UNIVERSITI PUTRA MALAYSIA

CHANGES IN NUTRITION IMPACT SYMPTOMS, NUTRITIONAL AND FUNCTIONAL STATUS AMONG HEAD AND NECK CANCER PATIENTS RECEIVING RADIOTHERAPY OR CHEMORADIOTHERAPY AT SELECTED HOSPITALS

NEOH MAY KAY

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By

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Thesis Submitted to the School of Graduates Studies, Universiti Putra Malaysia, in Fulfillment of the Requirement for the Degree of Master of Science

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August 2021

Chair : Zalina binti Abu Zaid, PhD
Faculty: Medicine and Health Sciences

Radiotherapy (RT) or concurrent chemoradiotherapy (CCRT) is the primary treatment for head and neck cancer (HNC). Any loss of weight during RT or CCRT will result in inconsistent radiation to the target region, which may decrease treatment efficacy. The study aimed to determine the changes in nutritional impact symptoms (NIS), nutritional and functional status and their associations with weight loss during treatment (RT or CCRT). This is an observational prospective study with weekly dietitian follow up HNC patients throughout the seven weeks of treatment; NIS, nutritional and functional status of patients were assessed along the treatment. The study subjects were HNC patients who hospitalized undergoing treatment at the National Cancer Institute, Putrajaya. Nutritional status was assessed with the Patient Generated Subjective Global Assessment (PG-SGA) at the baseline and end of the treatment. Head and Neck Symptoms Checklist (HNSC©) evaluated weekly NIS, 24-hour diet recall determined weekly dietary intake and Jamar Dynamometer measured weekly functional status of handgrip strength. Information on sociodemographic and clinical characteristics of the patients was obtained using a structured questionnaire. Data collection was done from March to December 2018. Primary analysis of dietary intake was conducted with Nutritionist Pro software. Statistical data analysis of changes over time was conducted with general linear model of repeated measures using IBM SPSS version 23. Fifty HNC patients, including 39 males (78%) and 11 (22%) females were recruited during data collection. The median age of HNC patients were 60 years old and the age range was 21 to 78 years old. At the end of treatment, the mean weight loss was 4.53 ± 2.87 kg (7.4%) and all patients were malnourished, where 32% were moderately malnourished and 68% were severely malnourished. Muscle mass decreased starting from week 4 ($p = 0.002$); fat mass and dietary intake decreased starting from week 3 ($p=0.022$; $p <0.001$); while oral nutritional supplements (ONS) intake increased from week

3 ($p < 0.001$). At the end of treatment, all HNC patients had xerostomia, altered taste and required ONS. The weight loss percentage was significantly related to change in NIS scores ($r = 0.434$, $p = 0.002$), indicating the higher NIS score difference during treatment in HNC patients, the greater weight loss percentage. A significant relationship between changes in total energy intake with weight loss percentage was found ($r = 0.297$, $p = 0.036$). It can be concluded that intensive nutrition intervention should began before the week 3 of treatment due to a significant change in muscle mass and fat mass. A minimum ONS recommendation of 500kcal starting at baseline, 800kcal at week 2, 1000 kcal at week 3, 1300kcal at week 4, and 1500kcal from week 5 until the end of treatment, by considering any NIS that interferes with eating. A routine biweekly nutrition intervention with NIS monitoring and ONS recommendation is suggested based on the results. Further research by implementing recommendation above should be done in intervention study to improve effectiveness of treatment outcomes by prevent high percentage of weight loss during treatment.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Master Sains

PERUBAHAN DALAM GEJALA KESAN PEMAKANAN, STATUS PEMAKANAN DAN STATUS FUNGSIAN DALAM KALANGAN PESAKIT KANSER KEPALA DAN LEHER YANG MENERIMA RADIOTERAPI ATAU KEMORADIOTERAPI DI HOSPITAL TERPILIH

