, cellulitis, ileus, perforation, pain, gastric metastases and anesthesia risks were reported (Locher et al., 2011). Furthermore, researchers have found that PEG dependence is a leading clinical predictor of quality of

life in this patient population. Body image disturbance and loss of swallow function were also predicted to be a consequences of prophylactic PEG tube placement.

A systematic review completed by Orphanidou et al., (2011) studied prophylactic feeding tubes for patients with locally advanced Head and Neck cancer undergoing combined chemotherapy and radiotherapy. The goals of this systematic review were to determine risks and benefits of prophylactic feeding tubes in the curative Head and Neck cancer population receiving combination chemotherapy/radiation and to make recommendations on the use of prophylactic feeding tubes and nutrition.

Studies were eligible for inclusion in the systematic review if they were published as full reports or publicly available abstracts in 1985 or later. Participants in these eligible studies were adult patients with squamous cell carcinoma of the head and neck receiving combined chemotherapy/radiation with curative intent, either as primary therapy or after surgery, who had a PEG tube placed prior to treatment. Twenty-one eligible studies were found. None were randomized or quasi-randomized trials. Available studies were descriptive, four were prospective and 11 studies included a control group.

Orphanidou et al., (2011) reported available evidence as weak. Therefore, the researchers could not conclude the effectiveness of prophylactic feeding tubes in the Head and Neck cancer population receiving concurrent chemotherapy and radiation in curative intended patients. Insufficient quality and quantity of the evidence, difficulty with data analysis and patients lost to follow up were identified as study limitations. Furthermore, the body of evidence reviewed could not support an evidence-based clinical practice guideline, however, recommendations were made.

Recommendations include using a comprehensive interdisciplinary approach in the care of the Head and Neck cancer patient before, during and after treatment commences (Orphanidou et al., 2011). Investigators also point out that having a nutritional screening and referral process in place to identify patient at risk or experiencing malnutrition is essential. Validated nutritional screenings tools are also necessary. Assessment and interventions are meant to optimize nutrition and fluid intake, consider patients for tube placement, provide symptom management and preserve swallow function. Rehab referral to speech and language pathology can focus on resumption of oral intake in an effort to prevent tube feed dependence.

The purpose of Alshadwi et al., (2013), literature review was to assess the current literature supporting the benefit of nutritional support, patient assessment and nutritional repletion, and the advantages and disadvantages of various alimentation modalities. Articles were reviewed that focused on the etiology and assessment of malnutrition and current nutritional treatments for cancer-induced anorexia and cachexia. Two hundred forty-eight articles were found and a summative view was formulated.

Investigators concluded that nutritional interventions should be initiated before cancer treatment begins (Alshadwi et al., 2013). Researchers summarized that gastrostomy tube placement before radiation therapy has been shown to prevent weight loss, treatment interruption, and dehydration (Alshadwi et al., 2013) and percutaneous endoscopic gastric tubes are preferred for patients who require tube feeds for more than thirty days.

One prospective multi-institution study of one hundred seventy two patients was reviewed. It compared PEG tubes with gastric tubes. According to this literature review,

gastric tubes had increased mortality rates and major complications. However, PEG tube placements were noted to have cancer cell seeding at the insertion site and tumor implantation after endoscopic placement (Alshadwi et al., 2013). Although reported as an incidence of up to one percent, it is worth noting. In conclusion, researchers summarized that for high risk Head and Neck cancer patients who are unable to consume nutrition by mouth, enteral feeding must be provided.

### ***Dysphagia***

Difficulty swallowing can be a presenting symptom in the Head and Neck cancer patient or a side effect of cancer treatment. The tumor location itself can often cause nutritional complications before treatment begins, with 5–52% of patients reporting dysphagia before undergoing CRT or RT (Platteaux et al., 2010). Dysphagia and swallow function can be measured by clinical swallow assessments or by video fluoroscopic swallow studies. More common indicators of swallowing problems are weight loss, food intake or need for PEG tube intervention (Langmore et al., 2012).

A randomized controlled clinical trial by Silander et al., (2013) followed Head and Neck cancer patients for two years to measure their energy intake, choice of energy sources and to assess problems with dysphagia. Energy intake is defined as oral, nutritional supplements, enteral and parenteral sources of nutrition. The objective was to explore when and for how long the patients had dysphagia and lost weight due to insufficient intake, and if having a PEG tube in place made a difference.

The population was identified as patients with stages III or IV oral or pharyngeal cancer and included curative patients. One hundred thirty-four patients were included and randomized to either a prophylactic PEG for early enteral feeding or nutritional care

according to clinical practice. At seven time points, weight, dysphagia, and energy intake was measured (Silander et al., 2013). Quality of life was measured using the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-35) (Silander et al., 2013). Food calculation software program AIVO Diet 32 analyzed intake data. Group comparisons were done using the Mann-Whitney U-test, Fisher's Exact test and Mantel-Haenszel  $\chi^2$  for comparisons. Statistical analysis was performed using SAS software. Findings were reported using statistically significant data analysis.

Both groups lost weight in the first six months due to insufficient energy intake and used enteral nutrition as their main intake source. No significant differences between groups were found. Neither of the groups reached their recommended protein requirements until six months after the start of treatment. Although dysphagia was prevalent, after one year, dysphagia had decreased, and oral intake was the main energy source for both groups. Study results concluded that a prophylactic PEG did not significantly improve enteral intake (Silander et al., 2013).

### ***Nutrition***

Nutritional management is very important in head and neck cancer patients to improve outcomes and to minimize significant temporary or permanent treatment-related complications such as severe weight loss (NCCN, 2020). All patients should be evaluated for nutritional risks and receive nutrition counseling by a registered dietician and have appropriate interventions made. Percutaneous endoscopic gastric tubes may be recommended prior to or during treatment for patients at high risk for significant weight loss and malnutrition.

Langmore et al., (2012) looked at whether PEG tube use caused dysphagia in Head and Neck Cancer patients undergoing radiotherapy. The first aim was to determine whether patients who received a prophylactic PEG had better or worse swallowing function, diet scores, or weight change outcomes than patients who did not receive a prophylactic PEG tube. The second aim of the study was to compare whether patients who used a feeding tube for all, some, or none of their nutrition, fared differently in terms of their swallow ability, diet level and weight change. A retrospective chart review was conducted for all Head and Neck cancer patients treated with radiation at the Boston University Medical Center from January 2003 to September 2008. Fifty nine patients met all inclusion and exclusion criteria.

