Identifying Patterns of Fatigue in Head and Neck Cancer Patients Post-Curative Intent Treatment

Nicole Elizabeth Kahler, MSN, RN, OCN, AGACNP-BC

Gastonia, North Carolina

Bachelors of Science in Nursing, University of North Carolina – Chapel Hill, 2006

Masters of Science in Nursing, University of Virginia, 2016

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Regina DeGennaro, DNP, CNS, RN, AOCN, CNL

Clareen Wiencek, PhD, RN, CNP, ACHPN

Leslie Blackhall, MD

Abstract

Background: Cancer-related fatigue (CRF) is a frequent and often debilitating symptom experienced by head and neck cancer (HNC) patients from diagnosis to survivorship. The trajectory and treatment of CRF is poorly understood and is inconsistently assessed by providers. Patient-reported outcomes (PRO) are an effective way to assess the progression of this symptom through the illness trajectory. *Objectives:* The aim of this project was to explore and describe the characteristics of HNC patients who completed their cancer treatment with curative-intent and to improve understanding of how their reported experience of fatigue changes over time. *Methods:* A retrospective, descriptive study was performed on medical records of HNC patients upon completion of curative-intent cancer treatment who were receiving palliative symptom management. Eight subjects met inclusion criteria and completed a total of 23 PRO surveys. Evidence to specifically identify PRO regarding CRF in the HNC patient population is limited, so this initial medical record review with PRO was an innovative approach to understanding the patient experience. *Findings:* No discernible pattern related to post-treatment fatigue was identified given the small sample size; however, several themes were revealed, including limited documentation of fatigue discussions, symptom clusters, patient- versus provider-reported Eastern Cooperative Oncology Group (ECOG) scores, and disparities in scores between health domains of interest. Future research on CRF for HNC patients receiving treatment with curative-intent and palliative symptom management could utilize a prospective design with specific time points for survey completion. Additionally, studies could adopt one standard measure of CRF, such as the PROMIS® fatigue scale.

Key Terms: Head and neck cancer, palliative care, cancer-related fatigue, patient-reported outcomes

Table of Contents

Identifying Patterns of Fatigue in Head and Neck Cancer Patients

Post-Curative Intent Treatment

Section I - Introduction

Cancer-related fatigue (CRF) is one of the most common side effects experienced by cancer survivors (Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, & Morrow, 2007). It is estimated that between 25-99% of cancer patients experience CRF at some point throughout treatment for their cancer, and roughly one-third of cancer patients continue to experience fatigue years after treatment has been completed (Servaes, Verhagen, & Bleijenberg, 2002). The National Comprehensive Cancer Network's Guidelines for Supportive Care defines CRF as a subjective feeling of physical, emotional or mental exhaustion related to cancer or its treatment that is persistent and out of proportion to the level of activity which restricts the person's normal functioning (National Comprehensive Cancer Network [NCCN], 2015). In comparison to the fatigue that non-cancer patients experience, CRF typically lasts longer, is more severe, and is not alleviated by rest (American Society of Clinical Oncologists, 2014). CRF can be experienced at any point from the time of diagnosis, including during and after treatment, and has been found to increase as the disease progresses (Stone & Minton, 2008), yet the mechanisms underlying CRF are not fully understood (Richardson, Ream, & Wilson-Barnett, 1998). NCCN Clinical Practice Guidelines recommend that all cancer patients be screened for fatigue at regular intervals and that treatment should begin promptly if warranted (2015).

As of January 1, 2014, the number of cancer survivors in America was estimated to be 14.5 million (American Cancer Society [ACS], 2016), and by 2022, the population of cancer survivors is expected to approach 18 million (ACS, 2012). As the number of survivors continues to rise, it becomes essential for oncology teams to understand who is most at risk for developing

fatigue, when during their cancer trajectory fatigue is most likely to cause the biggest issue, and what are the most efficacious ways to care for these patients and their symptoms. Earlier identification of those at risk for CRF and determining ways to manage their CRF can positively impact a variety of outcomes for patients, including physical functioning, symptom distress, and health-related quality of life (QOL) (Mitchell, Beck, Hood, Moore, & Tanner, 2007). While CRF has detrimental effects on physical, social, cognitive, and occupational functioning, and causes emotional and spiritual distress for patients and their families, it remains under-recognized and undertreated (Mitchell, et al., 2014).

The term "head and neck cancers" (HNC) is often used to describe multiple specific diagnoses located within close anatomical proximity to one another, such as cancers of the lip and oral cavity (most common), oropharynx, hypopharynx, larynx, salivary gland, and others (NCCN Clinical Practice Guidelines, 2015). HNC patients have some of the highest rates of fatigue among cancer patients in general (Hickok, et al., 2005), and fatigue has been reported as the symptom with the greatest burden by HNC patients even prior to receiving radiation therapy (Gunn, et al., 2013). HNC patients not only experience high symptom burden from the disease itself but also from the treatment. If a patient is being treated with curative-intent, the treatment regimen typically includes either adjuvant or neoadjuvant platinum-based chemotherapy, surgical resection, and daily radiation for up to seven concurrent weeks; these combinations of therapy can be very toxic and often lead to treatment delays as well as a myriad of persistent side effects even after treatment has been completed. (P. W. Read, personal communication, June 9, 2016). The location of the surgery and radiation is particularly problematic in HNC treatment as these modalities can cause severe issues with swallowing, nutrition and body image.

The Levine Conservation Model provided the theoretical framework for this project. This model's centerpiece is the concept of patient adaptation, which is essential for one to maintain their personal integrity and totality. If one is not able to adapt and conserve, an imbalance is imposed upon their totality; whereas if one is able to adapt and conserve, totality is maintained. Four domains are discussed in this model: conservation of energy, conservation of structural integrity, conservation of personal integrity, and conservation of social integrity (Levine, 1973). This framework is appropriate for this study because cancer and its treatment can cause great shifts in personal wellness. Medical center staff are perfectly poised to assist in the adaptation and successful conservation of energy and other domains related to CRF as demonstrated by this model.

The purpose of this project was to understand how CRF levels in the post-treatment period change for HNC patients receiving treatment with curative-intent and palliative symptom management. This study attempted to answer the following research question: How are the characteristics of head and neck cancer patients related to their level of fatigue post-treatment?

Section II - Review of the Literature

Fatigue is a substantial issue for the majority of cancer patients, and those with HNC are no different. Understanding what is currently known regarding the patterns and predictors of fatigue for HNC patients with curative-intent and palliative symptom management is essential so that this project may further contribute to that base knowledge. This literature review sought to determine the answer to the following question: In adult patients with HNC who are being treated with curative-intent, what is known about the patterns or predictors of fatigue before, during and after treatment? CRF is generally perceived as being the most significant during treatment with improvements noted once treatment has been completed; however, the feelings of

CRF can take months or even years to improve and some patients may never return to their pre-treatment levels of activity. While the overall burden of fatigue is abundant in the literature in cancer patients (Mitchell, et al., 2014), there is a gap in the evidence related to HNC patients and symptom management of fatigue for those being treated with curative-intent.

The electronic databases MEDLINE, CINAHL, Web of Science, and the Cochrane Library were systematically reviewed for possible relevant articles relating to the patterns or predictors of CRF in the HNC population. The inclusion criteria for this systematic review were as follows: 1) any study published within the last 10 years, and 2) any study assessing the patterns or predictors of fatigue before, during, or after treatment. Exclusion criteria were as follows: 1) any article for which the University of Virginia did not have full text access, 2) articles for which an English translation was not available, 3) studies focusing on the pediatric or adolescent population, 4) any study not specifically focusing on the fatigue patterns related to HNC, 5) any study assessing QOL where fatigue was not a specific outcome measure, and 6) any study not utilizing patient-reported outcome measures. No limiters were used with any of the searches. Each database was searched using the keywords “fatigue,” “predictor(s) or “pattern(s),” and “head and neck neoplasms” or “head and neck cancer.” MEDLINE yielded 15 citations, Web of Science yielded two citations, and both CINAHL and The Cochrane Library produced no citations. Removal of duplicate entries reduced the number to 14 articles, and after further title, abstract, and article review, the number of articles included in this systematic review was reduced to five. Ancestry searches yielded an additional two studies, bringing the total number of articles for inclusion in this systematic review to seven.

Results

Of the seven included studies, five examined fatigue in HNC patients before, during and after treatment with either radiotherapy or chemo-radiotherapy (Jereczek-Fossa, et al., 2007; Rogers, et al., 2008; Molassiotis & Rogers, 2012; Spratt, et al., 2012; Rosenthal, et al., 2014), and two studies assessed fatigue only prior to treatment initiation (Gunn, et al., 2013; Hanna, et al., 2015). Additionally, four of the studies included patients who were being treated with both curative- or palliative-intent (Jereczek-Fossa, et al., 2007; Rogers et al., 2008; Molassiotis & Rogers, 2012; Hanna, et al., 2015), whereas three studies solely included patients being treated with curative-intent (Spratt, et al., 2012; Gunn, et al., 2013; Rosenthal, et al., 2014). The duration of the studies varied from a one-time survey up to 30 months post-treatment completion (see Table 1). The limited available evidence suggests additional studies would benefit this patient population.

Jereczek-Fossa et al. (2007) prospectively analyzed 117 HNC patients being treated with radiation or chemo-radiation therapy to understand the fatigue level of these patients as they progressed through their treatment, as well as predictors of their fatigue. The majority of participants had squamous cell histology (76%), were male (79.5%), and had locally advanced (T3-4 or node-positive) disease (84%). Fatigue was measured by the Multidimensional Fatigue Inventory (MFI-20) questionnaire at baseline, weekly while receiving radiation, and at 10 and 40 days after completion of radiation. The average fatigue level increased significantly during the therapy (means±SD at baseline: 25.8±1.7), with a peak at Week 6 (33.7±1.8, $p < 0.0001$); fatigue scores began to decrease once treatment was complete. Additionally, the authors determined there were predictive factors for both on- and post-treatment levels of fatigue. On-treatment predictive factors included the presence of fatigue prior to beginning treatment ($p < 0.0001$), the use of chemotherapy as an additive to the radiation regimen ($p = 0.035$), patients who required

cortisone during radiation therapy ($p = 0.005$) and thyroid disease ($p = 0.032$). Post-treatment predictive factors of fatigue included the use of chemotherapy as an additive to the radiation therapy ($p < 0.001$) and those who required cortisone during radiation therapy ($p < 0.005$).