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Radioterapi (RT) atau kemoradioterapi bersamaan (CCRT) adalah rawatan utama untuk pesakit kanser kepala dan leher (HNC). Sebarang penurunan berat badan semasa RT atau CCRT akan menyebabkan radiasi yang tidak tepat ke kawasan sasaran yang dapat mengurangkan keberkesanan rawatan. Kajian ini bertujuan untuk menentukan perubahan dalam gejala kesan pemakanan (NIS), status pemakanan dan status fungsian dalam kalangan pesakit HNC semasa rawatan (RT atau CCRT). Ini adalah kajian prospektif dan perhatian yang menindaklanjuti pesakit HNC sepanjang tujuh minggu rawatan; gejala kesan pemakanan (NIS), status pemakanan dan status fungsian pesakit serta hubungan dengan kehilangan berat badan dinilai sepanjang rawatan yang jarang dilaporkan dalam literatur. Subjek kajian adalah pesakit HNC yang dimasukkan ke Institut Kanser Negara, Putrajaya untuk mendapatkan rawatan. Penilaian Global Subjektif yang dihasilkan oleh pesakit (PG-SGA) digunakan untuk menilai status pemakanan pada minggu pertama dan minggu terakhir. NIS dinilai dengan menggunakan Senarai Semak Gejala Kepala dan Leher (HNSC ©) pada setiap minggu, pengambilan makanan ditentukan oleh pengambilan makanan 24 jam pada setiap minggu dan status fungsian diukur melalui kekuatan pegangan tangan dengan Jamar Dynamometer pada setiap minggu. Soal selidik berstruktur digunakan untuk mendapatkan maklumat mengenai ciri sosiodemografi dan gambaran klinikal pesakit. Pengumpulan data dilakukan dari Mac hingga Disember 2018. Analisis utama pengambilan makanan dilakukan dengan perisian Nutritionist Pro. Analisis data statistik perubahan dari masa ke masa dilakukan dengan model linear umum pengukuran berulang menggunakan IBM SPSS versi 23. Lima puluh pesakit HNC, termasuk 39 lelaki (78%) dan 11 (22%) wanita direkrut semasa pengumpulan data. Umur pesakit HNC adalah 60 tahun dengan julat antara 21 hingga 78 tahun. Semua pesakit mengalami malnutrisi, di mana 16 (32%) malnutrisi serdehana dan 34 (68%) mengalami malnutrisi teruk dengan

penurunan berat badan 4.53 ± 2.87 kg (7.4%) pada akhir rawatan. Jisim otot menurun dengan ketara bermula dari minggu ke-4 ($p = 0.002$); jisim lemak dan pengambilan makanan menurun dengan ketara bermula dari minggu ke-3 ($p = 0.022$; $p < 0.001$); sementara pengambilan suplemen pemakanan oral (ONS) meningkat dengan ketara dari minggu ke-3 ($p < 0.001$). Semua pesakit HNC mengalami perubahan rasa, mulut kering dan memerlukan ONS pada akhir rawatan. Perubahan peratusan penurunan berat badan secara signifikan berkaitan dengan perubahan skor NIS ($r = 0.434$, $p = 0.002$), menunjukkan perbezaan skor NIS yang lebih tinggi semasa rawatan di kalangan pesakit HNC, peratusan penurunan berat badan yang lebih tinggi pada akhir rawatan. Hubungan yang signifikan antara perubahan penurunan berat badan peratusan dan jumlah pengambilan tenaga didapati ($r = 0.297$, $p = 0.036$). Ini dapat disimpulkan bahawa intervensi pemakanan intensif harus dimulakan sebelum minggu ke-3 rawatan yang berkaitan dengan perubahan ketara dalam jisim otot dan jisim lemak. ONS adalah dicadangkan bermula dengan paling minimum 500kkal, 800kkal pada minggu ke-2, 1000kkal pada minggu ke-3, 1300kkal pada minggu ke-4, dan 1500kkal dari minggu ke-5 hingga akhir rawatan, dengan mempertimbangkan sebarang NIS yang mengganggu makan. Intervensi pemakanan dengan perlaksanaan dua kali dalam setiap minggu rutin pemantauan NIS dan ONS dicadangkan berdasarkan hasil kajian ini. Penyelidikan lebih lanjut dengan melaksanakan cadangan di atas harus dilakukan dalam kajian intervensi untuk meningkatkan keberkesanan hasil rawatan dengan mencegah peratusan penurunan berat badan yang tinggi semasa rawatan.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the Master of Science. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
BIA	Bio Impedance Analysis
BMI	Body Mass Index
CCRT	Concurrent Chemoradiotherapy
EI	Energy Intake
ER	Energy Requirement
HGS	Handgrip strength
HNC	Head and Neck Cancer
HNSC©	Head and Neck Patient Symptom Checklist
kcal	Kilocalorie
MOH	Ministry of Health
NCI	National Cancer Institute
NCR	National Cancer Registry
NMRR	National Medical Research Registry
ONS	Oral Nutritional Supplements
PG-SGA	Patient-Generated Subjective Global Assessment
RT	Radiotherapy
SPSS	Statistical Package for Social Sciences
Stage I/II	Early stage of disease
Stage III/IV	Advanced stage of disease
UPM	Universiti Putra Malaysia
WHO	World Health Organisation