Analyses were conducted to determine the impact of PEG use on long-term diet level and weight change (Langmore et al., 2012). The investigators first evaluated whether patients who received prophylactic PEG had different outcomes (percentage of weight change and diet scores) than patients who did not receive a prophylactic PEG tube. Second, researchers assessed whether diet level at the end of radiation for all patients were associated with percentage of weight change and diet scores (Langmore et al., 2012). Data was collected at four capture points: the end of radiation and then again at 3, 6, and 12 months post placement. For each analysis, linear mixed-effects models were used to evaluate relationships. Kruskal-Wallis tests were used to analyze the association between diet status at baseline and diet scores at each time point. For the diet level analysis, Tukey-Kramer method was used to identify significant pairwise differences across the different baseline diet groups. Analysis was performed using SAS software.



Results showed no statistically significant differences of weight loss between the two groups at each time period (Langmore et al., 2012). In contrast to weight change results, the prophylactic PEG group had significantly worse diet outcomes than those who did not have prophylactic PEG tubes. However, those who did not receive prophylactic PEG's and those who maintained an oral, or a partial oral diet during radiation, had significantly better diet outcomes at all touch points post radiation (Langmore et al., 2012).

A 2017 study of early prophylactic feeding versus standard care in patients with Head and Neck cancer was completed by Brown et al. The purpose of the study was to evaluate the effectiveness of early prophylactic tube feeding compared to beginning tube feeding during treatment in patients undergoing prophylactic tube placement for patients with Head and Neck cancers. One hundred and seventy four patients were invited to participate in the study between September 2012 to June 2015 with 131 patients recruited then randomized. The primary outcome measure was the percentage of weight loss at three months post treatment (Brown et al., 2017). This was a single-center randomized controlled trial conducted in Queensland, Australia.

In the standard care arm, patients were started on enteral nutrition via their prophylactic gastrostomy by the dietitian when oral intake was less than 60 percent of estimated nutritional requirements for greater than ten days, if the patient was losing weight, if the patient required diet modification of texture, or if the patient experienced and increase in symptoms which impacted their nutritional status. The intervention group had enteral nutrition initiated via their prophylactic gastrostomy immediately following tube placement prior to the start of treatment. The prophylactic enteral nutrition was in

addition to their current oral intake and consisted of two 200ml bolus feedings daily (Brown et al., 2017). Data was analyzed and found no significant differences for weight loss, body composition or nutritional status. Researchers concluded that early intervention did not improve patient outcomes.

### ***P16 Tumor Suppressor Gene***

An important gene product that is involved in Head and Neck squamous cell carcinoma (HNSCC) pathogenesis is the p16<sup>INK4a</sup> (p16) protein, made by the *p16<sup>INK4a</sup> (CDKN2A)* gene. P16 is a cyclin-dependent kinase inhibitor that inhibits pRb phosphorylation and blocks cell cycle progression at the G1 to S check point (Lo et al., 1999). Loss of p16 expression by deletion, mutation, or hypermethylation is common in HNSCC (Worsham et al., 2006) and is associated with a worse prognosis (Namazie et al., 2009). P16 expression (p16 positive) has been correlated with improved outcomes in oral pharyngeal squamous cell carcinoma (Weinberger et al., 2004). The biologic significance of HPV positivity includes improved prognosis for patients with HPV positive HNSCC relative to HPV negative HNSCC (Ang et al., 2010) due in part to a better therapeutic response to chemo/radiotherapy (Fakhry, et al., 2008).

Verma et al., (2015) explored variables associated with poor prognosis in post-operative p16 positive oropharyngeal squamous cell carcinoma patients receiving adjuvant radiotherapy or chemo-radiotherapy in relation to feeding tube insertion timing. Ninety-seven patients were eligible for this retrospective chart review which took place between 1997 and 2009. Patients were grouped by those who had feeding tubes placed before radiation, patients who had feeding tubes placed during or after radiation, and patients who had no feeding tubes placed. These groups were analyzed for differential

tumor, patient, treatment, feeding tube characteristics as well as overall survival, disease free survival, and distant metastasis free survival (Verma et al., 2015).

The study population was identified as oropharyngeal cancer patients who were p16 positive, post-operative and adjuvant radiation candidates (Verma et al., 2015). After inclusion and exclusion criteria was met, ninety-seven patients were left for analysis. The primary endpoints were overall survival, disease free survival and distant metastases free survival. Kruskal-Wallis, Fisher Exact tests, Kaplan-Meier curves, Cox proportional Hazard Models and a backward stepwise model selection approach were performed for statistical analysis.

Results showed that pre-radiation feeding tube insertions were associated with higher tumor size and depth, tumor (T) but not node (N), overall stage, comorbidities, presence of chemotherapy, and less use of trans-oral laser microsurgery (Verma et al., 2015). Time from surgery to intensity modulated radiation therapy completion was statistically longer in patients receiving prophylactic PEG tubes. The feeding tubes were permanent in fifty-two percent of patient receiving prophylactic PEG tubes versus sixteen percent in the patient group who received PEG placement during or after treatment completion. Five year overall survival rates were highest in patients without feeding tubes (90%) and lowest in patients with feeding tubes placed prophylactically (50%). Five year disease free survival (DFS) was highest in the patients without feeding tubes (87.6%) and lowest for patients who had prophylactic PEG tubes placed (42.7%). Multivariate analysis showed that for both overall survival and disease free survival, feeding tube placement time and smoking history were statistically significant (Verma et al., 2015). This study concluded that early feeding tube insertion was correlated with a

poor prognosis. The presence of a feeding tube at the time of radiation consult can be used as an alternate marker in the p16 positive oropharyngeal squamous cell carcinoma patients to identify worse disease status alerting clinicians that this patient population is in a higher risk sub group.

### **PEG Tube Placement Timing**

For Head and Neck cancer patients undergoing treatment, there are two approaches to PEG tube feeding. Percutaneous endoscopic gastric tubes may be placed prophylactically in anticipation of patient needs prior to treatment, or reactively during treatment at a time when the patient is no longer able to meet their nutritional requirements (Bishop & Reed, 2015). Each method is associated with advantages and disadvantages. Advantages of prophylactic PEG insertion include decreases in weight loss, malnutrition and dehydration related hospitalizations and less treatment interruptions. Disadvantages to prophylactic tube placement include risks posed from surgery and non-use. Reactive tube placement, however, often interrupts treatment. There is no consensus on whether prophylactic versus reactive placement of PEG tubes is preferable in Head and Neck cancer patients (Locher et al., 2011).