Rogers et al. (2008) performed a cross-sectional one-time survey utilizing convenience sampling of 58 HNC patients treated in the outpatient setting to determine significant correlates of fatigue, sleep dysfunction, and cognitive dysfunction among HNC patients. Subjects were surveyed on many items including fatigue, sleep quality, cognitive function, depression, and physical activity; fatigue was measured by the Fatigue Symptom Inventory. The majority of the subjects had stage IV (60.3%) squamous cell carcinoma (93.1%); the pharynx was the most common site of primary disease (51.7%). The authors used bivariate analyses to determine that greater than average fatigue levels were statistically associated with multiple factors, including younger age ($r = -.39$, $p = 0.002$), history of prior radiation therapy ($r = .44$, $p = 0.001$), depression ($r = .64$, $p = .000$), and a more recent cancer diagnosis ($r = .29$, $p = 0.03$). Independent associations with higher fatigue, assessed by multiple linear regression analyses, included younger age ($\beta = -.022$), history of prior radiation ($\beta = 0.23$), depression ($\beta = 0.68$), and more current diagnosis of their cancer ($\beta = -0.25$). Rogers et al. concluded that those with HNC who are younger are more likely to experience greater amounts of fatigue than their older counterparts (2008).

Molassiotis and Rogers (2012) performed and analyzed qualitative quarterly interviews with 16 HNC patients over 12 months to appreciate the symptom experiences of these patients during and after treatment. Most of the participants were male (87.5%) and had oral or oropharyngeal cancer (87.5%) with a mean age of 61. The participants were equally split between receiving treatment with curative- versus palliative-intent. The theme of fatigue or

"tiredness" was expressed by most participants throughout the study. Rest or sleep did not relieve the fatigue that these patients experienced. For most participants, the fatigue continued for the duration of the study (12 months). The duration of this fatigue affected participants' abilities to return to activities they did prior to starting treatment, such as working.

Spratt et al. (2012) analyzed 87 patients who were undergoing treatment for oropharyngeal cancer at Memorial Sloan Kettering Cancer Center (MSKCC) to gain knowledge of the clinical correlates, patterns of time, and the severity of CRF in patients with HNC; all patients were being treated with curative-intent with either radiation or chemo-radiation (94%). CRF was measured by a form created by MSKCC; assessments were performed at baseline (time of consultation), during weekly treatment visits, then at multiple follow up appointments for up to 30 months post-radiation (median follow up = 14 months). The difference in mean baseline fatigue scores and those upon treatment completion were significantly different (0.76 & 6.89, respectively, $p = <.0001$). The highest rates of fatigue were seen at 1-2 weeks after completion of radiation (mean fatigue score 5.39, SD 2.73). None of the studied predictors of CRF were significant in this population, although the presence of pain was close (mean±SD of those with pain a) baseline: 0.93±1.44; b) difference of maximum post-treatment scores minus baseline: 6.63±2.61, $p = 0.06$). The authors determined that half of their subjects continued to report clinically significant levels of CRF 2 years post-treatment.

Gunn et al. (2013) analyzed 270 patients prior to beginning radiation or chemo-radiation using a prospective questionnaire model to assess the symptom patterns of those with HNC. Those with metastatic disease or those who received prior radiation therapy were excluded, although previous chemotherapy or surgery was allowed. Symptoms were assessed using the MD Anderson Symptom Inventory-Head and Neck Module (MDASI-HN) at baseline prior to

beginning treatment. The majority of the participants had squamous cell histology (77%); participants were placed into either low- (67.4%) or high-symptom burden (32.6%) groups. Fatigue was noted to be the most likely symptom to be rated as moderate-to-severe by the highest proportion of patients (mean MDASI-HN fatigue score±SD for entire cohort: 2.2±2.5); fatigue levels were reported to be higher in those patients who had received previous treatment, specifically chemotherapy (3.1±2.5).

Rosenthal et al. (2014) analyzed 149 patients with HNC prior to beginning treatment with radiation or chemo-radiation in a prospective study utilizing weekly patient-reported outcome measurements (MDASI-HN) during treatment to assess the symptom patterns and identify any factors potentially associated with the severity of the symptoms. Those with metastatic disease or those who received prior radiation therapy were excluded. Fatigue was rated as the most severe symptom during the first two weeks of treatment; during weeks six to seven, fatigue was reported as the fourth most severe symptom (behind problem tasting food, problem with mouth/throat mucus, and difficulty swallowing/chewing). Average overall symptom severity was worse for those who received chemo-radiation versus those who received radiation alone, particularly for fatigue (mean±SD, a) chemo-radiation: 4.06±2.12; b) radiation: 2.88±1.90, $p = .001$). The authors also determined that fatigue is often clustered with the symptoms of pain and drowsiness.

Hanna et al. (2015) retrospectively analyzed 748 treatment-naïve HNC patients for whom MDASI-HN data were available to examine their levels of symptom severity at the baseline stage. Fatigue was listed as one of seven most severe symptoms at baseline (mean fatigue severity±SD: 2.86±2.98; patients reporting severe fatigue = 16%), in addition to other symptoms such as disturbed sleep, sadness, and pain. Fatigue levels were not significantly different between

disease sites (non-mucosal, mucosal, or skull-based tumors); however, the levels of fatigue based on lymph node (LN) and tumor (T) staging were significantly different. Of those with N1-N3 staging, 36% reported moderate-to-severe fatigue compared to 27% of those with N0 staging ($p < .05$). Of those with T3 or T4 staging, 44% reported moderate-to-severe fatigue compared to 25% of those with T1 or T2 staging ($p < .05$).

Discussion

The reported studies provided a good background on which to proceed with this research proposal. All included studies illustrate that fatigue plays a significant role in the lives of HNC patients during the entire cancer trajectory from diagnosis to after completion of treatment. Several studies compared the reported levels of fatigue between patients treated with curative- versus non-curative-intent, which is important to differentiate as the treatments can vary widely (Hanna, et al., 2015; Jereczek-Fossa, et al., 2007; Molassiotis and Rogers, 2012; Rogers et al., 2008).

Identifying and understanding the fatigue patterns is the first step in developing the knowledge to design appropriate and effective interventions to reduce CRF in the HNC patient population. Having a greater understanding of the patterns of CRF typically described in the HNC population will allow clinicians to better educate patients regarding the levels of fatigue they should expect during specific periods of their cancer trajectory. A pattern of the most significantly reported CRF occurring during or shortly after treatment completion was discussed by several studies within the review of the literature (Jereczek-Fossa, et al., 2007; Gunn, et al., 2013; Rosenthal, et al., 2014). However, a pattern of prolonged recovery from CRF was also identified, noting incomplete resolution of CRF one to two years post-treatment (Molassiotis and Rogers, 2012; Spratt, et al., 2012).

Section III - Methods

Those diagnosed with cancer are forced to deal with many unpleasant side effects due to the disease itself as well as its treatment, and those with HNC are no exception. Due to often intense treatment modalities and the duration of curative radiation treatment or concurrent chemo-radiation, HNC patients frequently endure some of the highest levels of CRF (Hickok, et al., 2005). Due to these symptoms, evaluation and treatment by a palliative care team is often warranted.

This study provides a descriptive analysis of the HNC patients utilizing the services of the palliative care team to determine the patterns and frequency of fatigue experienced after completion of treatment for their cancer. The study attempted to answer the following research question: How are the characteristics of head and neck cancer patients who are being treated with curative-intent related to their level of fatigue post-treatment?

Project-Specific Definition of Terms

Palliative Care: Specialized healthcare for individuals with serious, potentially life-limiting illnesses, and is not specific to those with cancer. Palliative care can be instituted at any stage of the illness trajectory and focuses on symptom management and improvements in QOL for both the patient and the family (Center to Advance Palliative Care, *n.d.*). This term is distinct and different from hospice or end-of-life care.

Patient-reported outcomes (PRO): Any assessment of a patient's well-being and current condition of their health given by the patient, and that is free from analysis by any member of the patient's family or health care team (U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research, 2006). See Appendix A for the complete PROMIS® questionnaire bank utilized by the palliative care clinic.

Research Design

This study provided a retrospective, descriptive analysis of the patient characteristics, patterns and frequencies of CRF experienced by HNC patients who completed their treatment with curative-intent. The sample was obtained from the palliative medicine's CareTrack 4 database of patients evaluated by the palliative care clinic being treated with curative-intent for their cancers. The subjects were de-identified and coded to distinct study identification numbers in a separate master document, which was securely stored on a University server.

Sample Selection

In July 2015, the palliative care clinic at this academic institution began collecting PRO data from patients who were either currently or previously being treated by the cancer center for their cancer-related diagnoses. Only those patients who were currently or previously treated with curative-intent for their cancers were included in this database, known as CareTrack 4. Patients within the CareTrack 4 database completed PRO surveys at each visit to the palliative care clinic, but no more frequently than once per week, to assess their changes in fatigue, pain interference, QOL, depression, and anxiety.

This study analyzed a sample of HNC patients' records from July 1, 2015 to August 1, 2016. Included records were those of patients 18 years and older with a diagnosis of HNC treated with curative-intent who had completed their cancer treatment. Exclusion criteria included records of those patients not treated with curative-intent; those with a diagnosis of anything other than HNC, including thyroid, esophageal, or facial cancers; and records of those patients who did not complete treatment during the specified window of time. If a relapse occurred and treatment was administered during the specified window of time, only those surveys completed after the most recent treatment modality were included in the analysis. Any PROs completed prior to the

relapse were not included. At the time of data collection, the CareTrack 4 database included approximately 300 patient records. Of those 300 records, it was estimated there would be approximately 50 patient records included in this study.