CHAPTER 1

INTRODUCTION

1.1 Background

Head and neck cancer (HNC) is malignant in head and neck regions, including malignancies of the oral and nasal cavities, sinuses, salivary glands, pharynx, larynx and lymph nodes in the neck (Stewart & Wild, 2014). It is the sixth most common forms of cancer globally, contributing for almost 5% of new cancer cases in 2018 (Ferlay et al., 2019). From 2012 to 2016, a total of 115,238 new cancer cases were diagnosed among Malaysians and the data indicates that 7.8% (6110 males; 2924 females) of the cases belonged to HNC (Malaysia National Cancer Registry, 2019). HNC is among the top five leading cancers in Malaysia. It was the third most common cancer among Malaysian males and the sixth most common in Malaysian females in 2016 (Azizah AM. et al., 2019).

Many HNC patients are diagnosed at an advanced stage (Stage III or IV) and most of them are in nutritional vulnerability condition with a high risk of malnutrition (Dechaphunkul et al., 2013; Kubrak et al., 2010). HNC patients are often malnourished at the time of diagnosis, prior to the beginning or throughout treatment because of the catabolic condition caused by malignancy, tumour location that impair oral intake (Bower & Martin, 2009) and the intensity of treatments (Dechaphunkul et al., 2013; Jager-Wittenaar, Dijkstra, Vissink, Langendijk, et al., 2011a). Current treatment of HNC involves multimodality therapy such as surgery, radiotherapy (RT) and concurrent chemoradiotherapy (CCRT) (Bossola, 2015).

During treatment, weight may be compromised by symptoms that interfere with dietary intake. These are known as nutritional impact symptoms (NIS) which include the following symptoms: loss of appetite (LOA), taste changes, nausea, vomiting, swallowing difficulty, pain, dry/sore mouth, difficulty chewing, dental problems, thick saliva, anxiety, depression, and constipation (Kubrak et al., 2010). NIS symptoms that are exacerbated by treatment suppress appetite and weight maintenance extremely challenging (Kubrak, Olson, & Baracos, 2013a; Kubrak et al., 2010; Jager-Wittenaar et. al., 2007; Larsson, Hedelin, Johansson, & Athlin, 2005) .

In HNC patients, the side effects from RT with or without chemotherapy are common appearing throughout and immediately after completion of treatment. RT trigger NIS such as altered taste and smell, xerostomia, dysphagia and mucositis, create nutritional deficiency challenges due to difficulty in chewing and swallowing ability (Ravasco, Monteiro-Grillo, Marques Vidal, & Camilo, 2005; Langius et al., 2010) . CCRT has improved tumor control (Couch et al., 2007; Nguyen & Yueh, 2002) but is related with increased severity and

persistence of symptoms which may reduce dietary intake and resulting in weight loss throughout treatment (Couch et al., 2007).

Dysphagia is the most studied symptom impair oral intake in HNC patients either due to tumor obstruction or RT treatment (Dechaphunkul et al., 2013), but it is not the only symptom that affects nutritional status of these patients. In fact, symptoms such as xerostomia and oral mucositis also appear to suppress the appetite of HNC patients throughout RT treatment (Ogama & Suzuki, 2012). These side effects are frequent happen HNC patients, which affects the ability of the patient to eat and drink and increase the risk of malnutrition. Deterioration of nutritional status results in increased treatment related toxicity, which can extend the length of treatment (Vera-Llonch, Oster, Hagiwara, & Sonis, 2006).

