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Original Article

Assessment of Nutritional Status in Patients with Head and Neck Cancer Before Radiotherapy: A Single-center, Cross-sectional Study

Radyoterapi Öncesi Baş ve Boyun Kanseri Hastalarında Beslenme Durumunun Değerlendirilmesi: Tek Merkezli, Kesitsel Bir Çalışma

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ABSTRACT

Objective: It is important to assess nutritional status to determine the presence of malnutrition because poor nutritional status will reduce the efficacy and increase the side effects of radiotherapy. The aim of this research was to assess nutritional status by comparing several parameters, namely anthropometry, biochemistry, physical condition, and inflammatory parameters, with Patient Generated-Subjective Global Assessment (PG-SGA) as the gold standard.

Methods: A cross-sectional study with 78 subjects was conducted at the General Hospital Dr. Sardjito Yogyakarta, Indonesia, in 2022. The Malnutrition Screening Tool, Simple Nutrition Screening Tool, PG-SGA, and objective parameter data were used in the nutritional assessment. The objective parameters were determined by analyzing anthropometric data [body weight, mid-upper arm circumference (MUAC), and body fat], biochemical data (albumin and a complete blood profile), physical data (hand grip strength), and food intake data using the 1×24-hour recall method. The data were analyzed using One-Way ANOVA and the Kruskal-Wallis test.

Results: Malnutrition was found in 33.3% of pre-radiotherapy head and neck cancer (HNC) patients. Patients with good nutritional status did not experience weight loss, decreased appetite, gastrointestinal symptoms, decreased functional capacity, or fat and/or muscle deficit ($p<0.05$). The findings showed a significant relationship between PG-SGA and nutritional status based on body weight, weight loss, MUACs, handgrip strength, visceral fat, resting metabolic rate (RMR), and hemoglobin ($p<0.05$). A better nutritional status was associated with higher parameter values.

Conclusions: The method for nutritional status assessment in HNC patients undergoing radiotherapy can be performed by measuring body weight, weight loss, upper arm circumference, visceral fat, hemoglobin, and RMR in addition to PG-SGA as the gold standard.

Keywords: Head and neck cancer, nutritional status, malnutrition, PG-SGA, nutritional screening, nutritional assessment

ÖZ

Amaç: Kötü beslenme durumu radyoterapinin etkinliğini azaltacağından ve yan etkilerini artıracağından, malnütrisyon varlığını belirlemek için beslenme durumunu değerlendirmek önemlidir. Bu araştırmanın amacı, antropometri, biyokimya, fiziksel durum ve ayrıca enflamatuvar parametreler gibi çeşitli parametreleri altın standart olarak Hasta Tarafından Oluşturulan-Sübjektif Global Değerlendirme (PG-SGA) ile karşılaştırarak beslenme durumunu değerlendirmektir.

Yöntemler: Dr. Sardjito Genel Hastanesi Yogyakarta, Endonezya'da 2022 yılında 78 denekle kesitsel bir çalışma yürütüldü. Beslenme değerlendirmesinde Malnütrisyon Tarama Aracı, Basit Beslenme Tarama Aracı, PG-SGA ve objektif parametre verileri kullanıldı. Objektif parametreler antropometrik veriler [vücut ağırlığı, orta-üst kol çevresi (MUAC) ve vücut yağı], biyokimyasal veriler (albümin ve tam kan profili), fiziksel veriler (el kavrama gücü) ve 1×24 saatlik hatırlama yöntemi kullanılarak gıda alım verileri analiz edilerek belirlendi. Veriler Tek-Yönlü ANOVA ve Kruskal-Wallis testi kullanılarak değerlendirildi.

Bulgular: Radyoterapi öncesi baş ve boyun kanseri (BBK) hastalarının %33,3'ünde malnütrisyon saptandı. Beslenme durumu iyi olan hastalarda kilo kaybı, iştah azalması, gastrointestinal semptomlar, fonksiyonel kapasitede azalma ve yağ ve/veya kas eksikliği görülmedi ($p<0,05$). Bulgular, vücut ağırlığı, kilo kaybı, MUAC, el kavrama gücü, visseral yağ, istirahat metabolizma hızı (İMH) ve hemoglobin bazında PG-SGA ile beslenme durumu arasında anlamlı bir ilişki olduğunu gösterdi ($p<0,05$). Daha iyi beslenme durumu daha yüksek parametre değerleri ile ilişkilendirildi.