A study by Kramer et al., (2014) looked to examine the outcomes of PEG tube placement timing (prophylactic vs. reactive) on weight loss, tube duration and disease control in patients with Head and Neck cancer. The design was a historical cohort study with seventy-four patients identified for inclusion. The population included those Head and Neck patient's having received platinum-based chemotherapy and radiation as a primary modality and those patients with primary surgical resection having received adjuvant chemotherapy and radiation. Percutaneous endoscopic gastric tube timing was

determined by patient and/or physician preference to be either prophylactic (before radiation began) or reactive (after radiation began) (Kramer et al., 2014).

Data was gathered, tabulated and analyzed to determine the effect of PEG tube placement timing on nutritional status-in which weight gain and survival were determined. A second goal was to assess the effect of placement timing on PEG tube dependence and length of usage (Kramer et al., 2014). Student independent t-tests compared continuous variables and chi square and Fisher's exact tests analyzed categorical variables (Kramer et al., 2014). A hierarchical multiple regression analysis controlled confounders. Kaplan-Meier analysis looked to determine if timing had an effect on PEG use. Software then analyzed this data.

Researchers found that patients with prophylactic tube placement and advanced tumor stage had longer PEG tube duration. Patients receiving reactive PEG tubes had them in place for fewer days than those placed prophylactically (227 versus 139 days,  $p<.01$ ). No difference in percentage weight loss was found at 2, 6 or 12 months. Kramer et al., (2014) concluded that patients who receive reactive PEG tube placement may have them in for shorter durations of time without an increase in weight loss or worse outcomes. Furthermore, the study showed that having a prophylactic PEG tube did not significantly improve enteral intake.

A retrospective study by Lang et al., (2020) evaluated the period of time between radiation initiation and PEG tube placement. A secondary aim was to evaluate the course of weight change following PEG placement (Lang et al., 2020). A retrospective chart review was conducted for Head and Neck cancer patients undergoing radiotherapy alone, or chemotherapy/radiation between January 2010 and August 2017 at the University

Hospital of Heidelberg. All patients with Head and Neck cancer who underwent PEG tube placement before or during radiation were included in this study. Patients receiving either concurrent chemotherapy or immunotherapy with radiation were also included. One hundred and eighty six patients were included in this study.

A retrospective analysis was conducted to determine initial weight and nutritional intake prior to radiation initiation and then followed throughout treatment until completion. Demographic characteristics, body weight, body mass index (BMI), oral intake and patient-reported dysphagia and treatment related toxicities were examined (Lang et al., 2020). Statistical analysis was conducted and results presented as means and percentages. Kaplan-Meier estimates were calculated and Univariate analysis was conducted using logistic regression analysis. For comparison between groups, chi-squared and Student t-tests were performed. IBM SPSS software analyzed the data.

This study demonstrated that patients with an initial low BMI ( $<18.5$  kg/m<sup>2</sup>) and patients with pre-existing tumor-associated dysphagia were significantly more likely to receive earlier PEG placement. Therefore, the examiners concluded that this subset of patients should be closely monitored for weight loss and decreased oral intake to determine the need for early PEG tube placement in an attempt to maintain adequate nutrition, improve treatment tolerance and reduce side effects (Lang et al., 2020). Twenty six patients had PEG tube insertion prior to radiation due to dysphagia and reluctant weight loss. The remaining one hundred and sixty patients had PEG tube's placed during radiation therapy.

In conclusion, this literature review found no consensus to support prophylactic PEG tube placement for improved nutritional outcomes within the Head and Neck cancer

population prior to radiation/chemotherapy. Findings identify both benefits and harm. Additional research is needed to further this study topic and nutritional outcomes need specifying. Additional study topics may include patient compliance, effects of alcohol intake and insurance coverage for enteral products as they apply to the outcomes for Head and Neck Cancer patients receiving concurrent chemotherapy and radiation.

Surgery, radiation and chemotherapy are effective modalities used in combination or alone, to treat malignancies of the head and neck. However, surgery for head and neck cancer can lead to facial disfigurement and functional disorders which can have a deep impact on social interactions and emotional wellbeing. Body image disturbance, anxiety and dysfunctional coping are psychological consequences which can occur from disfiguring cancer treatment and PEG tube placement. Using Lazarus and Folkman's Theory of Stress, Adaptation and Coping, the emotional reactions to stress and relevant coping factors of the Head and Neck cancer patient will be explored.

## **Theoretical Framework**

Lazarus and Folkman's Theory of Stress, Adaptation and Coping evolved from Richard Lazarus' 1966 Appraisal Theory of Stress which is borrowed from the social sciences. It is considered a stress theory which both explains and describes the psychological response to stress. It is intended to be a practice level theory with meta-theoretical roots (Lazarus & Folkman, 1984 p. xi). The concept of stress has historical underpinnings beginning in the 14<sup>th</sup> century to present time with theoretical works developed from various disciplines including biology, psychology, and social science backgrounds (Lazarus & Folkman, 1984, p.3).

The basis of Lazarus's original stress theory describes how a person copes psychologically with stressful situations. Stress is considered to be a multitude of variables and processes. The Theory of Stress, Adaptation and Coping, later developed by Lazarus and Folkman, used this approach as the basis for their theoretical framework. This framework aimed to examine the concept, specify antecedents, processes and outcomes relevant to the overarching concept of stress (Lazarus & Folkman 1984, p. 12). The theory's intent was for practical use by a multitude of disciplines including nursing.

According to Lazarus and Folkman, there are two major factors which precede stress. These factors are called antecedents. The first antecedent is the person-environment relationship which includes values, beliefs, and social support among other factors. The second antecedent is appraisal which is divided into three cognitive subtypes. Primary appraisals refer to the judgments made about an event or stressor and secondary appraisals evaluate how the individual responds to them. After additional information has been received, the third subtype, re-appraisal occurs.



Coping, per Lazarus, is the process in which threat is perceived and the appraisal is managed (McEwen & Wills 2011, p. 289). The coping process is two-fold. Problem-focused coping changes the individual's relationship with their environment whereas emotional coping changes the situations meaning. The theory can be critiqued for not applying categories that are mutually exclusive and fully exhaustive (Andersen & Jarden, 2012 p. 26). Re-appraisal and adaptation are results of successful coping. According to Lazarus and Folkman, adaptation affects health, psychological well-being and social functioning interdependently.