Setting

This project was implemented in an academic medical center in Central Virginia. In 2012, the palliative care clinic at this institution established protocols to improve healthcare outcomes for patients with cancer and to reduce healthcare costs associated with this population. This project utilized PRO data as a way to longitudinally track patient health status and specific health-related outcomes. Patients completed the surveys at every visit to the palliative care clinic, but no more frequently than once per week; patients also had the option to complete the surveys at their home prior to their visits. Included on the surveys are five questions regarding pain interference, and four questions each regarding fatigue, anxiety, depression, and QOL, as well as additional questions assessing peripheral neuropathy, nausea and vomiting, and patient-reported Eastern Cooperative Oncology Group (ECOG) scores (see Appendix A). The surveys were always completed prior to the patient being seen by their provider so the results could be reviewed with the patient at the visit and a plan made to address any specific areas of concern.

All PRO and demographic data were stored in the patients' electronic medical record (EMR). Approval for this project was obtained from the Palliative Medicine Section Head at the academic institution.

Procedures

This study examined the retrospective data available from the palliative care clinic's eligible patient records in order to identify HNC patient records for analysis. At the time of data collection, there were approximately 300 patient records included in this database. Determination

of eligibility was manually performed by one researcher after review of each subject's EMR. The investigator examined all 300 charts within the palliative care database and manually extracted data from the subject's EMR if they met inclusion criteria. Those data were entered on an Excel workbook by the investigator.

Measures

The following demographic information was collected from eligible patient medical records: Age at diagnosis, gender, race/ethnicity, smoking history, and history of heavy alcohol use. Tumor and treatment specific information collected included diagnosis, year of diagnosis, anatomic location of the cancer, cancer stage, P16 staining status, type(s) of cancer treatment(s) received, date of treatment completion, and year(s) of relapse. Physical, psychosocial, and symptom management information collected included nutritional indicators (such as presence of a feeding tube or extreme weight loss), sleep indicators, and levels of fatigue, anxiety, pain interference, depression, quality of life, and patient-estimated ECOG scores. Additionally, whether or not fatigue was addressed by the provider at each time point was collected and, if yes, what intervention was recommended (see Table 2).

The PRO tool was developed in 2012 by the palliative care team for a Centers for Medicare and Medicaid Services Innovation project. This tool primarily utilized the National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS®) question bank during its development and was specifically designed as a tool to help identify cancer patients who may benefit from earlier palliative care interventions. Within the PROMIS® database, there are a total of 186 questions specific to the adult cancer patient population assessing the domains of anxiety, depression, fatigue, pain interference and physical functioning (Cella, et al., 2010). It was from these 186 questions that the University's palliative care clinic

PRO tool was derived. The tool was piloted in 2013 and adjustments were made to the tool based on the pilot results (Stukenborg, et al., 2014). The PROMIS® item bank has demonstrated broad validity and reliability testing with both quantitative and qualitative evaluations (Barsevick, et al., 2013).

Fatigue was measured using a variation of the PROMIS® Fatigue Short Form (SF) version 1 (see Appendix B). The PROMIS® Fatigue SF is a 7-item questionnaire which asks patients to answer fatigue-related questions using recall over the past seven days; answers range from never (1) to always (5). The seven items were initially selected from the 54-item bank of PROMIS® fatigue questions specific to the adult cancer patient population. The palliative care clinic's PRO tool utilized four of the seven questions; the questions were selected after review by physicians and patient stakeholders and based on national recommendations.

Cessna et al. (2016) determined the PROMIS® Fatigue SF scale demonstrated a Cronbach's alpha >0.86, providing evidence of good internal consistency and reliability within the cancer patient population. Additionally, Barsevick et al. (2013) determined that researchers utilizing the PROMIS® Fatigue item bank could synthesize short forms which could be tailored for use within individual clinical trials.

Each patient's answers to the PRO questionnaire were longitudinally tracked through the program and were seamlessly integrated into their EMR. Once answered by the patient, the scores for each answer were doubled, then all scores were averaged together. For example, if a person answered the four fatigue questions as rarely (1), rarely (1), always (5), and sometimes (3), their recorded scores were as follows: 2, 2, 10, 6 and their average fatigue score equaled 5. The scale was doubled to maintain a range consistent with most other clinical tools. In this study,

an average fatigue score of 6 or higher was assumed to be indicative of the patient experiencing at least moderate fatigue at that point in time.

In order to compare fatigue levels for the included patient records, the average fatigue scores after treatment completion were recorded. Additionally, the average pain interference, anxiety, depression, quality of life, physical functioning and patient-reported ECOG scores were also recorded. Within this database, higher averages for fatigue, pain interference, anxiety, depression, and ECOG were indicative of worse functioning within each domain. Conversely, higher average scores for QOL and physical functioning were indicative of better functioning within those domains.

Data Analysis

Data analysis was conducted with Microsoft Excel, which was used to organize and code the data. Numerical coding was performed for all variables and descriptive statistics were computed to describe the relationships between patient characteristics, levels of fatigue, and how fatigue compared to other PRO measures at each point in time.

Human Subjects Protection

This study received approval from the Institutional Review Board for Health Sciences Research (IRB-HSR). Because this study analyzed retrospective data and no additional information was collected directly from the patients, the need for informed consent was not necessary, per the IRB-HSR. In order to ensure the accuracy of transposed data during necessary audits, the subject's medical record number (MRN) was recorded. However, to maintain the subject's safety and privacy of this HIPAA-protected information, the MRN was coded to a distinct study identification number in a separate master document. The Excel workbook containing the subject's study identification number and their respective de-identified

information was stored separately from the master document. Both of these documents were stored on the F: drive of the medical center, which is used for securely storing sensitive information without the need for encryption.

Section IV - Results

At the time of data collection, there were approximately 300 patients in the CareTrack 4 database. Of those 300 patients, only 10 were initially deemed eligible for inclusion into the study. However, two of the 10 subjects were excluded as they had not completed any surveys. The median age of subjects at the time of diagnosis was 57 years. Six were male, two were female, five were Caucasian, three were African American, and none of the subjects identified themselves as Hispanic or Latino. All subjects, with one exception, had a history of tobacco or alcohol abuse, or both. The most common anatomic locations of the cancer were lip and oral cavity and the pharynx. P16 immunohistochemical staining, which correlates with oncogenic HPV positivity, was negative for the majority of subjects; however, two subjects had no documentation of P16 immunohistochemical staining. Squamous cell carcinoma (SCC) pathology occurred in seven of the eight subjects; the other subject had a pathology of papillary SCC, which is an unusual variant of the SCC pathology.

Case Study #1

Subject One had a cancer of the lip or oral cavity which was found to be papillary squamous cell carcinoma (SCC) diagnosed in 2016. The cancer was deemed to be stage IVa and was treated initially with surgery (mandibulectomy and unilateral neck dissection) followed by concurrent chemoradiation (cisplatin 100mg/m2 and a total of 60 Gy of radiation).

The first PRO survey was completed 9 days after the conclusion of chemoradiation. Fatigue was rated as 7.5, pain interference as 8, anxiety as 6, depression as 3, quality of life as 6,

physical functioning as 6, ECOG as 3. The second survey was completed 52 days after the conclusion of chemoradiation. At that time, fatigue was rated as 5, pain interference as 4, anxiety as 8, depression as 5.5, quality of life as 4, physical functioning as 9, and ECOG as 2. There were notable issues with pain interference, malnutrition, and sleep at both times of PRO completion, and the subject did have a feeding tube.

Case Study #2

Subject Two was found to have a SCC of the larynx, stage II at time of diagnosis in 2015 which was initially treated with concurrent chemoradiation (Cisplatin 100 mg/m2 and a total of 70 Gy of radiation). Recurrence was discovered in 2016, 463 days after initial diagnosis; unilateral neck dissection was then performed with curative-intent.

The first and only PRO survey available for this participant was completed 34 days after their surgery. At the time of PRO survey completion, this participant was noted to have issues with cachexia, weight loss and insomnia. Fatigue was rated as 4, pain interference as 4.66, anxiety as 5, depression as 2, quality of life as 6, physical functioning as 8, and ECOG as 2. Even though fatigue did not meet the criteria of moderate to severe (score of 6 or higher), it was still addressed in this visit's documentation. The patient was encouraged to increase the amount of physical activity and exposure to sunlight. The patient did not have a feeding tube, but did have other nutritional difficulties. It had been 446 days since completion of chemoradiation to the time of PRO survey completion. Having additional survey results would have been helpful in assessing how these quality indicators change over time for this subject.

Case Study #3

Subject Three was diagnosed with stage III SCC of the pharynx in 2014 which was initially treated with radiation only (70 Gy total). The patient experienced a relapse of disease in

2015 to one cervical lymph node as well as a solitary lung nodule, both of which were treated with a single dose of stereotactic body radiation therapy (SBRT) (40 Gy to cervical lymph node; 60 Gy to lung nodule).

After completion of SBRT, the patient completed five PRO surveys, the first of which was completed 34 days later. Fatigue was rated as 4.5, pain interference as 4, anxiety as 7, depression as 3, quality of life as 4, physical functioning as 4.5, and ECOG as 3. The next PRO survey was completed 97 days later, 131 days since treatment completion. Fatigue was rated as 5, pain interference as 5, anxiety as 3, depression as 2, quality of life as 4, physical functioning as 6, and ECOG as 3. The next PRO survey was completed 57 days later, 188 days since treatment completion. Fatigue was rated as 4, pain interference as 6, anxiety as 6, depression as 3, quality of life as 6, physical functioning as 6, and ECOG as 2. The fourth PRO survey was completed 33 days later, 221 days after treatment completion. Fatigue was rated as 4, pain interference as 5.33, anxiety as 3, depression as 2, quality of life as 4, physical functioning as 7, and ECOG as 2. The fifth and final PRO survey was completed 28 days later, 249 days after treatment completion. Fatigue was rated as 7, pain interference as 6.33, anxiety as 3.5, depression as 6, quality of life as 2, physical functioning as 5.5, and ECOG as 2. The patient did have a feeding tube in place, but it was noted the feeding tube was not being used as the patient was able to eat by mouth. Additionally, no issues with malnutrition or sleeping were documented. Of note, the patient did complete additional surveys; however, another relapse of disease was noted roughly three months after completion of the last analyzed PRO survey and, as such, it was not included in the analysis.