Sonuçlar: Radyoterapi gören BBK hastalarında beslenme durumunu değerlendirme yöntemi, altın standart olarak PG-SGA'ya ek olarak vücut ağırlığı, kilo kaybı, üst kol çevresi, visseral yağ, hemoglobin ve İMH ölçülerek yapılabilir.

Anahtar kelimeler: Baş ve boyun kanseri, beslenme durumu, malnütrisyon, PG-SGA, nütrisyonel tarama, nütrisyonel değerlendirme

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INTRODUCTION

Cancer was the first and second worldwide cause of premature death before the age of 70 in 91 of 172 countries in 2015. In 2018, there was a considerably high death rate for head and neck cancer (HNC) in the world, with approximately 330,000 cases out of 650,000 cases each year[1]. Data from Indonesia's Basic Health Research revealed that the prevalence of cancer in Indonesia has increased from 1.4 in 2013 to 1.8 per mile in 2018[2]. The World Health Organization Global Burden of Cancer Study (GLOBOCAN) reported 396,914 cancer cases and 234,511 deaths in Indonesia in 2020. Nasopharyngeal cancer as a type of HNC ranked the 4th most common cancer in men with 15,427 cases, accounting for 8.6% of all new cancer cases each year and more than 30% of the total[3].

Nutritional screening during 1-24 h of admission is the initial stage in assessing a patient's risk of malnutrition. Those at risk of malnutrition are distinguished from those who are not through the use of nutritional screening instruments. A dietician will provide additional intervention to patients at risk of malnutrition. Several nutrition screening tools are presently available to determine the risk of malnutrition, and each has benefits and drawbacks[4,5].

As previously mentioned, patients with cancer are at risk of experiencing malnutrition due to changes in metabolism and pathophysiology of the cancer itself as well as side effects of cancer treatment or therapy. It was revealed that 51% of cancer patients had nutritional issues, 43% were at risk, and 9% were malnourished. The degree of malnutrition is mostly related to the stage and location of the cancer, where malnutrition often occurs in HNC, gastroesophageal, upper gastrointestinal, pancreatic, and advanced lung cancer[6]. 30% of HNC patients experienced malnutrition before radiotherapy[7]. Other studies have shown an increased prevalence of malnutrition in patients with HNC from 11.9% before therapy to 49.4% after radiotherapy or chemoradiotherapy. Patients who were at risk of malnutrition before therapy had a lower survival rate than those who were at risk during therapy or were not at risk of malnutrition[8]. Malnutrition increases the risk of infection, delayed wound healing, impaired heart and lung function, depression, muscle weakness, poor quality of life, post-operative complications, decreased chemotherapy and radiotherapy response, and mortality in patients with HNC[9].

Prior to radiotherapy, it is crucial to pay close attention to the patient's nutritional status, as it will determine the success of the treatment. Patients at risk of malnutrition have lower body mass index (BMI), mid-upper arm circumference (MUAC), albumin, and hemoglobin (Hb) levels and longer length of stay than those without risk of malnutrition[10]. It is essential to perform screening and assessment of the risk of malnutrition to determine the right nutrition intervention as a way to improve the quality of life of HNC patients, especially those suffering from esophageal cancer[11]. Nutritional management can prevent weight loss, severe malnutrition, dysphagia, and health status in patients with HNC undergoing radiotherapy or radio chemotherapy, enhance therapy tolerance, and boost energy intake and quality of life[12]. Thus, a good nutritional status before radiotherapy is essential to avoid nutritional decline owing to side effects of radiotherapy. The purpose of this study was to assess the prevalence of malnutrition and nutritional status factors in patients with HNC before radiotherapy.

Cancer growth is linked to inflammation[13]. Inflammation precedes cancer and promotes all phases of carcinogenesis. Cancer cells and surrounding stromal and inflammatory cells generate an inflammatory tumor microenvironment through well-orchestrated reciprocal interactions. Approximately 15-20% of all cancers are caused by infection, prolonged inflammation, or autoimmunity at the same tissue or organ site[14].