Coping theory is becoming increasingly relevant with the rising prevalence of chronic diseases including cancer. The theory is particularly useful to oncology nurses working with head and neck cancer patients who may not experience symptom relief. Educating patients about effective coping strategies could provide benefit and potentially improve quality of life for this patient population. Lazarus and Folkman's Theory of Stress, Adaptation and Coping has been utilized extensively in research as it relates to head and neck cancer patients and coping.

A study by Andersen and Jarden (2012) explored how head and neck cancer patient's coped with radiation and associated side effects. The qualitative study applied Lazarus and Folkman's theory of coping to the final stage of the study's research analysis. Nine patients were eligible for study but only five were participants. Semi-structured interviews were completed on this convenience sample.

General meaning was extrapolated from the interviews and themes were developed. The Theory of Stress, Adaptation and Coping was applied to the findings through further analysis to bring the main themes to a conceptual level (Andersen &

Jarden, 2012, p. 26). The research question, “Which coping strategies do the patients apply?” was answered in five main themes: Flying away, Recruiting help, Finding my place, Cognitive Control and Coping. All main themes identified coping strategies which were action oriented and improved quality of life when controlled by the patient.

Hulbert-Williams et al., (2012), also explored Lazarus and Folkman’s Theory of Stress, Adaptation and Coping in full. Their aim was to investigate the validity of the prescribed cognition-emotion relationships as outlined by Lazarus, using improved methodological and statistical approaches. Their sample included 160 cancer patients diagnosed with curative intent in which a diagnosis of psychosocial adjustment to cancer was made.

A repeat measures design was used. A self-reported questionnaire was completed soon after diagnosis, and at three and six month follow ups. Data on appraisals, core-relational themes and emotions were collected. Twelve core relational themes were identified and the three most common included self-blame, loss/helplessness and threat.

Data collected in the study supported the structure of Lazarus and Folkman’s theory and identified its sound empirical base. It was suggested by Hulbert-Williams et al. (2012) that larger scale research is needed using more complex statistical testing. The above research studies are examples that Lazarus and Folkman’s theory continues to be relevant to the nursing profession.

The above research examples support the testability and usefulness of Lazarus and Folkman’s Theory of Stress, Adaptation and Coping. The theory has been applied extensively in nursing research and has been shown useful in practice. Emotional wellbeing and effective coping is desired in all patient populations. Proper assessment of

stress and coping will provide holistic care and provide proper referral for psycho-social, supportive or palliative interventions. The application of stress theory to nursing practice is important. It provides a framework for nurses to assess the effects of stress and the coping processes that patients use. Identifying coping resources and support structures and educating patients about them may facilitate effective coping strategies. Research nurses, administrators, educators and bed-side nurses alike can incorporate Lazarus and Folkman's theory into practice. Next, a discussion of methodology.

## **Method**

### **Purpose**

The purpose of this proposed research was to describe nutritional outcomes of weight, body mass index, total protein and albumin and their relative change in the Head and Neck cancer population receiving concurrent chemotherapy/radiation in those patients with prophylactic percutaneous gastrostomy (PEG) tubes versus those without.

### **Design**

The proposed study is a descriptive retrospective chart review of all Head and Neck cancer patients treated with concurrent chemotherapy/radiation between January 1, 2000 and December 31, 2019 who are eligible. Patient's electronic medical record data meeting the criteria will be collected and analyzed.

### **Sample and Site**

A convenience sample of all adult patients diagnosed with Head and Neck cancer was obtained. Inclusion criteria for this study consisted of male and female patients with Head and Neck cancer who received chemotherapy and radiation at Sturdy Memorial Hospital and Brigham and Women's/Sturdy Memorial Radiation Oncology Center. All patients with Head and Neck cancer originating from sites which include the nasopharynx, oropharynx, oral cavity and hypopharynx, regardless of HPV status were included. This study also included adult patients who were treated with curative intent for stages I-IV cancer with squamous cell pathology and had PEG tubes placed either before (prophylactically) or during (reactively) chemotherapy/radiation administration. Exclusion criteria omitted patients with Stage 0 Head and Neck cancer, patients with recurrent or metastatic disease and those who did not complete chemotherapy/radiation.

Patients with histological Head and Neck cancer pathology types other than squamous cell and patients treated with palliative intent were excluded.

### **Procedures**

Institutional Review Board approval was obtained at Sturdy Memorial Hospital and Rhode Island College prior to the study. Other ethical considerations included research ethics and compliancy training (CITI program), HIPPA, data protection and patient confidentiality.

### **Measurement**

The data collection plan identified for this retrospective chart review included recording quantitative data found within the hospital's electronic medical record systems which included Meditech, Centricity, Intellidose, Intellidose TXM and/or Cerner. Data collection included the Eastern Cooperative Oncology Group performance status, ICD-10 code, tissue of origin, cancer stage, treatment protocol, PEG tube placement and timing of tube placement. Weight, body mass index, total protein and albumin levels were captured at baseline, prior to beginning cancer treatment and again upon completion of treatment. The data was collected and analyzed by one evaluator. A Microsoft Excel spread sheet was used for data organization, management, and storage.

### **Dissemination**

The proposed research will be disseminated as a major paper on the Rhode Island College Digital commons website. A poster presentation will be completed. The poster will also be presented at the Sturdy Memorial Hospital quality fair. Professional publication will be considered.

## Results

A total of 45 medical records were reviewed to obtain a cohort of 28 patients with Head and Neck Cancer who received concurrent chemotherapy and radiation and who had percutaneous endoscopic gastrostomy tubes placed. Group A included 27 subjects (n=27) who had a percutaneous endoscopic gastrostomy tube placed prior to the initiation of concurrent chemotherapy and radiation and Group B included 1 subject (n=1) who had a percutaneous endoscopic gastrostomy tube placed after chemotherapy and radiation was initiated. Data collected for both Group A and Group B included weight, body mass index, total protein, and albumin levels. The mean, median and range were computed for all categories of data collected and then compared between the two groups, then at two catch points, prior to and upon completion of concurrent chemotherapy and radiation. Table 1 summarizes the data collected in both Group A and Group B of patients prior to the start of concurrent chemotherapy and radiation. Table 2 summarizes the data in both groups of patients upon completion of concurrent chemotherapy and radiation.