Consequences of malnutrition in HNC included reduced immune function, increased risk of infection, impaired wound healing, diminished quality of life (QoL), and increased fatigue (Jager-Wittenaar, Dijkstra, Vissink, Van Oort, et al., 2011b; Langius et al., 201 3a; Ravasco et al., 2005). Various studies reported malnutrition attributed around 10-20% to death among cancer patients (Sesterhenn et al., 2012; Pressoir et al., 2010; Wie et al., 2010) rather than malignancy itself. Treatment breaks including cytotoxic agent's dosage reduction or radiation timing modification or definite cessation of treatment bring an impact in anticancer treatment associated with decreased of overall survival and locoregional control rate (Kubrak et al., 2013a; Cannon et al.,2014; Capuano et al., 2008).

Malnourished patients have lower handgrip strength (Norman et al., 2011; Flood et al., 2014), which is related to decreased protein synthesis due to decreased oral intake, which causes muscle fibre atrophy and decreased muscle mass, resulting in muscle function impairment. Muscle mass loss can occur before weight loss is observed, as a decline in muscle function frequently occurs prior to detectable weight loss (Norman et al., 2011), explaining why muscle function responds to nutritional depletion earlier. According to Norman et al. (2005), low body composition muscles have significantly lower handgrip strength. Reduced handgrip strength is associated with the highest relative risks of morbidity and mortality (Chen, Huang, & Hung, 2011). Handgrip strength has been shown to be an excellent predictor of protein loss, which has been linked to long-term mortality. In weight loss monitoring, early identification of impaired nutritional status with decreased muscle function and at risk of losing functional status is critical.

Garabige et al. (2007) reported that early nutritional management has reduced weight loss, treatment interruptions and the incidence of mucositis throughout radiotherapy. Based on the results reported, it has become important that nutritional status of patient should be taken consideration in the management of patient, as it influences the patient's tolerance to treatment. An early and

substantiated nutrition intervention for prevention of malnutrition is therefore required to improve treatment efficacy in cancer patients.

Nutrition intervention includes nutritional counseling, oral nutritional supplements (ONS), enteral or parenteral, and combined interventions, should be administered according to the patient's energy and protein requirements, and tolerability (Jann Arends et al., 2017). Several studies have shown beneficial effects of improvement of QOL scores, greater energy and protein intake and less nutritional deterioration in the ONS group compared to the without ONS group in HNC patients (Ravasco et al., 2005; Nayel, El-Ghoneimy & El-Hadad, 1992). Most of the ONS is liquids that can be less early satiety and easier to digest than solids when individuals are ill, poor appetite or are without dentition (Hubbard, Elia, Holdoway, & Stratton, 2012).

Symptom assessment is often adopted in the HNC population to restore dietary intake and to minimise unintentional weight loss, especially throughout treatment (Kubrak et al., 2013a). The head and neck symptoms checklist (HNSC) is an assessment tool specifically design for HNC patients. The HNSC provides specific information that applicable for HNC patients as it contains a severity assessment which interfere with eating that allows the health care provider to monitor progression of NIS and to develop appropriate interventions throughout treatment. HNSC is simple, convenient to use, more comprehensive and specific to HNC patients than Patient-Generated Symptom Global Assessment (PG-SGA) (Schmidt, Olson, Kubrak, Parliament, & Ghosh, 2013). This checklist documents contains five additional NIS (lack of energy, depression, difficulty chewing, thick saliva, and anxious) particular to HNC patients that are not usually included in the others symptoms assessment. In addition, HNSC is useful in assessing NIS to monitor oral intake, nutrition assessment, nutrition intervention, and control unintentional weight loss (Schmidt et al., 2013).

A few clinical studies on HNC patients have shown a significant relationship between NIS and decreased oral intake, weight loss, and diminished functional status (Jann Arends et al., 2017; Jager-Wittenaar et al., 2007; Kubrak et al., 2013a). A research by Farhangfar et al. (2014) found that patients with multiple NIS or greater total symptoms scores are more prone to have reduced oral intake and weight loss (Farhangfar et al., 2014). There is a need to use a standardized and comprehensive measurements for early intervention based on the results to support the need for proactive symptom management. Whereas the research by Kubrak et al. (2013b) demonstrate that some symptoms in the HNSC are key determinants of the impact of NIS on dietary intake and weight loss throughout treatment. This support HNSC is a valid tool in evaluate NIS among HNC patients for strengthening interventional approaches to nutrition care (Kubrak et al., 2013a).