The involvement of inflammation in the pathogenesis of malnutrition is significant. Increased systemic inflammation can substantially increase the risk of malnutrition. Changes in serum levels of pro-inflammatory factors are potential predictors of malnutrition, and the effect of oral nutritional supplements is pronounced in patients who show no symptoms of persistent inflammatory activity. Increased muscle catabolism, also known as sarcopenia, is caused by inflammation and is associated with a decline in nutritional status and clinical outcomes[15].

Radiation has two effects on tumor patients' immune systems as a holistic treatment. Radiation kills tumor cells but also non-selectively kills immune cells, resulting in low immune function and suppressed immunological response. Inflammatory factor levels were considerably increased before radiotherapy in esophageal cancer patients, intensified after radiotherapy, and positively linked with myelosuppression and irradiation volume. In addition, immunological parameter recovery improved patient prognosis[16].

This study aimed to determine the nutritional status of HNC patients before undergoing radiotherapy by comparing several parameters of nutritional status (anthropometric, biochemical, physical condition) and inflammation with Patient-Generated Subjective Global Assessment (PG-SGA) as the gold standard.

MATERIALS and METHODS

Study and Patients

Ethical approval for this study was obtained from the ethics commission of The Medical and Health Research Ethics Committee of the Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Indonesia, with ethical clearance number KE/FK/0316/EC/2022 (approval date: 23.03.2022). A cross-sectional study was conducted in the Radiotherapy Unit of Dr. Sardjito General Hospital Yogyakarta, Indonesia, from April to November 2022. Samples were selected using the consecutive sampling method involving patients diagnosed with HNC who were scheduled to undergo radiotherapy at the radiology department of Dr. Sardjito General Hospital. The subjects were selected on the basis of the inclusion criteria of patients over 18 years old and willing to participate in signing an informed consent form. Patients who could not stand upright were excluded from the study because they could not be weighed.

Data Collection

This study used nutritional status assessment using anthropometry, biochemistry, physical examination, and intake as the research instrument. Anthropometric measurements include measurements of body weight, height, BMI, weight loss, and upper arm circumference. BMI is measured by the ratio of body weight (kg) to height (m) [BMI = weight (kg)/height (m^2)] and is classified as malnourished if <18.5 kg/m^2. Weight change formula: (current weight-usual weight). Patients' height was measured with a stadiometer, upper arm circumference was measured using medline and classified as malnourished if <23.5 cm; body weight, body fat, visceral fat, and resting metabolism were measured with Omron brand Type HBF 378 digital scales. Handgrip strength was measured for physical measurement using a handgrip dynamometer. Food intake was measured using the 1×24-hour food recall interview method for further analysis using nutrisurvey software. Albumin levels in blood were analyzed using ABX Pentra 400 by colorimetric method with normal values of 3.5-5 g/dL for all genders; Hb levels, leukocyte, lymphocyte, and neutrophil profiles were analyzed using a hematology analyzer. The neutrophil-to-lymphocyte ratio (NLR) was calculated by a simple ratio between neutrophils and lymphocytes, with <5 indicated as normal. Normal Hb values for females were 12 g/dL and for males were 13 g/dL; total lymphocyte cell <1500 cells/mm^3 indicated malnutrition.

The nutritional status of cancer patients was evaluated at the beginning of the study using two screening instruments: the Malnutrition Screening Tool (MST) and the Simple Nutrition Screening Tool (SNST). The MST comprises two questions with points ranging from 0 to 7[17]. SNST is a six-question simple nutritional screening tool devised in Indonesia that excludes anthropometric measurements and weight loss[5]. Both screening tools were used in this study because they have simpler questions, are subjective, do not require measurement, are simple to use, and are suitable for Indonesian conditions. The cut-off point for each nutrition screening tool is as follows: MST ≥2 and SNST ≥3. Comprehensive nutritional status was assessed using the gold standard PG-SGA, which provides additional information regarding nutritional symptoms and short-term weight loss. The PG-SGA is divided into two sections. The patient completes the first section using a checkbox format, while the second section is a physical examination. Malnutrition criteria were determined based on the results of the PG-SGA scores, which were categorized into three groups: those scored 0-3 (non-malnourished /score A), 4-8 (moderate malnutrition/score B), and ≥9 (severe malnutrition/score C)[18].