Table 1 Comparison between Group A and Group B Pre-treatment

	<b>Weight</b>	<b>Body Mass Index</b>	<b>TP</b>	<b>Albumin</b>
<b>Group A</b>				
<b>Prophylactic PEG tube placement pre-treatment</b>				
Mean	179.5	27.2	7.2	3.4
Median	136.5	22.9	7.1	3.6
Range	96-235	15.4-49.9	5.8-8.1	2.5-4.2
<b>Group B</b>				
<b>Reactive PEG tube placement pre-treatment</b>				
Mean	248	34.6	6.2	4
Median				
Range				

*Table 2 Comparison between Group A and Group B Post-treatment*

	<b>Weight</b>	<b>Body Mass Index</b>	<b>TP</b>	<b>Albumin</b>
<b>Group A</b>				
<b>Prophylactic PEG tube placement post-treatment</b>				
Mean	169.6	25.7	6.8	3.3
Median	131.5	22.1	6.7	3.3
Range	93-340	14.8-47.4	5.7-8.6	2.4-4.3
<b>Group B</b>				
<b>Reactive PEG tube placement post-treatment</b>				
Mean	230	32.1	6.1	3.7
Median				
Range				

Table 1 compares the weight, body mass index, total protein, and albumin scores for two groups of patients, those who had PEG tubes placed prophylactically (Group A) and those who had PEG tubes placed reactively (Group B) prior to concurrent chemotherapy and radiation beginning. The weight range in Table 1 group A was between 89 and 358 pounds with the mean weight being 179.5 pounds. The mean body mass index for group A was 27.2 with the range being between 15.4 and 49.9. The mean total protein level was 7.2 with the range being between 6 and 9.1. The mean albumin level was 3.4 with the range being between 2.5 and 4. Group B contained only one patient (N=1). Therefore, the measurements of weight, body mass index, total protein and albumin reflect both the value and mean of this small data set of one patient. The patient's in Group A who had prophylactic PEG tubes placed prior to treatment weighed

less, had lower body mass indexes and albumin levels but had higher total protein levels when compared to the one patient in Group B.

Table 2 compares the weight, body mass index, total protein, and albumin scores for two groups of patients, those who had PEG tubes placed prophylactically (Group A) and those who had PEG tubes placed reactively (Group B) upon completion of concurrent chemotherapy and radiation. The weight range in Table 2 Group A was between 88 and 340 pounds with the mean weight being 169.6 pounds. The mean body mass index for Group A was 25.7 with the range being 14.8 and 47.4. The mean total protein level was 6.8 with the range being between 5.7 and 8.6. The range for albumin was 2.4 and 4.1 with the mean being 3.3. Group B consisted of one patient (N=1), therefore, the measurements of weight, body mass index, total protein, and albumin, reflect both the individual value and the mean of this one patient data set.

*Table 3 Comparison of average change percentages between Group A and Group B at end of treatment*

	<b>% Weight change</b>	<b>%BMI change</b>	<b>%Total Protein change</b>	<b>%Albumin change</b>
<b>Group A Prophylactic Peg Tubes</b>	-5.48%	-5.35%	-4.4	-1.88
<b>Group B Reactive Peg Tubes</b>	-7.26	-7.23	-1.61	-7.5

Table 3 compares the average percent change in weight, BMI, total protein, and albumin levels for patients with prophylactic PEG tubes (Group A) versus patients who had PEG tubes placed reactively (Group B) at the completion of treatment. Patients with



prophylactic PEG tubes (Group A) had a 5.48% average decrease in weight upon completion of treatment whereas the one patient with a reactive PEG tube (Group B), had a 7.26% decrease in weight. Average decrease in body mass index for patients upon treatment completion was 5.35% in Group A and 7.23% for the one patient in Group B. The average percentage of decrease in total protein levels were greater in Group B (-1.61%) than in Group A (-4.4 %). Albumin percentage decrease was also greater in Group B (-7.5% versus -1.88%). This data suggests a greater percentage of weight loss, decreased body mass index and albumin with less of a percentage decrease in total protein for patients with reactive PEG tubes placed when measured upon completion of concurrent chemotherapy/radiation treatment for Head and Neck Cancer.

### **Summary and Conclusions**

Approximately 35% to 60% of all patients with Head and Neck cancers are malnourished at the time of their diagnosis because of tumor burden and obstruction of intake or the anorexia and cachexia associated with their cancer (Alshadwi et al., 2013). When administration of intensive multimodal treatments is concurrent, severe, and often debilitating effects can compromise the patient's ability to maintain adequate nutrition and hydration (Orphanidou et al., 2011). Patients unable to maintain adequate oral intake have greater rates of weight loss, hospitalization and forced treatment breaks (Bishop & Reed, 2015). In Head and Neck cancer patients undergoing definitive chemotherapy and radiation, there are two approaches to percutaneous endoscopic gastric tube feeding-first to insert the tubes prior to treatment in anticipation of inadequate intake or second to insert a tube when patients are no longer able to meet their nutritional requirements (Bishop & Reed, 2015). There is no consensus on the optimal timing of PEG tube placement for patients undergoing therapy for Head and Neck cancer (Kramer et al., 2014).

The purpose of this study was to describe nutritional outcomes in the Head and Neck cancer population receiving concurrent chemotherapy and radiation in those patients with prophylactic endoscopic gastric tubes versus those with reactive tube placements. This study was guided by Lazarus and Folkman's Theory of Stress, Adaptation and Coping. A retrospective chart review was conducted, and forty-five charts were reviewed. Twenty-eight patients met the studies inclusion criteria and were subsequently separated into two groups. Group A was Head and Neck cancer patients with prophylactic endoscopic gastric tubes and Group B was Head and Neck cancer

patients with reactive prophylactic endoscopic gastric tubes. A data collection tool was developed based on literature and clinical experience which included patient weight, body mass index, total protein, and albumin levels. Weight, body mass index, total protein and albumin levels were captured at baseline, prior to beginning cancer treatment and again upon completion of treatment then compared between the two groups. The average change percentages of weight, body mass index, total protein and albumin were also compared between Group A and Group B. The final sample size of Group A included twenty-seven patients (n=27) and Group B had a final sample size of 1 patient (n=1).