Case Study #4

Subject Four was diagnosed with stage IVa SCC of the pharynx in 2015. P16 staining was not available for this individual. Treatment with radiation only was employed (total dose of 70 Gy) and there was no evidence of recurrence at the time of analysis.

The first and only PRO survey was completed 42 days after completion of radiation. Fatigue was rated as 4.5, pain interference as 4.66, anxiety as 2.5, depression as 2, quality of life as 4, physical functioning as 9.5, and ECOG as 1. The subject did have a feeding tube in place and nutritional issues were documented. This participant reported low levels of anxiety and depression, moderate levels of fatigue, pain interference, and quality of life, and a high level of physical functioning. Once again, having additional survey results would have been helpful in assessing how these quality indicators change over time for this subject.

Case Study #5

Subject Five was the only one who had no history or tobacco or alcohol abuse. This patient was initially diagnosed with SCC of the lip or oral cavity in 2010. At that time, treatment consistent solely of a unilateral hemiglossectomy. Approximately six years later, a recurrence of disease was discovered. This time, a unilateral partial glossectomy and unilateral neck dissection was performed, followed by radiation (total of 60 Gy).

The first PRO survey was completed 14 days after treatment completion. Fatigue was rated as 4, pain interference as 6.66, anxiety as 3.5, depression as 2, quality of life as 4, physical functioning as 9, and ECOG as 1. The second PRO was completed 27 days later, 41 days after treatment completion. Fatigue was rated as 3, pain interference as 7.33, anxiety as 5, depression as 2, quality of life as 4, physical functioning as 9.5, and ECOG as 1. The final PRO survey was completed 28 days later, 69 days after treatment completion. At that time, fatigue was rated as 4.5, pain interference as 6.33, anxiety as 4.5, depression as 2, quality of life as 6, physical

functioning as 9, and ECOG as 1. The patient had a feeding tube, although there were no documented issues with malnutrition or other nutritional deficiencies. However, there were reported issues with sleeping, including insomnia and possible sleep apnea.

Case Study #6

Subject Six was diagnosed with stage IVa SCC of the larynx in 2014. The disease was initially treated with concurrent chemoradiation (carboplatin AUC of 5; total dose of 70 Gy). Hepatotoxicity occurred after a single dose of carboplatin which resulted in the discontinuation of any further doses of chemotherapy. Chemoradiation provided an incomplete disease response which led to a subsequent bilateral neck dissection. Disease recurrence was noted in 2016 which was treated with a total laryngectomy. Subject six had a history of a previous lung malignancy diagnosed in 2013 treated with surgical resection alone.

The first PRO survey was completed 24 days after treatment completion. Fatigue was rated as 2.5, pain interference as 7.66, anxiety as 5.5, depression as 2, quality of life as 8, physical functioning as 10, and ECOG as 2. The second PRO survey was completed 32 days later, 56 days after surgical resection. Fatigue was rated as 4, pain interference as 4.33, anxiety as 3.5, depression as 2.5, quality of life as 8, physical functioning as 10, and ECOG as 0. The third PRO survey was completed 31 days later, 87 days after surgery. Fatigue was rated as 4, pain interference as 3.66, anxiety as 5, depression as 2, quality of life as 10, physical functioning as 10, and ECOG as 0. The final PRO survey was completed 33 days later, 120 days after surgery. Fatigue was rated as 4, pain interference as 2 , anxiety as 3, depression as 2, quality of life as 6, physical functioning as 10, and ECOG as 1.

The patient did have a feeding tube, but no issues with malnutrition or sleep were documented. Fatigue management was not reported in any of the corresponding progress notes.

Case Study #7

Subject Seven was diagnosed with stage IVb SCC of the pharynx in 2015. Treatment consisted of neoadjuvant chemotherapy with paclitaxel (175 mg/m2) and carboplatin (AUC of 5) administered every 21 days for four cycles. Thereafter, concurrent chemoradiation with weekly cisplatin (30 mg/m2; 70 Gy total) was utilized. No surgical resection took place. The patient completed their only PRO survey 80 days after completion of treatment.

Greater than two months after treatment completion, fatigue was reported as 10, pain interference as 8.33, anxiety as 3, depression as 2, physical functioning as 7, quality of life as 4, and ECOG was estimated to be 3. This subject did have a feeding tube in place and nutritional issues were reported, as were issues with insomnia due to thick saliva producing a cough. Even though fatigue was rated 10/10, the issue was not addressed by the clinician within the documentation.

Case Study #8

Subject Eight was diagnosed with stage IVa SCC of the lip or oral cavity in 2015. Documentation of P16 staining status was not found in the medical record review. Treatment consisted of surgical resection and unilateral neck dissection follow by radiation (total of 60 Gy). No chemotherapy was utilized and at the time of analysis, there was no documentation of recurrence.

There were six PRO surveys completed by the patient. The first was completed 91 days after the completion of radiation. Fatigue was rated as 7.5, pain interference as 8, anxiety as 8.5, depression as 7, quality of life as 6, physical functioning as 8, and ECOG as 3. The second PRO survey was completed 42 days later, 133 days after finishing treatment. Fatigue was rated as 5.5, pain interference as 8.33, anxiety as 3.5, depression as 6, quality of life as 4, physical functioning

as 8, and ECOG as 2. The third PRO survey was completed 27 days later, 160 days after treatment completion. Fatigue was rated as 6, pain interference as 9.33, anxiety as 5, depression as 8.5, quality of life as 4, physical functioning as 8.5, and ECOG as 2. The fourth PRO survey was completed 28 days later, 188 days after treatment completion. Fatigue was rated as 6, pain interference as 8, anxiety as 8, depression as 8, quality of life as 4, physical functioning as 9, and ECOG as 1. The fifth PRO survey was completed 29 days later, 217 days after treatment completion. Fatigue was rated as 4.5, pain interference as 8.66, anxiety as 4.5, depression as 7, quality of life as 4, physical functioning as 9, and ECOG as 2. The final PRO survey was completed 28 days later, 245 days after radiation completion. Fatigue was rated as 6, pain interference as 9.66, anxiety as 5.5, depression as 7, quality of life as 4, physical functioning as 8.5, and ECOG as 2.

The patient did have a feeding tube, and at each time point, the problem of "moderate malnutrition" was documented; however, as time progressed the patient was noted to be gaining weight and taking more nutrition by mouth. Issues with insomnia were noted during the first three time points. Fatigue was never specifically addressed in the documentation; however, efforts to deal with depression were documented at every time point.

Section V - Discussion

A total of 23 PRO measures were completed by the eight subjects. The earliest PRO survey was completed nine days after treatment completion; the latest survey was completed 249 days after treatment completion. The average length of time after treatment completion to PRO survey completion was 108 days (3.6 months). Three subjects completed the PRO survey only once; Subject Eight completed the most surveys (six). The fatigue scores ranged from 2.5 to 10 with a mean fatigue score of 5.1. (see Appendix C). Due to the low number of eligible subjects

for this study and the paucity of completed PRO surveys, the aim of identifying patterns of fatigue post-curative intent treatment was not met. However, several themes were detected among the data.

Understanding and Discussing Fatigue

The mean patient-reported fatigue score was 5.1, which was lower than expected. A mean fatigue score of six or higher is indicative of at least moderate fatigue, and only four of the eight subjects demonstrated a fatigue score of six or higher at seven different time points throughout the data collection window. Even when fatigue was noted to be problematic by the patient, it was rarely addressed by the clinician within the visit documentation.

Of the seven times fatigue was scored at six or higher, only once was there clinician guidance in the documentation of ways to manage or reduce fatigue. Instructions documented by clinicians included increasing the amount of sunlight exposure as well as the amount of physical activity; however, these were documented under the plan of "integrative" and not specifically identified to mitigate fatigue.

The highest recorded mean fatigue score was a 10 (Subject Seven, 80 days after completion of chemoradiation), but there was no mention of ways to mitigate or manage the fatigue symptoms in the documentation for this subject's visit. Additionally, fatigue was often recorded to be problematic within the review of systems or physical exam, but there was no mention of it within the assessment or plan.

As subjects were not required to complete these surveys at any point in time, perhaps those with less fatigue self-selected to complete PRO surveys more frequently. This could provide another explanation as to the unexpectedly low reported levels of fatigue within this population. The emotional state of the subject at the time of PRO survey completion could have

also affected the way the subject's fatigue was perceived and rated (Ahlberg, Ikman, Gaston-Johansson, & Mock, 2003).

Symptom Clusters

Symptom clusters within the head and neck cancer population are generally divided into two categories: gastrointestinal-related and HNC specific symptoms (Xiao, et al., 2013). Within the realm of the HNC symptoms, pain interference and fatigue often occur together. Of the four subjects who experienced moderate to high levels of fatigue (Subjects 1, 3, 7 & 8), pain interference was also noticeably increased at those time points as well. However, there were times when pain interference was rated as high and fatigue was not rated as at least moderate. There did not appear to be any discernable pattern as to when fatigue peaked; for some subjects for whom multiple data points were available, fatigue was rated to be worse closer to the time of treatment completion; for others, fatigue was rated as more severe as time out from treatment progressed. Shepherd and Fisher (2004) determined that two weeks post-treatment completion for oral and oropharyngeal cancer patients treated with curative-intent was the worst from a quality of life perspective and most functions improved to baseline at the three month mark. Again, given the small number of subjects in this study, no patterns to the domains were identified.

Patient-Reported ECOG Scores

One interesting aspect of the palliative care clinic's PRO survey is the use of patient-reported ECOG scores. Traditionally, ECOG scores are assigned by providers and patients report their perceived quality of life; the palliative care clinic's PRO survey directed the subjects estimate both ECOG and QOL. The provider-assessed ECOG scores range from zero (best functioning) to five (dead). Within the PRO surveys, the spectrum ranged from zero (I am fully

active) to four (I need much help caring for myself, and I spend nearly all day in bed or in a chair). None of the eight subjects scored their ECOG as four, and it appeared that for the subjects where multiple data points were available, the ECOG improved with time. Subject Eight is an exception to this, however, as an improvement in ECOG was noted as time progressed initially and then ECOG worsened from a one to a two greater than 200 days after treatment completion. Disparity between how patients perceive their performance status and how it is perceived by their providers has been well documented (Schnadig, et al., 2008; Atkinson, Andreaotti, Roberts, Saracino, Hernandez, & Basch, 2015; Liu, et al., 2016).