Statistical Analysis

IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp. was used to examine the statistical data. Descriptive data were used to provide comparative data on patient characteristics in each group. Patient characteristics in each group were compared and presented descriptively. Nutritional status parameters were compared in the form of anthropometric, biochemical, and nutrient intake data between 3 groups to be analyzed using One-Way ANOVA for data with normal distribution and Kruskal-Wallis for data with non-normal distribution. Post-hoc tests were also used for multiple comparisons of the three categories. Pairwise comparison was used for Kruskal-Wallis test, while Bonferroni was used for ANOVA. Chi-square was used to analyze nutrition screening data (MST, SNST) with PG-SGA.

RESULTS

Sixty-four percent (n=50) of the patients included in the study were male. Most subjects (n=36 or 46%) had cancer in the pharynx, especially the nasopharynx. Based on the stage of cancer, 36.4% (n=16) with stage IV cancer experienced malnutrition. Those in the moderate and severe malnutrition group mostly had previously undergone chemotherapy or surgery, as described in Table 1.

Table 1. Patient's characteristics.

Nutritional parameters	PG-SGA			
	Well nourished (score 0-3)	Moderately malnourished (score 4-8)	Severely malnourished (score ≥9)	p-value
n (%)	52 (66.7)	17 (21.8)	9 (11.5)	-
Age, n (%)				
Adult (<60 years)	30 (61.2)	11 (22.4)	8 (16.3)	0.199
Elderly (≥60 years)	22 (75.9)	6 (20.7)	1 (3.4)	
Sex, n (%)				
Male	41 (71.9)	10 (17.5)	6 (10.5)	0.244
Female	11 (52.4)	7 (33.3)	3 (14.3)	
Cancer location, n (%)				
Pharynx*	25 (73.5)	5 (14.7)	4 (11.8)	-
Larynx	12 (75)	3 (18.8)	1 (6.3)	-
Salivary gland*	4 (57.1)	3 (42.9)	0 (0)	0.296
Paranasal and nasal cavity	4 (57.1)	2 (28.6)	1 (14.3)	-
Oral cavity*	6 (75.0)	1 (12.5)	1 (12.5)	-
Tongue	1 (16.7)	3 (50)	2 (33.3)	-
Cancer stage, n (%)				
Not identified	9 (56.3)	6 (37.5)	1 (6.3)	0.276
I + II	5 (83.3)	1 (16.7)	0 (0)	
III	10 (83.3)	2 (16.7)	0 (0)	
IV	28 (63.6)	8 (18.2)	8 (18.2)	
Treatment history, n (%)				
Surgery and chemotherapy	28 (57.1)	13 (26.5)	8 (16.3)	0.056
Never had therapy before	24 (82.8)	4 (13.8)	1 (3.4)	

PG-SGA: Patient Generated-Subjective Global Assessment

*Cancer location: Pharynx (nasopharynx, oropharynx); salivary gland (mucoepidermoid, parotid); oral cavity (maxilla, mandibule, gingiva, palatum)

In the severe malnutrition group, as shown in Table 2, more subjects experienced weight loss, decreased appetite, gastrointestinal disorders or symptoms, decreased functional capacity, and decreased fat and muscle reserves compared with the group with moderate malnutrition or good nutritional status. The MST and SNST screening results revealed that 94% and 72.9% of HNC patients who were not at risk of malnutrition had good nutritional status, respectively, based on PG-SGA ($p<0.001$).

Table 3 shows some significant differences between nutritional status as indicated by the anthropometric parameters in the form of MUAC, grip strength, body weight, and changes in body weight, visceral fat, and resting metabolism. In addition, nutritional status as indicated by biochemical data showed significant differences in Hb levels between groups with good nutritional status and those with moderate and severe malnutrition. It was clear that the more severe the malnutrition condition, the lower the anthropometric parameters and Hb levels. In the inflammatory data, a more severe degree of malnutrition was associated with an increase in neutrophils and NLR, but the difference was not statistically significant.

DISCUSSION

Malnutrition was found in 33.3% of pre-radiotherapy HNC patients and was classified as moderate or severe. Malnutrition affects up to 3-52% of HNC patients during the pre-therapy phase[19]. An increase in the prevalence of malnutrition occurs up to 88% in patients with HNC during therapy and during the rehabilitation period. The data on subject characteristics denote that there were more men than women who suffered from HNC (64% vs. 36%). In the severe malnutrition group, almost

Table 2. Nutrition impact symptom and nutritional screenings.