Table 1 compared weight, body mass index, total protein and albumin levels between patients who had percutaneous endoscopic gastric tubes placed prophylactically and reactively prior to beginning concurrent chemotherapy and radiation. The mean weight, body mass index and albumin were lower in patients with prophylactic tubes (Group A) when compared to those with reactive tubes placed (Group B) prior to starting cancer treatment. Lower weight, body mass index and albumin levels in Group A indicates that those patients having feeding tubes placed prophylactically may have had significant pre-treatment weight loss, significant airway obstruction or severe dysphagia.

Table 2 compared the same data sets between patients who had percutaneous endoscopic gastric tubes placed prophylactically versus reactively at the completion of their cancer treatment. Again, average weight, body mass index and albumin levels were found to be lower in patients with prophylactic tubes (Group A) when compared to those with reactive tubes placed (Group B). This finding suggests that despite early

intervention with gastric tube placement, patients continued to lose weight and show signs of nutritional impairment upon completion of cancer treatment.

Table 3 compared weight loss, body mass index, total protein, and albumin percent changes in patients with prophylactic percutaneous gastric tubes (Group A) against those with reactive percutaneous gastric tubes (Group B) at the completion of treatment. Although both groups had decreases in weight, body mass index, total protein and albumin from their pre-treatment measures, patients with reactive tubes placed had a greater percentage of decline in all touch points except total protein. This data identified that prophylactic timing of tube placement did not prevent malnutrition and may not have a significant impact on patients overall nutritional outcomes.

This study had many limitations. This research was limited by a small sample size, in part, due to the low incidence of Head and Neck cancers which are relatively rare and account for less than five percent of all cancer cases diagnosed in the United States yearly. The study also took place in a community hospital setting, that lacks a designated Head and Neck cancer clinic, which may have further attributed to the small sample size. Other study limitations included the exclusion criteria. Nine patients had no percutaneous gastric tubes placed, one patient never used their tube for artificial nutrition, three patients did not complete their planned treatment protocols, and four medical records had incomplete data sets. Therefore, these seventeen patients were excluded from the study. The most significant limitation was the small sample size of patients with reactive percutaneous endoscopic gastric tubes (N=1).

It was noted in the patient's medical records that of the twenty-seven patients who had gastric tubes placed prophylactically, only nine patients started artificial nutrition prior to their cancer treatment. These nine patients had an average of twenty-six days of artificial nutrition prior to starting their cancer treatments. The remaining eighteen patients started using artificial nutrition on an average of nineteen days after concurrent chemotherapy and radiation started despite having had prophylactic percutaneous endoscopic gastric tubes placed prior to their treatment's initiation. Factors that may have influenced artificial nutrition start time were personal preference, insurance approval for artificial nutrition and gastric tube complications. Other factors for delaying artificial nutrition could not be discerned. The one patient with a reactive percutaneous endoscopic gastric tube had it placed eighteen days after treatment began and artificial nutrition was started the same day. It is important to recognize that timing of tube placement does not always coincide with timing of artificial nutrition commencing. There is currently no consensus in the literature to guide the timing of tube placement. Understanding the reasons that artificial nutrition is not started at time of tube placement could glean pertinent information, identify barriers to care and help guide practice.

In summary, this research study described the nutritional outcomes in Head and Neck cancer patients receiving concurrent chemotherapy and radiation who had percutaneous endoscopic gastric tubes placed either prophylactically or reactively. The study results identified that all patients, despite timing of tube placement, lost weight and showed signs of worsening nutritional status. This was evidenced by decreases in body mass index, total protein, and albumin in both patient groups. Identifying and eliminating factors associated with delayed enteral nutrition may hasten tube to feed time and

enhance patients overall nutritional status. More research is needed to assist clinicians in choosing high risk patients who will likely benefit from gastric tube placement and low risk patients who can forgo tube placement all together. Next, recommendations and implications for advanced nursing practice will be discussed.

### **Recommendations and Implications for Advanced Nursing Practice**

The advanced practice registered nurse (APRN) plays a vital role in accurately assessing the Head and Neck cancer patient prior to receiving concurrent chemotherapy and radiation to determine if prophylactic feeding tube placement is indicated. A risk assessment tool can be developed by the APRN using NCCN recommendations for prophylactic percutaneous endoscopic gastric tube placement. For those patients who do not require prophylactic PEG tube placement, the APRN can work collaboratively with the Registered Dietician (RD) to monitor patient's nutritional status using validated malnutrition screening tools. Tracking patient's weight, body mass index, total protein, and albumin changes in addition to malnutrition screenings can be useful to identify patients who may require reactive PEG tube placements. The APRN helps to coordinate care and has appropriate referral processes in place to expedite surgical placement of these tubes for patients with Head and Neck cancer.

Another innovative APRN strategy to enhance Head and Neck cancer patients overall nutritional status is in the development of a pre-habilitation clinic. An interdisciplinary approach to the care of the Head and Neck cancer patient would provide advanced practice nurse assessment and medical management prior to cancer treatment initiation. The multidisciplinary team of registered dieticians, physical therapists, speech and language pathologists, social workers, case managers and chaplains could facilitate patient centered care, improve patient satisfaction, and enhance overall outcomes. Patients and families would be educated early to prepare patients for cancer treatment and allow for early interventions to enhance patients overall nutritional status.

A follow up clinic led by advanced practice nurses can allow for more frequent outpatient visits and more intense symptom management once active treatment has started. Frequent follow up appointments for patients in active treatment may decrease emergency room visits, prevent admissions, enhance nutritional outcomes, and improve quality of life. The APRN plays a pivotal role in improving health care value and potentially decreasing the burden on the healthcare system by avoiding inappropriate use of healthcare resources by preventing unnecessary emergency room visits and avoiding admissions.

This study identified that despite the timing of percutaneous endoscopic gastric tube placement, all patients lost weight and had worse nutritional outcomes upon treatment completion. In addition, the timing of PEG tube placement did not always coincide with artificial nutrition initiation. Sixty-seven percent of patients with prophylactic PEG tubes began using artificial nutrition an average of nineteen days after the cancer treatment began. Additional research is needed to determine the factors associated with delays in time to tube feed so that barriers to early nutritional support can be identified and mitigated. Excellent nutrition management is essential to improve the Head and Neck cancer patient's overall wellbeing and minimize weight loss.