The length of RT or CCRT for HNC patients is set at approximately six to seven weeks and the dose of RT is planned by radiologist and oncologist. This is a

crucial time for nutrition assessment, intervention and monitoring due to the fast changes in oral intake that affected by NIS. HNC patient may gradually experience multiple NIS that needs a different intensity of nutrition intervention along the treatment. Early nutrition intervention allows patients tolerate better to treatment which helps to achieve the best treatment outcomes (Santarpia, Contaldo, & Pasanisi, 2011; Garabige et al., 2007) but the progression of NIS affects energy intake remains to be clearly defined with HNSC over the time throughout treatment. If HNSC can help in identify the severity of NIS to determine the intensity of dietary intervention, there should be a simple weekly screening through HNSC that can be used as a nutrition assessment for all HNC patient receiving RT or CCRT regardless inpatient or outpatient.

1.2 Problem statement

The side effects arise from RT or CCRT treatment may suppress appetite, results in decrease oral intake and ultimately weight loss. Weight loss throughout RT is common in HNC patients. Two studies found that RT exacerbated acute side effects and weight loss happen following two weeks of RT or CCRT (Raber-Durlacher, Elad, & Barasch, 2010; Rodríguez-Caballero et al., 2012). However, a systematic review has indicated that weight loss begins at one week of RT, concluded that nutrition intervention should be implemented early in treatment and that weight monitoring should start at the first week of RT or CCRT, especially in patients vulnerable to weight loss (Langius et al., 2013b). Hence, intensive dietary intervention is recommended before problem arises, rather than expecting reduced oral intake and weight loss to occur throughout RT or CCRT treatment.

Langius et al. (2013) found that weight loss can have a significant effect on patient survival in a cohort study of 1340 HNC patients. They revealed that critical weight loss of more than 5% weight loss is associated with a 1.7-fold increased risk of dying in HNC patients. Previous studies reported multiple complications associated with critical weight loss treatment including treatment complication, reduce treatment effectiveness, increased mortality rate, longer hospital stay and lower survival rate (Argiris, Li, & Forastiere, 2004; Couch et al., 2007; Nguyen & Yueh, 2002).

Any weight loss throughout treatment will reduce treatment effectiveness in which required to replan the treatment with the term of “adaptive RT”. This term “adaptive RT” refers to different procedures that take into account anatomical and functional changes that can influence RT/CCRT dose distribution (Grégoire et al., 2012). The loss of body weight involves skeletal mass disrupts the capability to preserve calorie. Muscle mass loss due to inadequate dietary intake will restrict the essential fuel to maintain optimal functional ability. Various studies reported that muscle function responds faster to reduce food intake than other nutritional indices (Bourdel-Marchasson, Joseph & Dehail, 2001; Pichard et al., 2004).

Handgrip strength is a common indicator of muscle function. It is applicable to evaluate the short period functional changes before anthropometric and biochemical changes occur (Norman et al., 2011). Repetitive radiotherapy causes lethargy in HNC patients along the treatment and handgrip strength measurement is useful for patients who have muscle weakness around lower limb (Norman, Stobäus, Gonzalez, Schulzke, & Pirlich, 2011). This is important in monitoring HNC patients who lose muscle strength throughout treatment due to lack of energy intake with weight loss problem.

The European Society for Clinical Nutrition and Metabolism (ESPEN) advises using ONS apart from counselling in cases when insufficient intake of normal foods to prevent nutritional deterioration. Enteral tube feeding is recommended if having severe dysphagia and decreased energy intake (Jann Arends et al., 2017). In order to identify patients that require intensive nutritional intervention, further research is needed to observe their energy intake, NIS and the weight loss throughout treatment by schedule. In addition, subgroups which positively impact from an early nutritional support need to be identified. To date, none of the studies investigate about the changes of NIS, nutritional status and oral intake especially ONS intake throughout RT or CCRT treatment.