Nutritional parameters	PG-SGA			
	Well nourished (score 0-3)	Moderately malnourished (score 4-8)	Severely malnourished (score ≥9)	p-value
Weight loss, n (%)				
No	47 (94.0)	3 (6.0)	0 (0)	**<0.001**
Yes	5 (17.9)	14 (50.0)	9 (32.1)	
Decrease in dietary intake, n (%)				
No	52 (83.9)	9 (14.5)	1 (1.6)	**<0.001**
Yes	0 (0)	8 (5.0)	8 (50.0)	
Gastrointestinal symptoms, n (%)				
No	49 (83.1)	9 (15.3)	1 (1.7)	**<0.001**
Yes	3 (15.8)	8 (42.1)	8 (42.1)	
Decrease in functional capacity, n (%)				
No	46 (74.2)	12 (19.4)	4 (6.5)	**0.006**
Yes	6 (37.5)	5 (31.3)	5 (31.3)	
Deficit fat and/or muscle, n (%)				
No	52 (74.3)	13 (18.6)	5 (7.1)	**<0.001**
Yes	0 (0)	4 (50.0)	4 (50.0)	
MST, n (%)				
Not at risk	48 (94.1)	3 (5.9)	0 (0)	**<0.001**
Risk	4 (14.8)	14 (51.9)	9 (33.3)	
SNST, n (%)				
Not at risk	51 (72.9)	16 (22.9)	3 (4.3)	**<0.001**
Risk	1 (12.5)	1 (12.5)	6 (75)	

MST: Malnutrition Screening Tools, SNST: Simple Nutrition Screening Tool, PG-SGA: Patient Generated-Subjective Global Assessment

Table 3. Comparison of nutritional parameters.

Parameters	PG-SGA				
	Well nourished (score 0-3)	Moderately malnourished (score 4-8)	Severely malnourished (score ≥9)	p-value	95% CI
Nutritional parameters					
Actual weight, kg**	63.16±16.26[a]	54.72±10.64[a,b]	52.70±16.31[b]	**0.048**	0.002-0.022
Weight change, kg**	1.61±5.17[a]	-1.45±2.12[b]	-5.02±2.41[b]	**<0.001**	-0.093- -0.04
BMI, kg/m2*	23.64±4.94	22.32±4.40	20.00±4.00	0.093	0.003-0.067
MUAC, cm*	26.28±4.40[a]	24.12±3.30[a,b]	22,67±3.85[b]	**0.028**	0.013-0.082
HGS, kg**	27.54±12.46[a]	19.38±7.92[b]	20.48±5.53[a,b]	**0.017**	0.004-0.03
Visceral fat, %**	9.54±6.59[a]	6.72±4.21[a,b]	4.92±3.62[b]	**0.045**	0.007-0.057
Albumin, g/dL*	4.17±0.46	4.10±0.54	3.86±0.42	0.169	-0.16-0.634
Hemoglobin, g/dL*	12.65±1.89[a]	10.94±2.84[b]	10.73±1.58[b]	**0.003**	0.044-0.177
TLC, cell/mm3*	1420.50±806.4	1113.85±545.0	1540±1206	0.318	0.000-0.000
RMR*	1455.1±274.6[a]	1288.2±153.2[b]	1270.2±303.7[a,b]	**0.024**	0.000-0.001
Inflammation parameters					
Lymphocyte*	1.71±0.65	1.45±0.60	1.72±0.79	0.185	-0.117-0.366
Neutrophile*	4.82±2.13	4.91±3.10	5.98±3.21	0.433	-0.99-0.027
NLR**	1.88±0.32	1.76±0.44	1.67±0.50	0.190	-0.030-0.799

PG-SGA: Patient Generated-Subjective Global Assessment, BMI: Body mass index, MUAC: Mid-upper arm circumference, HGS: Hand grip strength, TLC: Total lymphocyte cell, RMR: Resting metabolic rate, CI: Confidence interval, NLR: Neutrophil-to-lymphocyte ratio

*One-Way ANOVA test, **Kruskal-Wallis test, [a,b]Post-Hoc test (Bonferroni for ANOVA and Pair wise comparison for Kruskal-Wallis test), with distinct letters denoting statistically significant differences

80% had undergone chemotherapy. Cancer therapy, either chemotherapy or chemoradiotherapy, is a strong predictor of malnutrition in patients with HNC, where there is an increased risk of malnutrition by 5x higher than that in patients without chemoradiotherapy[20].