In conclusion, there is no consensus in the literature to guide appropriate timing for percutaneous endoscopic tube placement in the Head and Neck cancer patient treated with combination chemotherapy and radiation. Patient and provider preference continues to be the mainstay for decision making. Randomized studies are needed in multicenter, large cancer intensive sites with a high volume of Head and Neck cancer patients to determine best timing of tube placement with the desired goal of achieving optimal



nutritional outcomes. APRN's must participate in and utilize current research to change the standard of care in this complex patient population. Evidence-based practice and a multi-disciplinary innovative approach may improve patient care and enhance nutritional outcomes in this vulnerable patient population.

## References

- Alshadwi, A., Nadershah, M., Carlson, E. R., Young, L. S., Burke, P. A., & Daley, B. J. (2013). Nutritional considerations for Head and Neck Cancer Patients: A review of the literature. *Journal of oral and maxillofacial surgery: Official Journal of the American Association of Oral and Maxillofacial Surgeons*, 71(11), 1853–1860. <https://doi.org/10.1016/j.joms.2013.04.028>.
- American Cancer Society. (2021) Cancer Facts & Figures 2021. *American Cancer Society*. <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2021/cancer-facts-and-figures-2021.pdf>
- Andersen, K., & Jarden, M. (2012). Coping with radiotherapy for Head and Neck Squamous Cell Carcinoma: A Qualitative Exploration. *Nursing Science*, 104(32), 25-29. <https://doi.org/10.1177/010740831203200206>.
- Ang, K., Harris, J., Wheeler, R., Weber, R., Rosenthal, R., Nguyen-Tân, P., Westra, W., Chung, C., Jordan, R., Lu, C., Kim, H., Axelrod, R., Silverman, C., Redmond, K., & Gillison, M. (2010). Human Papilloma and survival of patients with Oropharyngeal Cancer. *The New England Journal of Medicine*, 363, 24-25. DOI: 10.1056/NEJMoa0912217
- Bishop, S., & Reed, W.M. (2015). The provision of Enteral Nutritional support during definitive chemoradiation in Head and Neck Cancer Patients. *Journal of Medical Radiation Sciences*, Dec;62(4): 267-276.

- Brown, T. E., Banks, M. D., Hughes, B., Lin, C. Y., Kenny, L. M., & Bauer, J. D. (2017). Randomized controlled trial of early prophylactic feeding vs standard care in patients with Head and Neck Cancer. *British Journal of Cancer*, *117*(1), 15–24. <https://doi.org/10.1038/bjc.2017.138>.
- Cady, J. (2007). Nutritional support during radiotherapy for Head and Neck Cancer: The role of prophylactic feeding tube placement. *Clinical Journal of Oncology Nursing*, *116*, 875-880.
- Cooper, J.S., Fu, K., Marks J., & Silverman, S. (1995). Late effects of radiation therapy in the Head and Neck region. *International Journal of Radiation*, *31* (5), 1141-1164.
- Dropkin, M. (1999). Body image and quality of life after Head and Neck cancer surgery. *Cancer Practice*, *7*(6), 309-313. DOI: 10.1046/j.1523-5394.1999.76006.x.
- Fakhry, C., Westra, W., Li, S., Cmelak, A., Ridge, J., Pinto, H., Forastiere, A., & Gillison, M., (2008). Improved survival of Patients with Human Papillomavirus–Positive Head and Neck Squamous Cell Carcinoma in a prospective clinical trial. *Journal of the National Cancer Institute*, *100*(4), 20, 261–269. [doi.org/10.1093/jnci/djn011](https://doi.org/10.1093/jnci/djn011).
- Hulbert-Williams, N.J., Morrison, V., Wilkinson, C., & Neal, R.D. (2012). Investigating the cognitive precursors of emotional response to cancer stress: Re-testing Lazarus’s transactional model. *British Journal of Health Psychology*, *18*, 97-121. DOI:10.1111/j.2044-8287.2012.02082.x
- Kasozi, R., Choudhary, A., Andrus, K., Wong, R., Randall, R., Orovets, C., Bali, G., Karapetyan, L., Gibson, M., Fu, P., & Sloan, J. (2018). Use of percutaneous

endoscopic gastrostomy tube feeding support in Head and Neck Cancer.

*International Journal of Radiation Oncology*, 100 (5), 1401-1402.

<https://doi.org/10.1016/j.ijrobp.2017.12.243>.

Kramer,S., Newcomb,M., Hessler,J., & Siddiqui, F. (2014). Prophylactic versus reactive peg tube placement in Head and Neck Cancer. *Otolaryngology-Head and Neck Surgery Foundation*, 150 (3), 407-412. DOI: 10.1177/0194599813517081.

Lang, K., ElShafie, R. A., Akbaba, S., Koschny, R., Bougatf, N., Bernhardt, D., Welte, S. E., Adeberg, S., Häfner, M., Kargus, S., Plinkert, P. K., Debus, J., & Rieken, S. (2020). Percutaneous endoscopic gastrostomy tube placement in Patients with Head and Neck Cancer treated with radiotherapy. *Cancer Management and Research*, 12, 127–136. <https://doi.org/10.2147/CMAR.S218432>.

Langmore,S., Krisciunas,G., Vasques Miloro,K., Evans,S., & Cheng,D. (2012). Does peg use cause dysphagia in Head and Neck Cancer Patients? *Dysphagia*, 27 (2),1-9. DOI: 10.1007/s00455-011-9360-2.

Languis, J., Van Dijk A.M., Doornaert, P., Kruiuzenga, H.M., Langendijk, J.A., Leemans, C.R., Weijs, P.J. & Verdonck-de Leeuw, I.M., (2013). More than 10% weight loss in Head and Neck Cancer patients during radiotherapy is independently associated with deterioration in quality of life. *Nutrition Cancer*, 65(1), 76-83. DOI: 10.1080/01635581.2013.741749.

Lazarus, R., & Folkman, S. (1984). Stress, appraisal, and coping. *New York, NY: Springer Publishing Company, Inc.*

Lees, J. (1999). Incidence of weight loss in Head and Neck Cancer patients on commencing radiotherapy treatment at a regional oncology center. *European*

*Journal of Cancer Care. Sep;8(3):133-136. DOI: 10.1046/j.1365-2354.1999.00156.x.*

Lo, Y., Wong, I., Zhang, J., Tein, M., Ng, M., & Hiem, M. (1999). Quantitative analysis of aberrant *p16* methylation using real-time quantitative methylation-specific polymerase chain reaction. *Cancer Research*, Aug;59(16) 3899-3903.