Many researches focused on the effect of weight loss and energy intake pretreatment and post treatment, mainly emphasis on the effect of treatment. (Jager-Wittenaar et al., 2011a; Kubrak et al., 2013a; M. G. van den Berg et al., 2006; Van Der Laan et al., 2015) .However, there is a lack of specific assessment tool to monitor NIS throughout treatment that can affects energy intake and weight status throughout the RT or CCRT treatment. In order to establish strategies to reduce malnutrition in patients with HNC, it is necessary to understand the changes in energy intake from dietary and ONS intake at which points throughout the treatment period occur. Compliance with nutritional intervention may be increased when patients' dietary changes and ONS intake are taken consideration. At present, there is not much data about energy intake of dietary changes and the consumption of ONS throughout treatment.

NIS assessment should be repeated at regular intervals such as weekly, fortnightly or monthly to evaluate the need for nutritional intervention and track its effectiveness. Nutritional intervention should identify problems included xerostomia, smell and taste changes, nausea, vomiting, mucositis, constipation and diarrhea that likely to affect intake (Jann Arends et al., 2017). In the absence of published literature on analysis NIS using HNSC, the analysis of factors contributing to decrease energy intake is important to assess the efficacy of intensive nutrition intervention to reduce weight loss dur throughout ing treatment. Once the healthcare team has a better understanding on the contribution of factors, they will be able to provide higher quality care to assist, support and improve the energy intake of these patients during the difficult time of ongoing cancer treatments.

In brief, identification impact of RT or CCRT through NIS changes over time conveys useful information concerning the progression of patients' ability in consuming energy intake from diet throughout treatment. Therefore, this research proposed important to follow HNC patients throughout RT or CCRT by identifying NIS, as symptoms which are not present before treatment may occur secondary to treatment, and affects dietary intake or nutritional status later throughout treatment. This significance of measuring the weekly change of NIS through HNSC is considered as a screening tool to monitor factors affecting energy intake especially symptoms that interfere with eating and weight loss in HNC throughout treatment.

Currently, dietitians in Malaysia practice a standardize nutrition intervention according to MNT guidelines in Malaysia for cancer patients. There are no local studies to investigate prospectively the changes in nutrition impact symptoms, nutritional and functional status in HNC patients throughout RT/CCRT. It is critical to conduct this study in order to gather more information about changes that can be made to improve current dietary intervention for better treatment outcomes. In view of high prevalence of HNC incidence in Asian countries, it is important to study the changes as a preliminary data to develop nutrition management guideline specific in HNC patients throughout treatment.

1.2.1 Research Questions

Several research questions were addressed as follows:

1. What is the magnitude of change in weight of HNC patients throughout RT or CCRT?
2. What are the changes in NIS of HNC patients throughout RT or CCRT?
3. What are the changes in the nutritional status of HNC patients throughout RT or CCRT?
4. What are the changes in the functional status of HNC patients throughout RT or CCRT?
5. Is there any association between changes in nutrition impacts symptoms, nutritional status and functional status with weight loss throughout RT or CCRT?

1.3 Significance of the study

During RT or CCRT, weight monitoring is essential as this treatment required head mask to ensure accurate radiation delivery to target area by correctly position the patient. Any loss of weight throughout RT or CCRT will affect the target area with inaccurate radiation, which can minimise the treatment effectiveness (Capuano et al., 2008). Therefore, nutrition intervention become most important to minimize weight loss throughout radiotherapy and ought to be continuously monitored even though completed radiotherapy (Kubrak et al., 2013a; Jager-Wittenaar et al., 2011a).

Currently, there is no established nutrition management guideline for HNC patients according to NIS changes over time throughout RT or CCRT treatment. This essential assessment is recommended to performed on a regular basis to evaluate and then adjust an appropriate nutritional management especially energy intake from oral food as well as ONS according to nutritional status throughout treatment. Relevant data is very important to develop a framework or standard protocol for specific nutrition management to prevent aggressive weight loss in HNC patients.

We performed a longitudinal study of baseline and throughout treatment of HNC patients receiving RT or CCRT treatment. This research is therefore intended to determine changes in nutritional status, functional status, NIS and energy intake among HNC patients throughout radiotherapy and to investigate the relationship with weight changes throughout treatment. Based on the findings of this analysis, a clearer description of how NIS affects energy intake and nutrition status throughout RT or CCRT could be obtained. More nutrition intervention studies should be designed to identify early signs to help avoid high unintentional weight loss and improve treatment outcomes. The results of the RT or CCRT related NIS evaluation, including nausea, vomiting and decreased appetite, which affect energy intake may indicate the need for early NIS screening to enhance nutrition intervention such as timing of ONS or enteral tube feeding initiation.