Disparities in Domains

It is generally viewed as helpful to have patient-reported data with which to assess symptoms and tolerance. Regarding fatigue, four questions were selected for the palliative care clinic's PRO survey from the PROMIS® Fatigue SF; these questions were selected after review by physicians and patient stakeholders and based on national recommendations. The validity and reliability of tailored questionnaires utilizing the PROMIS® Fatigue item bank questions has been established (Barsevick, et al., 2013). In reviewing the 23 available PRO surveys, there were several instances where the reported averages and ratings were incongruent. For example, Subject 6 reported consistently high levels of physical function and QOL at each time point; however, at the time of the first post-treatment survey (24 days), high levels of pain interference were reported and ECOG was rated as a 2 ("I can't do any work, but I can care for myself"). Additionally, Subject 1 reported high levels of pain interference, fatigue, and poor ECOG, but rated physical functioning and QOL as moderate to high. These discrepancies could be due to patient perceptions of what is most distressing to them individually, as what effects one person's QOL can be perceived differently to another individual. However, it may be the case that the

questions that were chosen for each domain do not accurately reflect the domains they are seeking to measure. Ahlberg, Ikman, Gaston-Johansson, & Mock (2003) noted that higher levels of activity are associated with less fatigue, but this was not consistently noted within this study.

Strengths & Limitations

Strengths of this study include the ability to build on the body of knowledge regarding the patterns of fatigue in this specific HNC population. As palliative care becomes more readily employed in this and other institutions, providing a better understanding of how this group of cancer patients treated with curative-intent may continue to experience fatigue after treatment is complete can improve knowledge and understanding for clinicians and patients. The cancer center at this academic institution recently started a cancer rehabilitation program run by a physical medicine and rehabilitation physician. This program is geared specifically for cancer patients post-treatment to maximize their quality of life in survivorship. The physical therapy department is involved and actively seeking ways to work with the cancer center, indicating increased demand for rehabilitative services in this population. This study also provides supplementary information regarding symptom clusters that are assessed in the HNC population.

Additionally, this is the first time the PRO survey data from this palliative care population have been analyzed from the perspective of fatigue. Systematic triggers are currently in place to alert palliative care clinicians of high pain interference, anxiety, and depression scores; however, no such trigger exists for fatigue, as it was assumed the vast majority of patients would trigger for high levels of fatigue at most visits. This study provides evidence that perhaps those assumptions should be challenged within the HNC population previously treated with curative-intent. Feasibility for a fatigue trigger within the HNC population could be explored as

this may serve to be a useful tool to identify those patients who might benefit from early fatigue symptom management.

Limitations of this study include the use of only retrospective data, which does not allow for strict control over what variables were collected. The included patients were asked to complete the PRO surveys at each visit to the clinic, however their participation in the completion of the surveys was not mandatory. This resulted in large amounts of missing data, which certainly limited the extent to which data could be interpreted. The small sample size is another limitation. The limited number of subjects and available PRO survey data meant that no meaningful statistical analyses could be run or interpreted.

Another limitation of this descriptive study is the inability to describe rationale for the occurrence of the symptom of fatigue within this patient population. However, this study has provided a good basis on which to move towards correlating this populations' symptom of fatigue with other factors such as mood and functional status in the future. A larger sample size and more predictable times of data collection would be beneficial in producing a data set more amenable to meaningful statistical analysis and correlation.

Nursing Practice Implications

This study will contribute to the growing body of knowledge regarding CRF in the HNC patient population seeking curative-intent treatment. With this knowledge, clinicians may be able to provide more specific education to HNC patients receiving palliative care treatment prior to treatment initiation about the level of fatigue they may experience and its possible duration. Additional education provides patients the ability to more accurately anticipate their clinical course and could lead to more predictable outcomes. Furthermore, this information may be used

by other providers, including physical therapists who may incorporate these findings into their teaching and exercise interventions, dieticians, and social workers.

Implications for Future Research

This descriptive study provides a platform on which further research studies could expand. However, the retrospective design of this trial is limiting. Future research on CRF for this patient population should utilize a prospective design with specific time points for survey completion; additionally, studies should adopt one standard measure of fatigue, such as the PROMIS® fatigue scale. In order to further research efforts around the understanding of fatigue, we must continue to ask patients about this symptom in order to define ways to manage it (Erickson, Spurlock, Kramer, & Davis, 2013). Furthermore, NCCN Clinical Practice Guidelines recommend that all cancer patients be screened for fatigue at regular intervals and that treatment should begin promptly if warranted (2015). There has been much research on fatigue within the cancer population as a whole, but the amount of fatigue research specific to the HNC population is lacking. Even more scarce are data regarding the post-treatment effects on fatigue within the HNC population. This requires the continued pursuit of knowledge and research. There is an opportunity to compare the levels of fatigue of HNC patients within the palliative care database to those patients with other types of cancers to determine if levels of fatigue are comparable in the post-treatment setting.

Products of the DNP Project

The results of this study will be submitted for publication to a peer-reviewed journal, the Clinical Journal of Oncology Nursing. The results will be submitted for consideration as a poster presentation to the 2017 International Cancer Education Conference, the 2017 Virginia Doctor of Nursing Practice Conference, as well as the 2018 Virginia Council of Nurse Practitioner's

conference. The results will be discussed in detail with the palliative care physicians and staff who care for these patients on a daily basis.

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Table 1.

Patterns and burden of fatigue in HNC patients before, during, and/or after receiving treatment.

Citation	Size, Sample Description, Study Aim	Methods, Measures	Questionnaire, Interview Frequency	Outcomes
Jereczek-Fossa et al. (2007)	117 Italian HNC patients treated with radiation or chemo-radiation Analyze fatigue levels during and after radiation treatment & assess how other variables affect the patients	Prospective study, convenience sampling MFI-20	Questionnaires at baseline, weekly during radiation treatment, 10 days & 40 days radiation completion	Average fatigue increased during radiation reaching peak at week 6, then slowly decreased upon completion of treatment
Rogers et al. (2008)	58 American patients with a diagnosis of HNC Understand what factors correlate with fatigue for HNC patients.	Cross-sectional study, convenience sampling FSI	One questionnaire only at time of consent	Fatigue was closely linked to the following factors: younger age (β= -0.22), prior exposure to radiation therapy (β= 0.23), a more recent cancer diagnosis (β= -0.25), & depression (β= 0.40)
Molassiotis & Rogers (2012)	16 English HNC patients with any stage of disease and any treatment history Gain a deeper understanding of the symptom experience for those with HNC within the first year of diagnosis	Qualitative study with interviews	Quarterly interviews over 12 months (T1-T4)	Fatigue ("tiredness") was the second theme to become known to the authors as it was expressed by most patients. The fatigue appeared to continue at T2, mildly improve at T3 and was deemed "unrelenting" at T4, although this meaning is ambiguous
Sprat et al. (2012)	87 American oropharyngeal cancer patients Better understand the timing, correlates, & severity of fatigue specifically in oropharyngeal cancer patients	Prospective study, convenience sampling MSKCC CRF form	Questionnaires at baseline, weekly during radiation, & multiple follow up appointments up to 30 months post-radiation	The difference in mean baseline fatigue scores (0.76, SD 1.36) & the mean fatigue scores at time of treatment completion (6.89, SD 2.44) was significant ($p<.0001$). Levels of fatigue peaked within the first 1-2 weeks after completion of

Citation	Size, Sample Description, Study Aim	Methods, Measures	Questionnaire, Interview Frequency	Outcomes
				radiation (mean fatigue score 5.39, SD 2.73).
Gunn et al. (2013)	270 American HNC patients without prior radiation exposure Gain an understanding of the symptom patterns present prior to beginning treatment with radiation; explore variations in those patterns based on sub-groups; & correlate those with higher symptom burdens to other factors	Prospective study, convenience sampling MDASI-HN	One questionnaire only prior to beginning treatment	Fatigue was noted to be the most likely symptom to be rated as moderate-to-severe by the highest proportion of patients (mean MDASI-HN fatigue score±SD for entire cohort: 2.2±2.5); fatigue levels were reported to be higher in those patients who had received previous treatment, specifically chemotherapy (3.1±2.5).
Rosenthal et al. (2014)	149 HNC patients Gain an understanding of the symptom patterns present during treatment with radiation or concurrent chemo-radiation; explore symptoms based on sub-groups; & identify factors associated with the severity of symptoms	Prospective study, convenience sampling MDASI-HN	Questionnaires weekly during treatment	Fatigue rated as the most severe symptom during weeks 1 & 2 of treatment; during weeks 6-7, fatigue was reported as the fourth most severe symptom. Average overall symptom severity was worse for those who received chemo-radiation versus those who received radiation alone, particularly for fatigue (mean±SD, a) chemo-radiation: 4.06±2.12; b) radiation: 2.88±1.90, p = .001). Fatigue is often clustered with the symptoms of pain and drowsiness.
Hanna et al. (2015)	748 American, treatment-naïve HNC patients Gain an understanding of the symptom severity in treatment-naïve HNC	Retrospective study, convenience sampling MDASI-HN	Questionnaire data available at baseline prior to patients beginning treatment	Fatigue was listed as one of seven most severe symptoms at baseline (mean fatigue severity±SD: 2.86±2.98; patients reporting severe fatigue = 16%). No difference in fatigue levels between disease sites;

Citation	Size, Sample Description, Study Aim	Methods, Measures	Questionnaire, Interview Frequency	Outcomes
	patients; explore variations in symptoms based tumor location; & correlate disease factors with symptom severity and interference			however, the levels of fatigue based on lymph node (LN) and tumor (T) staging were significantly different. Of those N1-N3 staging, 36% reported moderate-to-severe fatigue compared to 27% of those with N0 staging ($p < .05$). Of those with T3 or T4 staging, 44% reported moderate-to-severe fatigue compared to 25% of those with T1 or T2 staging ($p < .05$).