Although the results in this study showed that cancer stage and therapy history in patients with HNC with nutritional status did not show significant results. However, literature studies have shown that HNC patients with poor nutritional status are associated with early death in stage III and IV disease[21]. Chemoradiation is often linked to mucositis, odynophagia, dysgeusia, nausea, vomiting, dysphagia, and tiredness, all of which make it difficult to eat[22]. Surgery releases stress hormones and inflammatory agents, catabolizing glycogen, fat, and protein and releasing glucose, amino acids, and free fatty acids into the circulation[23]. This can cause patients with a history of chemoradiation or previous surgical intervention to have a worse nutritional status than patients who have not undergone such therapy.

The duration of cancer diagnosis and the timing of their previous therapy remain unknown in this study. A prior study reported that cancer is a persistent ailment that frequently leads to significant weight reduction, perhaps progressing to cachexia. This phenomenon arises from an elevation in the metabolic rate among individuals with cancer, which progressively intensifies and impairs the body's capacity to fulfill these requirements. As the duration of a patient's cancer diagnosis increases, their body's energy reserves will also increase. This can lead to malnutrition and a decline in their nutritional state[24]. The research subjects exhibited a range of cancer stages, including a notable number of subjects with early-stage cancer. The study by Deng et al.[25] revealed that individuals with advanced HNC are more susceptible to malnutrition. This is primarily attributed to the heightened metabolic rate caused by the rapid growth of cancer cells and the intensified inflammatory response. Consequently, there is an elevated demand for energy and increased protein breakdown, reducing muscle mass[25].

Furthermore, some research participants had undergone cancer treatment in the form of surgical intervention or chemotherapy before radiotherapy. Zeidler et al.[26] reported a significant alteration in the patient's weight and nutritional condition over the course of cancer treatment. A study by Bach et al.[27], 2020 found a notable alteration in the body weight of colorectal cancer patients before surgery and up to 7 days post-surgery. There was a reduction in weight of approximately 1.8 kg from pre-surgery to 7 days post-surgery. Treatment administered to patients with HNC has a lasting impact on their nutritional status, persisting for several months after the completion of treatment. It may take up to 3 months for their nutritional status to partially recover, but it does not fully return to its pre-treatment level[27]. In a study conducted by Mulasi et al.[28] in 2018, it was found that the nutritional status, as measured by the PG-SGA score, deteriorated throughout chemoradiotherapy and continued to decrease until the completion of treatment. However, the score started to improve between 1 and 3 months after the treatment. In addition, there was a decrease in body weight over the course of the therapy, which continued for up to one month after the therapy. Nevertheless, after three months post-therapy, there was an increase in body weight, although it did not return to the initial weight before treatment[28].

Signs of malnutrition were also observed from the weight loss experienced by all subjects in the group of patients with severe malnutrition. Most patients with severe malnutrition complained of gastrointestinal symptoms. The main cause of malnutrition in cancer patients is anorexia associated with disturbances in taste, such as changes in the perception of taste and smell, which can inhibit food intake. Malnutrition is characterized by decreased functional capacity in addition to decreased food intake and body weight, whereas severe malnutrition is closely associated with a decrease in muscle mass with or without a decrease in fat mass[29].

Cancer can have a very harmful effect on nutritional status. Not only do cancer cells take nutrients from the patient's body, but treatment and the physiological consequences of cancer itself can interfere with maintaining adequate nutrition[18]. From Table 2, it appears that the more severe the malnutrition, the lower and the less patients' weight. Nausea, diarrhoea, changes in smell and taste, medication side effects, stress, and discomfort have all been linked to decreased food intake and eventually, weight loss in patients with more severe malnutrition. In addition, the screening results revealed that a higher PG-SGA score indicates a greater risk of malnutrition. Previous studies have revealed that SNST and MST have high sensitivity and specificity for determining cancer patients at risk of malnutrition[30]. This is because both the MST and SNST nutrition screening tools have parameterized questions measuring weight loss and appetite reduction. Furthermore, the SNST contains fatigue questions that describe the patient's medical history.