Locher, J. L., Bonner, J.A., Carroll, W.R., Caudell, J.J., Keith, J.N., Kilgore, M.L., Ritchie, C.S., Roth, D.L., Tajeu, G.S., & Allison, J.J. (2011). Prophylactic percutaneous endoscopic gastrostomy tube placement in treatment of Head and Neck Cancer: A Comprehensive review and call for evidence-based medicine. *Journal of Parenteral and Enteral Nutrition*, 35, 365-37. DOI:10.1177/0148607110377097.

Locher, J.L., Bonner, J.A., Carroll, W.R., Caudell, J., Kilgore, M., Ritchie, C., Roth, D.L., Tajeu, G., Yuan, Y., & Allison, J. (2012) Gastrostomy tube placement and use in patients with Head and Neck Cancer. *Head and Neck*. 34:422–428.

Madhoun, M., Blankenship, M., Blankenship, D., Krempl, G., & Tierney, W.M. (2011). Prophylactic peg placement in Head and Neck Cancer: How many feeding tubes are unused (and unnecessary)? *World Journal of Gastroenterology*. 17(8):1004-1008. DOI: 10.3748/wjp.v17.i8/1004.

McEwen, M., & Wills, E. M. (2011). Theoretical basis for Nursing. Philadelphia, PA: *Lippincott Williams & Wilkins*.

Namazie, A., Alavi, S., Olopade, O., Pauletti, G., Aghamohammadi, N., Aghamohammadi, M., Gornbein, J., Calcettera, T., Slamon, D., Wang, M., & Srivatsan, E. (2009). Cyclin D1 amplification and p16(MTS1/CDK4I) deletion

correlate with poor prognosis in Head and Neck Tumors. *The Laryngoscope*. 112(3): 472-481. DOI:10.1097/00005537-200203000-00013.

National Comprehensive Cancer Network (2021). *NCCN Clinical Practice Guidelines in Oncology/Head and Neck Cancers*.

[https://www.nccn.org/professionals/physician\\_gls/PDF/head-and-neck.pdf](https://www.nccn.org/professionals/physician_gls/PDF/head-and-neck.pdf).

Nugent, B., Lewis, S., & O'Sullivan, J.M. (2013). Enteral feeding methods for nutritional management in patients with Head and Neck Cancers being treated with radiotherapy and/or chemotherapy. *Cochrane Database of Systematic Reviews*, Issue 1. Art. No.: CD007904. DOI: 10.1002/14651858.CD007904.pub3

Orphanidou, C., Biggs, K., Johnston, M.E., Wright, J.R., Bowman, A., Hotte, S.J., Esau, E., Myers, C., Lafleur, M., Sheehan, B., & Griffin, M.A. (2011). Prophylactic feeding tubes for patients with locally advanced Head-and-Neck Cancer undergoing combined chemotherapy and radiotherapy-systematic review and recommendations for clinical practice. *Current Oncology*, 18 (4), 191-201.

Platteaux N., Dirix, P., Dejaeger, E., & Nuyts, S. (2010) Dysphagia in Head and Neck Cancer Patients treated with chemoradiotherapy. *Dysphagia*, 25(2):139–152  
DOI:10.1007/s00455-009-9247-7.

Riera L., Sandiumenge A., Calvo C., Bordas, J.M., Alobid, I., & Llach, J., Bernal, M. (2002) Percutaneous endoscopic gastrostomy in Head and Neck Cancer Patients. *ORL* 64:32-34. DOI: 10.1159/000049265.

Sachdev, S., Refaat, T., Bacchus, I., Sathiaseelan, V., & Mittal, B. (2015). Age most significant predictor of requiring enteral feeding in Head-and-Neck Cancer Patients. *Radiation Oncology*, 10:93. DOI: 10.1186/s13014-015-0408-6.

- Salas, S., Baumstarck-Barrau K, Alfonsi, Digue, L., Bagarry D., Feham N., Bensadoun, R.J., Pignon T., Loundon, A., Deville, J.L., Zanaret, M., Favre, R., Duffaud,F., & Auguier, P. (2009). Impact of the prophylactic gastrostomy for unresectable Squamous Cell Head and Neck Carcinomas treated with radio-chemotherapy on quality of life: Prospective randomized trial. *Radiotherapy Oncology*. 93:503-509.
- Scolapio, J.S., Spangler, P.R., Romano, M.M., McLaughlin, M.P., & Salassa, J.R. (2001). Prophylactic placement of gastrostomy feeding tubes before radiotherapy in patients with Head and Neck Cancer: Is it worth-while? *Journal of Clinical Gastroenterology*, 33:215-217.
- Silander,E., Jacobsson,I., Berteus-Forslund, H., & Hammerlid, E. (2013). Energy intake and sources of nutritional support in patients with Head and Neck Cancer-a randomized longitudinal study. *European Journal of Clinical Nutrition*,67, 47-52.
- Siegel R, Miller, K., & Jemal A. (2015) A Cancer Journal for Clinicians. *American Cancer Society Journals, Jan-Feb*;65(1):5-29. DOI: 10.3322/caac.21254.
- Thomsen, T.G., Rydahl-Hansen,S., & Wagner,L. (2010). A review of potential factors relevant to coping in patients with advanced cancer. *Journal of Clinical Nursing*, 19, 3410-3426. DOI:10.1111/j.1365-2702.2009.03154.x.
- Verma,V., Liu,J., Eschen,L., Danieleley,J. Spencer,C., & Lewis,J. (2015). Pre-radiotherapy feeding tube identified a poor prognostic subset of postoperative p16 positive Oropharyngeal Carcinoma Patients. *Radiation Oncology*, 10 (8), 1-9. DOI: 10.1186/s13014-0314-3.

- Weinberger, P., Yu, Z., Haffty, B., Kowalski, D., Harigopal, M., Sasaki, C., Rimm, D., & Psyrri, A. (2004). Prognostic significance of p16 protein levels in Oropharyngeal Squamous Cell Cancer. *Clinical Cancer Research*, 10(17) 5684-5691; DOI: 10.1158/1078-0432.CCR-04-0448.
- Worsham M.J., Chen, K.M., Meduri V., Nygren, A., Erramim, Schouten, J., & Benniger, M. Epigenetic events of disease progression in Head and Neck Squamous Cell Carcinoma. *Arch Otolaryngol Head Neck Surgery*, 2006;132(6):668–677. DOI:10.1001/archotol.132.6.668.