Note. HNC = Head & Neck Cancer; MFI = Multidimensional Fatigue Inventory; FSI = Fatigue Symptom Inventory; MSKCC CRF = Memorial Sloan Kettering Cancer Center Cancer-Related Fatigue; MDASI-HN = MD Anderson Symptom Inventory-Head & Neck Module

Table 2.

Sources of variables of interest

Variable	Measure or Tool
Fatigue, anxiety, depression, pain interference, QOL, patient-reported ECOG score	PRO surveys
Demographics *Age* *Gender* *Race* *Smoking history* *ETOH history*	EMR, progress notes
Tumor Characteristics *Diagnosis* *Year of diagnosis* *Anatomic location of cancer* *Cancer stage* *P16 staining status*	Pathology reports, progress notes
Cancer Treatment Plan *Type(s) of cancer treatment* *Date of treatment completion* *Year(s) of relapse*	Progress notes
Physical, psychosocial, symptom management	Progress notes

Note. QOL: quality of life. PRO: patient-reported outcomes. EMR: electronic medical record.

ECOG: Eastern Cooperative Oncology Group.

Appendix A

PROMIS® Questionnaire Bank Utilized by Palliative Care Patient-Reported Outcome Survey

Please respond to each question by marking one box per row.

Question	Answers				
In the past 7 days, I felt anxious.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt worried.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt nervous.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt tense.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt worthless.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt helpless.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt depressed.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt hopeless.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often did you feel tired?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often did you run out of energy?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often were you too tired to think clearly?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often were you too tired to take a bath or shower?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10

In the past 7 days, how much did pain interfere with your enjoyment of life?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with your ability to concentrate?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with your day to day activities?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with your enjoyment of recreational activities?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with doing your tasks away from home (e.g. getting groceries, running errands)?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10

Are you able to do chores such as vacuuming or yard work?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2
Are you able to dress yourself, including tying shoelaces and doing buttons?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2
Are you able to get on and off of the toilet?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2
Are you able to wash and dry your body?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2

In the past 7 days ... How often have you had watery stools?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often has your stool been hard?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel sick to your stomach?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you vomit?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you have a loss of appetite?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel short of breath?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel numbness, tingling, or burning in your hands or feet?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did pain from numbness, tingling, or burning in your hands or feet interfere with your day to day activities?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel that your faith gave you strength to cope with your illness?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10

In the past 7 days, how would you rate your quality of life?	Excellent Score = 10	Very Good Score = 8	Good Score = 6	Fair Score = 4	Poor Score = 2

Please select the statement that best describes you today.	I am fully active Score = 0	I can't do heavy work, but can do some light work Score = 1	I can't do any work, but I can care for myself Score = 2	I need some help caring for myself. And I spend most of the day in bed or on a chair Score = 3	I need much help caring for myself, and I spend nearly all day in bed or on a chair Score = 4

Note. PROMIS® = Patient-Reported Outcomes Measurement Information System.

Appendix B

PROMIS Item Bank v. 1.0 - Fatigue -Short Form 7a

Fatigue - Short Form 7a

Please respond to each question by marking one box per row.

In the past 7 days…

		Never	Rarely	Sometimes	Often	Always
FATEXP20	How often did you feel tired?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP5	How often did you experience extreme exhaustion?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATEXP18	How often did you run out of energy?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP33	How often did your fatigue limit you at work (include work at home)?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP30	How often were you too tired to think clearly?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP21	How often were you too tired to take a bath or shower?.....	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
FATIMP40	How often did you have enough energy to exercise strenuously?.....	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

Appendix C

PATIENT-REPORTED OUTCOME DATA

Subject	*Days Since Treatment Completion*	*Fatigue*	*Pain Interference*	*Anxiety*	*Depression*	*Physical Functioning*	*QOL*	*ECOG*
1	9	7.5	8	6	3	7	Good	3
	52	5	4	8	5.5	9	Fair	2
2	34	4	4.66	5	2	8	Good	2
3	34	4.5	4	7	3	4.5	Fair	3
	131	5	5	3	2	6	Fair	3
	188	4	6	6	3	6	Good	2
	221	4	5.33	3	2	7	Fair	2
	249	7	6.33	3.5	6	5.5	Poor	2
4	42	4.5	4.66	2.5	2	9.5	Fair	1
5	14	4	6.66	3.5	2	9	Fair	1
	41	3	7.33	5	2	9.5	Fair	1
	69	4.5	6.33	4.5	2	9	Good	1
6	24	2.5	7.66	5.5	2	10	Very Good	2
	56	4	4.33	3.5	2.5	10	Very Good	0
	87	4	3.66	5	2	10	Excel.	0
	120	4	2	3	2	10	Good	1
7	80	10	8.33	3	2	7	Fair	3
8	91	7.5	8	8.5	7	8	Good	3
	133	5.5	8.33	3.5	6	8	Fair	2
	160	6	9.33	5	8.5	8.5	Fair	2
	188	6	8	8	8	9	Fair	1
	217	4.5	8.66	4.5	7	9	Fair	2
	245	6	9.66	5.5	7	8.5	Fair	2

Note. Fatigue, pain interference, anxiety, depression, & physical functioning: scale of 2 -10; ECOG scale of 0-4. Worst fatigue, pain interference, anxiety, depression = 10. Worst physical functioning = 0. Worst ECOG = 4. QOL: quality of life. ECOG: Eastern Cooperative Oncology Group. Excel: excellent.

Appendix D

IRB Approval

University of Virginia
Institutional Review Board for Health Sciences Research
HIPAA Privacy Board

IRB - HSR # 19399		
Event: Approval Protocol Modification - Expedited	**Type:** Protocol	**Sponsor(s):** **Sponsor Protocol #:** **Principal Investigator:** Regina DeGennaro, RN-C, MSN, AOCN, CNL
Title: Identifying Patterns of Fatigue in Head and Neck Cancer Patients Post-Curative Intent Treatment		
Assurance: Federal Wide Assurance (FWA)#: 00006183		
Certification of IRB Review: The IRB-HSR/HIPAA Privacy Board abides by 21CFR50, 21CFR56, 45CFR46, 45CFR160, 45CFR164, 32CFR219 and ICH guidelines. This activity has been reviewed in accordance with these regulations.		
Event Date: 01/30/17 **Protocol Expiration Date:** 11/06/17 **Number of Subjects:** 15 **HSR Protocol Version Date:** 01/27/17 **Data Security Plan Date:** 10/21/16		
Current Status: Open to enrollment		
Consent Version Dates:		
Committee Members (did not vote):		
Comments: The IRB determined the modification met the criteria for approval per the federal regulations and was approved. Modification expedited: minimal risk/minor changes. The revised IRB protocol included the following key changes: 1) Pg7, exclusion criteria: Revised one of the exclusion criterion to allow the inclusion of more subject records. 2) Pg 7-8: Added data points to be collected, which would allow a greater understanding of confounding factors related to fatigue. This study was previously granted waiver of consent for the main study, there is no consent to be revised.		
The IRB-HSR official noted below certifies that the information provided above is correct and that, as required, future reviews will be performed and certification will be provided.		
Name: Hein T. Ng, PhD **Title:** Member, Institutional Review Board for Health Sciences Research **Phone:** 434-924-9634 **Fax:** 434-924-2932		**Name and Address of Institution:** Institutional Review Board for Health Sciences Research PO Box 800483 University of Virginia Charlottesville, VA 22908
Approval:		**Date:**

Appendix E

Manuscript

Understanding Fatigue in Head and Neck Cancer Patients Post-Curative Intent Treatment

Nicole Kahler, DNP, RN, AGACNP-BC, OCN,

University of Virginia Cancer Center, Augusta

Regina DeGennaro, DNP, CNS, RN, AOCN, CNL,

University of Virginia School of Nursing

Abstract

Background: Cancer-related fatigue (CRF) is a frequent and often debilitating symptom experienced by head and neck cancer (HNC) patients from diagnosis to survivorship. The trajectory and treatment of CRF is poorly understood and inconsistently assessed by providers. Patient-reported outcomes (PRO) are an effective way to assess the progression of this symptom through the illness trajectory.

Objectives: The aim of this project was to explore and describe the characteristics of HNC patients who completed their cancer treatment with curative-intent and to improve understanding of how their reported experience of CRF changes over time.

Methods: A retrospective, descriptive study was performed on medical records of HNC patients upon completion of curative-intent cancer treatment who were receiving palliative symptom management.

Findings: Eight subjects met inclusion criteria and completed a total of 23 PRO surveys. No discernible pattern related to post-treatment CRF was identified given the small sample size; however, several themes were revealed. Future research on CRF for HNC patients receiving treatment with curative-intent and palliative symptom management could utilize a prospective design with specific time points for survey completion. Additionally, studies could adopt one standard measure of fatigue, such as the PROMIS® fatigue scale.

Key Words: Head and neck cancer, palliative care, cancer-related fatigue, patient-reported outcomes

Understanding Fatigue in Head and Neck Cancer Patients

Post-Curative Intent Treatment

Introduction

Cancer-related fatigue (CRF) is one of the most common side effects experienced by cancer survivors (Hofman, Ryan, Figueroa-Moseley, Jean-Pierre, & Morrow, 2007). It is estimated that between 25-99% of cancer patients experience CRF at some point throughout treatment for their cancer, and roughly one-third of cancer patients continue to experience fatigue years after treatment has been completed (Servaes, Verhagen, & Bleijenberg, 2002). The National Comprehensive Cancer Network's Guidelines for Supportive Care defines CRF as a subjective feeling of physical, emotional or mental exhaustion related to cancer or its treatment that is persistent and out of proportion to the level of activity which restricts the person's normal functioning (National Comprehensive Cancer Network [NCCN], 2015). CRF can be experienced at any point from the time of diagnosis, including during and after treatment, and has been found to increase as the disease progresses (Stone & Minton, 2008), yet the mechanisms underlying CRF are not fully understood (Richardson, Ream, & Wilson-Barnett, 1998).