Another notable finding is related to the evaluation of the nutritional status of lean body mass, one of which is the MUAC measurement[31]. Table 3 shows that the MUAC in the non-malnourished group is greater than that in the moderate and severe malnourished group, which reflects that malnutrition will reduce lean body mass due to the dismantling of energy reserves that come from sources other than fat stores.

Grip strength is a general indicator of muscle strength because it is associated with upper body strength. Table 3 shows that the grip strength of the non-malnourished group was greater than that of the moderately and severely malnourished group. Another study disclosed that there was no significant correlation between the PG-SGA scores, which indicated a relationship between the incidence of malnutrition and the handgrip strength of cancer patients, but individuals who were malnourished tended to have lower grip strength[32].

Visceral fat was significantly lower in cancer patients who had lost weight than in patients without weight loss. Low visceral fat content indicates a state of malnutrition. The decrease in body fat in cancer patients results from a proinflammatory process[9]. This fact is apparent from Table 3, which indicates lower visceral fat and higher weight loss at more severe degrees of malnutrition. Apart from indicating malnutrition, visceral fat is also associated with the severity of cancer. Visceral fat was found to be lower in patients with advanced cancer than in those with an early stage cancer[33].

Reduced food intake and metabolic disturbances [such as increased resting metabolic rate (RMR), insulin resistance, impaired lipolysis, and proteolysis] are caused by systemic inflammation and cancer cell-derived catabolic factors. This systemic inflammation increases RMR in cancer patients, which has a strong correlation with weight loss. RMR expenditure is the quantity of energy expended in 24 h without loss of lean body mass[34].

The results of this study indicate that the more severe the degree of malnutrition, the lower the patient's intake and the lower the RMR. RMR is linked to appetite and energy intake and regulates energy homeostasis. Consequently, when energy intake is inadequate, patients tend to have a lower RMR[35].

Malnutrition in patients with cancer can be assessed by screening and nutritional examination through anthropometry, assessment of muscle function and strength, food intake, laboratory tests such as albumin, prealbumin, and transferrin, immune and inflammatory biomarkers, and assessment of quality of life. Serum protein measurements can provide indirect information about the levels of visceral proteins, for example albumin, which are also frequently used in nutritional status screening[36]. Table 3 denotes that albumin levels are within the normal range and show no significant difference between the 3 groups. High or low levels of albumin in the body can be attributed to various factors, such as food intake, especially protein, inflammatory response, and malnutrition[37]. Serum albumin only has a prognostic value for the prevalence of malnutrition, where there is a relationship between serum albumin levels and malnutrition, but it cannot be used as a marker of nutritional status. Albumin is a better indicator of inflammation than nutritional status[38].

Table 3 implies that the more severe the degree of malnutrition, the lower the average Hb level. Malnourished cancer patients had lower Hb levels than those who were not malnourished[39]. Interleukin-6 and reactive oxygen species stimulate hepcidin, which depletes ferroportin and limits iron absorption from the small intestine and macrophages, resulting in an iron deficit for heme synthesis in cancer-related malnutrition. In addition, cancer metabolism disorders of nutrients often occur, including glucose metabolism disorders, which can cause low Hb levels. This is due to the Krebs cycle's impact on the availability of substrates for heme synthesis[40].

Chronic inflammation is the pathological basis of malignancy in humans. Malignancy occurs at sites of chronic inflammation, and inflammatory cells are found at the time of tumor tissue biopsy. Tissue damage (physical, chemical, infection) will trigger an inflammatory response, which is an important mechanism against damage-causing agents and initiates the process of tissue repair by forming an immune response. Low lymphocyte and neutrophil counts are linked to poor prognosis in patients with advanced cancer[38]. On this basis, the indicators of inflammation only describe the malignancy of the disease, but do not describe the level of malnutrition; thus, there is no difference in the levels of inflammatory indicators, be it in the form of leukocytes, lymphocytes, or neutrophils, between the two groups.

The majority of HNC patients (66.7%) had good nutritional status prior to radiotherapy in this study. Therefore, nutritional screening and assessment are important to perform prior to radiotherapy so that they can serve as the basis for future nutritional interventions, even before treatment or therapy begins. Particularly in patients at moderate to high risk of malnutrition.