Therefore, this study is the first kind in Malaysia to identify the prevalence and magnitude of weight changes in HNC and the association of nutrition impact symptoms, nutritional status and functional status with weight loss throughout RT or CCRT. The results of this study may be applied to the current literature on weight changes in HNC throughout RT or CCRT, which could help to improve nutrition intervention.

1.4 Study Objectives

1.4.1 General Objective

To determine changes in nutrition impact symptoms, nutritional and functional status and their association with weight loss among head and neck cancer patients receiving radiotherapy (RT) or concurrent chemoradiotherapy (CCRT) in National Cancer Institute.

1.4.2 Specific objectives

a. To determine and compare baseline data (socio-demographic, clinical characteristic, NIS, nutritional status and functional status) and changes between well-nourished and malnourished HNC patients

b. To determine the magnitude of weight loss among HNC patients throughout RT or CCRT
c. To determine changes of head and neck cancer patients throughout RT or CCRT in
    i. Nutrition impact symptoms
    ii. Nutritional status (muscle mass, fat mass, laboratory parameters, type of diet, total energy and protein intakes, dietary energy and protein intakes, oral nutritional supplement (ONS) energy and protein intakes and Patient-Generated Subjective Global Assessment (PG-SGA) scores)
    iii. Functional status (handgrip strength)
d. To determine the association between changes in nutrition impact symptoms, nutritional status and functional status with weight loss among head and neck cancer patients throughout RT or CCRT

1.5 Conceptual Framework

Figure 1.1 illustrates the dependent and independent variables in the present study. The dependent variable was weight changes. Weight changes often occur among HNC patients throughout the 7 weeks of radiotherapy with weight loss rather than weight gain commonly reported. Weight change in this study was defined as the difference in weight from baseline to end of RT or CCRT. Percentage of weight loss >5% was further categorized as critical weight loss (Langius et al., 2016).

Independent variables were nutrition impact symptoms, nutritional status included body composition (muscle mass and fat mass), laboratory parameters (albumin, hemoglobin, white blood cells), energy and protein intake (oral food & oral nutritional supplements) and functional status (handgrip strength). The changes of nutrition impact symptoms, body composition, energy and protein intakes as well as functional status were assessed at weekly basis while laboratory parameters was measured at baseline (week 1), middle (week 4) and end of treatment (week 7). There associations between changes in NIS, nutritional status and functional status with weight loss in HNC throughout 7 weeks of RT or CCRT were evaluated.

HNC patients were categorized into well-nourished and malnourished groups in this study. The overall changes and changes of both groups has been observed throughout the 7 weeks of RT/CCRT. Cancer stage is the potential confounding factors in this study but not included in the exclusion criteria as the radiotherapy impact on nutritional deterioration combined with deficiencies in nutritional intake, nutrition impact symptoms and muscle function were similar in all stages (Anandavadivelan et al., 2016; Kubrak et al., 2013).