By the year 2022, the population of cancer survivors is expected to approach 18 million (American Cancer Society, 2012). It is essential for oncology teams to understand who is most at risk for developing fatigue, when during their cancer trajectory fatigue is most likely to cause the biggest issue, and what are the most efficacious ways to care for these patients and their symptoms. While CRF has detrimental effects on physical, social, cognitive, and occupational functioning, and causes emotional and spiritual distress for patients and their families, it remains under-recognized and undertreated (Mitchell, et al., 2014).

The term “head and neck cancers” (HNC) is used to describe multiple specific diagnoses located within close anatomical proximity to one another, such as cancers of the lip and oral cavity (most common), oropharynx, hypopharynx, larynx, salivary gland, and others (NCCN Clinical Practice Guidelines, 2015). HNC patients have some of the highest rates of fatigue among cancer patients (Hickok, et al., 2005), and fatigue has been reported as the symptom with the greatest burden by HNC patients even prior to receiving radiation therapy (Gunn, et al., 2013).

The purpose of this project was to understand how CRF levels in the post-treatment period change for HNC patients receiving treatment with curative-intent and palliative symptom management. This study attempted to answer the following research question: How are the characteristics of head and neck cancer patients related to their level of fatigue post-treatment?

The theoretical framework utilized was the Levine Conservation Model, which is appropriate for this population as cancer and its treatment can cause great shifts in wellness. This framework describes the conservation of energy, as well as social, structural, and personal integrity as essential to patient adaptation (Levine, 1973).

Review of the Literature

The electronic databases MEDLINE, CINAHL, Web of Science, and the Cochrane Library were systematically reviewed for possible relevant articles relating to the patterns or predictors of CRF in the HNC population. The inclusion criteria for this systematic review were as follows: 1) any study published within the last 10 years, and 2) any study assessing the patterns or predictors of fatigue before, during, or after treatment. Exclusion criteria were as follows: 1) any article for which the University of Virginia did not have full text access, 2) articles for which an English translation was not available, 3) studies focusing on the pediatric or

adolescent population, 4) any study not specifically focusing on fatigue patterns related to HNC, 5) any study assessing QOL where fatigue was not a specific outcome measure, and 6) any study not utilizing patient-reported outcome measures. No limiters were used with any of the searches. Each database was searched using the keywords “fatigue,” “predictor(s) or “pattern(s),” and “head and neck neoplasms” or “head and neck cancer.” Five articles were included in this systematic review; ancestry searches yielded two additional studies bringing the total number of included articles to seven.

Results

Five studies examined fatigue in HNC patients before, during and after treatment with either radiotherapy or chemo-radiotherapy (Jereczek-Fossa, et al., 2007; Rogers, et al., 2008; Molassiotis & Rogers, 2012; Spratt, et al., 2012; Rosenthal, et al., 2014), and two studies assessed fatigue prior to treatment initiation (Gunn, et al., 2013; Hanna, et al., 2015). Four studies included patients who were being treated with both curative or palliative intent (Jereczek-Fossa, et al., 2007; Rogers et al., 2008; Molassiotis & Rogers, 2012; Hanna, et al., 2015), whereas three studies solely included patients being treated with curative-intent (Spratt, et al., 2012; Gunn, et al., 2013; Rosenthal, et al., 2014). The duration of the studies varied from a one-time survey up to 30 months post-treatment completion. All included studies illustrate that fatigue plays a significant role in the lives of HNC patients during the entire cancer trajectory from diagnosis to after completion of treatment. While the overall burden of cancer fatigue is abundant in the literature (Mitchell, et al., 2014), there is a gap in the evidence related to HNC patients and symptom management of fatigue for those being treated with curative-intent.

Methods

This study provides a descriptive analysis of HNC patients utilizing services of the palliative care team to determine the patterns and frequency of fatigue experienced after completion of treatment for their cancer.

Project-Specific Definition of Terms

Palliative Care: Specialized healthcare for individuals with serious, potentially life-limiting illnesses, and not specific to those with cancer. Palliative care can be instituted at any stage of the illness trajectory and focuses on symptom management and improvements in QOL for the patient and family (Center to Advance Palliative Care, *n.d.*). This term is distinct and different from hospice or end-of-life care.

Patient-reported outcomes (PRO): Any assessment of a patient's well-being and current condition of health given by the patient, and free from analysis by any member of the patient's family or health care team (U.S. Department of Health and Human Services FDA Center for Drug Evaluation and Research, 2006).

Research Design

This study provided a retrospective, descriptive analysis of patient characteristics, patterns and frequencies of CRF experienced by HNC patients who completed treatment with curative-intent.

Sample Selection

Patients who were currently or previously treated with curative-intent were included in the palliative care database. Patients within the database completed PRO surveys at each visit to the palliative care clinic, but no more frequently than once per week, to assess changes in fatigue, pain interference, QOL, depression, and anxiety.

This study analyzed a sample of HNC patients' records from July 1, 2015 to August 1, 2016. Included records were those of patients 18 years and older with a diagnosis of HNC treated with curative-intent who had completed cancer treatment. Exclusion criteria included records of those patients not treated with curative-intent; those with a diagnosis of anything other than HNC, including thyroid, esophageal, or facial cancers; and records of patients who did not complete treatment during the specified window of time. If a relapse occurred and treatment was administered during the specified window of time, only those surveys completed after the most recent treatment modality were included in analysis. Any PROs completed prior to relapse were not included. This study received approval from the Institutional Review Board for Health Sciences Research (IRB-HSR).

Setting

This project was implemented in an academic medical center in Central Virginia. The palliative care clinic utilized PRO data as a way to longitudinally track patient health status and specific health-related outcomes. Patients completed surveys at every visit to the palliative care clinic, but no more frequently than once per week; patients also had the option to complete surveys at home prior to visits. Included on the surveys are five questions regarding pain interference, and four questions each regarding fatigue, anxiety, depression, and QOL, as well as questions assessing peripheral neuropathy, nausea and vomiting, and patient-reported Eastern Cooperative Oncology Group (ECOG) scores (Appendix A). The surveys were completed prior to the patient being seen by their provider so results could be reviewed with the patient at the visit and a plan made to address any specific areas of concern.

All PRO and demographic data were stored in the patients' electronic medical record (EMR). Approval for this project was obtained from the Palliative Medicine Section Head at the academic institution.

Measures

The following demographic information was collected from eligible patient medical records: Age at diagnosis, gender, race/ethnicity, smoking history, and history of heavy alcohol use. Tumor and treatment specific information collected included diagnosis, year of diagnosis, anatomic location of the cancer, cancer stage, P16 staining status, type(s) of cancer treatment(s) received, date of treatment completion, and year(s) of relapse. Physical, psychosocial, and symptom management information collected included nutritional indicators (such as presence of a feeding tube or extreme weight loss), sleep indicators, and levels of fatigue, anxiety, pain interference, depression, quality of life, and patient-reported ECOG scores. Additionally, whether or not fatigue was addressed by the provider at each time point was collected and, if yes, what intervention was recommended (Table 1).

The PRO tool was developed in 2012 by the palliative care team for a Centers for Medicare and Medicaid Services Innovation project. This tool primarily utilized the National Institutes of Health Patient-Reported Outcomes Measurement Information System (PROMIS®) question bank during its development and was specifically designed as a tool to help identify cancer patients who may benefit from earlier palliative care interventions.

Fatigue was measured using a variation of the PROMIS® Fatigue Short Form (SF) version 1 (Appendix B). The PROMIS® Fatigue SF is a 7-item questionnaire which asks patients to answer fatigue-related questions using recall over the past seven days; answers range from never (1) to always (5). The palliative care clinic's PRO tool utilized four of the seven questions;

these were selected after review by physicians and patient stakeholders and based on national recommendations.

Each patient's answers to the PRO questionnaire were longitudinally tracked through the program and were seamlessly integrated into their EMR. In this study, an average fatigue score of 6 or higher was assumed to be indicative of the patient experiencing at least moderate fatigue at that time point. Higher averages for fatigue, pain interference, anxiety, depression, and ECOG were indicative of worse functioning within each domain. Conversely, higher average scores for QOL and physical functioning were indicative of better functioning within those domains.

Data Analysis

Data analysis was conducted with Microsoft Excel, which was used to organize and code the data. Numerical coding was performed for all variables and descriptive statistics were computed to describe relationships between patient characteristics, levels of fatigue, and how fatigue compared to other PRO measures at each point in time.

Results

At the time of data collection, there were approximately 300 patients in the palliative care database. Of those 300 patients, only 10 were initially deemed eligible for inclusion into the study. However, two of the 10 subjects were excluded as they had not completed surveys, providing a total of eight subjects. The median age of subjects at time of diagnosis was 57 years. Six were male, two were female, five were Caucasian, three were African American, and none of the subjects identified as Hispanic or Latino. All subjects, with one exception, had a history of tobacco or alcohol abuse, or both. The most common anatomic locations of cancer were lip and oral cavity and pharynx. P16 immunohistochemical staining, which correlates with oncogenic HPV positivity, was negative for the majority of subjects; however, two subjects had no

documentation of P16 immunohistochemical staining. Squamous cell carcinoma (SCC) pathology occurred in seven of the eight subjects; the other subject had a pathology of papillary SCC, which is an unusual variant of the SCC pathology.

Discussion

A total of 23 PRO surveys were completed by the eight subjects. The earliest PRO survey was completed nine days after treatment completion; the latest survey was completed 249 days after treatment completion. The average length of time after treatment completion to PRO survey completion was 108 days (3.6 months). Three subjects completed the PRO survey only once; Subject Eight completed the most surveys (six). The fatigue scores ranged from 2.5 to 10 with a mean fatigue score of 5.1. (Appendix B). Several themes were detected among the data.

Understanding and Discussing Fatigue

The mean patient-reported fatigue score was 5.1. A mean fatigue score of six or higher is indicative of at least moderate fatigue, and only four of the eight subjects demonstrated a fatigue score of six or higher at seven different time points throughout the data collection window.

Of the seven times fatigue was scored at six or higher, only once was there clinician guidance in the documentation of ways to manage or reduce fatigue. Instructions documented by clinicians included increasing amount of sunlight exposure as well as amount of physical activity; however, these were documented under the plan of "integrative" and not specifically identified to mitigate fatigue.

The highest recorded mean fatigue score was a 10 (Subject Seven, 80 days after completion of chemoradiation), but there was no mention of ways to mitigate or manage the fatigue symptoms in the documentation for this subject's visit. Additionally, fatigue was often

recorded to be problematic within review of systems or physical exam, but there was no mention of it within the assessment or plan.

As subjects were not required to complete these surveys at any point in time, perhaps those with less fatigue self-selected to complete PRO surveys. This could provide another explanation as to the unexpectedly low reported levels of fatigue within this population. The emotional state of the subject at the time of PRO survey completion could have also affected the way the subject's fatigue was perceived and rated (Ahlberg, Ikman, Gaston-Johansson, & Mock, 2003).

Patient-Reported ECOG Scores

One interesting aspect of the palliative care clinic's PRO survey is the use of patient-reported ECOG scores. Traditionally, ECOG scores are assigned by providers and patients report perceived quality of life; the palliative care clinic's PRO survey directed the subjects to estimate both ECOG and QOL (Table 2). None of the eight subjects scored their ECOG as four, and it appeared that for most of the subjects where multiple data points were available, the ECOG improved with time. Disparity between how patients perceive their performance status and how it is perceived by their providers has been well documented (Schnadig, et al., 2008; Atkinson, Andreaotti, Roberts, Saracino, Hernandez, & Basch, 2015; Liu, et al., 2016).

Disparities in Domains

Regarding fatigue, four questions were selected for the palliative care clinic's PRO survey from the PROMIS® Fatigue SF; these questions were selected after review by physicians and patient stakeholders and based on national recommendations. The validity and reliability of tailored questionnaires utilizing the PROMIS® Fatigue item bank questions has been established within the literature (Barsevick, et al., 2013). In reviewing the 23 available PRO surveys, there

were several instances where reported averages and ratings were incongruent. These discrepancies could be due to patient perceptions of what is most distressing to them individually, as what effects one person's QOL can be perceived differently to another individual. However, it may be the case that questions that were chosen for each domain do not accurately reflect domains they are seeking to measure.

Strengths & Limitations

Strengths of this study include the ability to build on the body of knowledge regarding patterns of fatigue in this specific HNC population. As palliative care becomes more readily employed in this and other institutions, providing a better understanding of how this group of cancer patients treated with curative-intent may continue to experience fatigue after treatment is complete, can improve knowledge and understanding for clinicians and patients.

This is the first time the PRO survey data from this palliative care population have been analyzed from the perspective of fatigue. Systematic triggers are currently in place within this palliative care clinic to alert clinicians of high pain interference, anxiety, and depression scores; however, no such trigger exists for fatigue, as it was assumed the vast majority of patients would trigger for high levels of fatigue at most visits. This study provides evidence that perhaps those assumptions should be challenged within the HNC population previously treated with curative-intent. Feasibility for a fatigue trigger within the HNC population could be explored as this may serve to be a useful tool to identify those patients who might benefit from early fatigue symptom management.

Limitations of this study include use of only retrospective data, which do not allow for strict control over what variables were collected, as well as small sample size. The included patients were asked to complete the PRO surveys at each visit to the clinic, however participation

was not mandatory. This resulted in large amounts of missing data, which limited the extent to which data could be interpreted.

Another limitation of this descriptive study is the inability to describe rationale for occurrence of the symptom of fatigue within this patient population. However, this study has provided a good basis on which to move towards correlating this populations' symptom of fatigue with other factors such as mood and functional status in the future.

Conclusion

CRF within the HNC population treated with curative-intent remains poorly understood. Utilizing PRO data provides a useful tool in assessing this devastating symptom in real-time. In order to further research efforts around understanding fatigue, we must continue to ask patients about this symptom in order to define ways to manage it (Erickson, Spurlock, Kramer, & Davis, 2013). Future research on CRF for this patient population could utilize a prospective design with specific time points for survey completion. Studies should adopt one standard measure of fatigue, such as the PROMIS® fatigue scale.

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Table 1.

Sources of variables of interest

Variable	Measure or Tool
Fatigue, anxiety, depression, pain interference, QOL, patient-reported ECOG score	PRO surveys
Demographics *Age* *Gender* *Race* *Smoking history* *ETOH history*	EMR, progress notes
Tumor Characteristics *Diagnosis* *Year of diagnosis* *Anatomic location of cancer* *Cancer stage* *P16 staining status*	Pathology reports, progress notes
Cancer Treatment Plan *Type(s) of cancer treatment* *Date of treatment completion* *Year(s) of relapse*	Progress notes
Physical, psychosocial, symptom management	Progress notes

Note. QOL: quality of life. PRO: patient-reported outcomes. EMR: electronic medical record.

ECOG: Eastern Cooperative Oncology Group.

Table 2.

Provider- versus patient-reported ECOG score meanings

Score	Provider-Reported	Patient-Reported
0	Fully active, able to carry on all pre-disease performance without restriction	I am fully active
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light house work, office work	I can't do heavy work, but can do some light work
2	Ambulatory and capable of all self care but unable to carry out any work activities. Up and about more than 50% of waking hours	I can't do any work, but I can care for myself
3	Capable of only limited self care, confined to bed or chair more than 50% of waking hours	I need some help caring for myself. And I spend most of the day in bed or on a chair
4	Completely disabled. Cannot carry on any self care. Totally confined to bed or chair	I need much help caring for myself, and I spend nearly all day in bed or on a chair
5	Dead	N/a

Note. ECOG = Eastern Cooperative Oncology Group. N/a = not applicable. Adapted from Oken, M. M., Creech, R. H., Tormey, D. C., Horton, J., Davis, T. E., McFadden, E. T. & Carbone, P. P. (1982). Toxicity and response criteria of the Eastern Cooperative Oncology Group. *American Journal of Clinical Oncology. 5*(6), 649-55.

Appendix A

PROMIS® Questionnaire Bank Utilized by Palliative Care Patient-Reported Outcome Survey

Please respond to each question by marking one box per row.

Question	Answers				
In the past 7 days, I felt anxious.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt worried.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt nervous.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt tense.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt worthless.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt helpless.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt depressed.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, I felt hopeless.	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often did you feel tired?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often did you run out of energy?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often were you too tired to think clearly?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days, how often were you too tired to take a bath or shower?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10

In the past 7 days, how much did pain interfere with your enjoyment of life?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with your ability to concentrate?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with your day to day activities?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with your enjoyment of recreational activities?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10
In the past 7 days, how much did pain interfere with doing your tasks away from home (e.g. getting groceries, running errands)?	Not at all Score = 2	A little bit Score = 4	Somewhat Score = 6	Quite a bit Score = 8	Very much Score = 10

Are you able to do chores such as vacuuming or yard work?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2
Are you able to dress yourself, including tying shoelaces and doing buttons?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2
Are you able to get on and off of the toilet?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2
Are you able to wash and dry your body?	Without any difficulty Score = 10	With a little difficulty Score = 8	With some difficulty Score = 6	With much difficulty Score = 4	Unable to do Score = 2

In the past 7 days ... How often have you had watery stools?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often has your stool been hard?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel sick to your stomach?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you vomit?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you have a loss of appetite?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel short of breath?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel numbness, tingling, or burning in your hands or feet?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did pain from numbness, tingling, or burning in your hands or feet interfere with your day to day activities?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10
In the past 7 days ... How often did you feel that your faith gave you strength to cope with your illness?	Never Score = 2	Rarely Score = 4	Sometimes Score = 6	Often Score = 8	Always Score = 10

In the past 7 days, how would you rate your quality of life?	Excellent Score = 10	Very Good Score = 8	Good Score = 6	Fair Score = 4	Poor Score = 2

Please select the statement that best describes you today.	I am fully active Score = 0	I can't do heavy work, but can do some light work Score = 1	I can't do any work, but I can care for myself Score = 2	I need some help caring for myself. And I spend most of the day in bed or on a chair Score = 3	I need much help caring for myself, and I spend nearly all day in bed or on a chair Score = 4

Note. PROMIS® = Patient-Reported Outcomes Measurement Information System.

Appendix B

PATIENT-REPORTED OUTCOME DATA

Subject	*Days Since Treatment Completion*	*Fatigue*	*Pain Interference*	*Anxiety*	*Depression*	*Physical Functioning*	*QOL*	*ECOG*
1	9	7.5	8	6	3	7	Good	3
	52	5	4	8	5.5	9	Fair	2
2	34	4	4.66	5	2	8	Good	2
3	34	4.5	4	7	3	4.5	Fair	3
	131	5	5	3	2	6	Fair	3
	188	4	6	6	3	6	Good	2
	221	4	5.33	3	2	7	Fair	2
	249	7	6.33	3.5	6	5.5	Poor	2
4	42	4.5	4.66	2.5	2	9.5	Fair	1
5	14	4	6.66	3.5	2	9	Fair	1
	41	3	7.33	5	2	9.5	Fair	1
	69	4.5	6.33	4.5	2	9	Good	1
6	24	2.5	7.66	5.5	2	10	Very Good	2
	56	4	4.33	3.5	2.5	10	Very Good	0
	87	4	3.66	5	2	10	Excel.	0
	120	4	2	3	2	10	Good	1
7	80	10	8.33	3	2	7	Fair	3
8	91	7.5	8	8.5	7	8	Good	3
	133	5.5	8.33	3.5	6	8	Fair	2
	160	6	9.33	5	8.5	8.5	Fair	2
	188	6	8	8	8	9	Fair	1
	217	4.5	8.66	4.5	7	9	Fair	2
	245	6	9.66	5.5	7	8.5	Fair	2

Note. Fatigue, pain interference, anxiety, depression, & physical functioning: scale of 2 -10; ECOG scale of 0-4. Worst fatigue, pain interference, anxiety, depression = 10. Worst physical functioning = 0. Worst ECOG = 4. QOL: quality of life. ECOG: Eastern Cooperative Oncology Group. Excel: excellent.