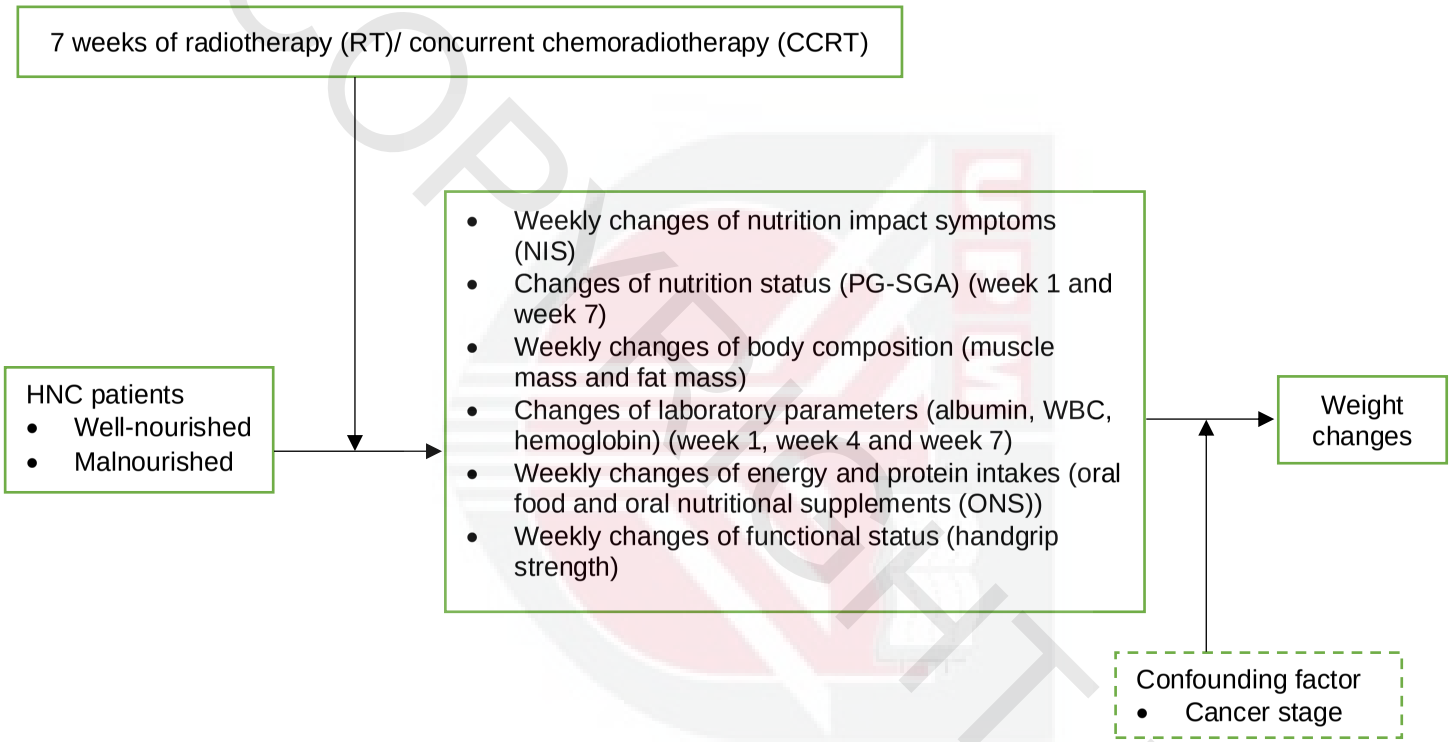

Figure 1.1: Conceptual Framework

1.6 Study Hypothesis

1. H1: There is a significant change in weight throughout RT or CCRT.
2. H1: There is a significant change in nutrition impact symptoms throughout RT or CCRT
3. H1: There is a significant change in nutritional status throughout RT or CCRT
4. H1: There is a significant change in functional status throughout RT or CCRT
5. H1: There are a significant association between changes in nutrition impact symptoms, nutritional status and functional status with weight loss among head and neck cancer patients throughout RT or CCRT

1.7 Glossary of terms

Cancer is a disease characterized by the development of abnormal cells outside their natural borders, which can then invade adjacent areas of the body and/or spread to other organs. Other common words used are malignant, tumours and neoplasms (National Cancer Institute, 2017).

Head and Neck cancer is classified as cancers arising in the oral cavity, oropharynx, hypopharynx, nasopharynx, larynx, nasal fossa, paranasal sinuses, and salivary glands (National Cancer Institute, 2017).

Radiotherapy is the use of high-energy radiation from x-rays, gamma rays, neutrons, protons, and other sources to destroy cancer cells and suppress tumors. Other common words used are irradiation and radiation therapy (National Cancer Institute, 2017).

Concurrent chemoradiotherapy is the combination of radiotherapy and chemotherapy treatment that is delivered at the same time. Chemotherapy treatment uses drugs to stop the cancer cells from developing, either by destroying cells or by preventing them from dividing (National Cancer Institute, 2017).

Nutrition impact symptoms are symptoms occur during cancer treatments procedures (nausea, vomiting, diarrhea, constipation, dysgeusia, depression, anxiety, pain) which deteriorates dietary intake (Kubrak et al., 2010).

Nutritional assessment is an approach to assess different aspects of nutrition included dietary intake, medical and medication history, anthropometric and physical examination as well as laboratory tests to identify nutritional status. (Ottery, 2000)

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