This study has certain limitations, specifically the heterogeneity of cancer stages and the interval between cancer diagnosis and radiotherapy initiation. In addition, there was variation in the treatment administered to the research participants before radiotherapy, as well as differences in the time interval between previous treatment and radiotherapy. Furthermore, a subset of subjects had no prior experience with cancer therapy. This can exert an influence on the advancement of cancer, thereby affecting the nutritional health of the individual. Therefore, it is advisable to conduct more studies to narrow down the scope, such as investigating advanced HNC cases that have not undergone any cancer treatment previously.

CONCLUSION

The method for assessing nutritional status in HNC patients undergoing radiotherapy can be performed by measuring body weight, weight loss, upper arm circumference, visceral fat, Hb, and RMR in addition to PG-SGA as the gold standard.

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Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the ethics commission of The Medical and Health Research Ethics Committee of Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada, Indonesia with ethical clearance number KE/FK/0316/EC/2022 (approval date: 23.03.2022).

Informed Consent: The participants/patients gave their written informed consent to take part in this study. Individual(s) provided written informed consent for the publication of any potentially identifiable images or data in this article.

Author Contributions

Surgical and Medical Practices: S.S., F.N.K., A.S.S., M.H., E.E., Concept: S.S., F.N.K., M.H., Design: S.S., Data Collection and/or Processing: F.N.K., M.H., E.E., Analysis and/or Interpretation: S.S., F.N.K., A.S.S., Literature Search: S.S., A.S.S., Writing: F.N.K., A.S.S.

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REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68:394-424.
2. Kementerian Kesehatan Republik Indonesia. Hasil utama riskesdas 2018. Riset Kesehatan Dasar. Jakarta, Indonesia; 2018.
3. WHO. Indonesia Fact Sheets: Cancer [Internet]. Globocan. 2020. Available from: https://gco.iarc.fr/today/data/factsheets/populations/360-indonesia-fact-sheets.pdf
4. Rasmussen HH, Holst M, Kondrup J. Measuring nutritional risk in hospitals. Clin Epidemiol. 2010;2:209-16.
5. Susetyowati, Hadi H, Hakimi M, Asdie AH. Development, validation and reliability of the simple nutrition screening tool (SNST) for adult hospital patient in Indonesia. Pakistan J Nutr. 2014;13:157-63.
6. Marshall KM, Loeliger J, Nolte L, Kelaart A, Kiss NK. Prevalence of malnutrition and impact on clinical outcomes in cancer services: A comparison of two time points. Clin Nutr. 2019;38:644-51.
7. Kono T, Sakamoto K, Shinden S, Ogawa K. Pre-therapeutic nutritional assessment for predicting severe adverse events in patients with head and neck cancer treated by radiotherapy. Clin Nutr. 2017;36:1681-5.
8. Liu W, Gao L, Huang X, et al. Pretreatment nutritional risk as a prognostic factor in head and neck cancer patients receiving radiotherapy or chemoradiotherapy. Asia Pac J Clin Nutr. 2019;28:223-9.
9. Talwar B, Donnelly R, Skelly R, Donaldson M. Nutritional management in head and neck cancer : United Kingdom National Multidisciplinary Guidelines. J Laryngol Otol. 2016;130:32-40.
10. Susetyowati, Hadi H, Hakimi M, Asdie AH. Comparison of Nutrition Screening and Assessment Parameters in Predicting Length of Hospital Stay. J Nutr Med Diet Care. 2018;4:1-9.
11. Cao J, Xu H, Li W, et al. Nutritional assessment and risk factors associated to malnutrition in patients with esophageal cancer. Curr Probl Cancer. 2021;45:100638.
12. Yanni A, Dequanter D, Lechien JR, et al. Malnutrition in head and neck cancer patients: Impacts and indications of a prophylactic percutaneous endoscopic gastrostomy. Eur Ann Otorhinolaryngol Head Neck Dis. 2019;136:27-33.
13. Korniluk A, Koper O, Kemona H, Dymicka-Piekarska V. From inflammation to cancer. Ir J Med Sci. 2017;186:57-62.
14. Greten FR, Grivennikov SI. Inflammation and Cancer: Triggers, Mechanisms, and Consequences. Immunity. 2019;51:27-41.
15. Zheng K, Liu X, Ji W, Lu J, Cui J, Li W. The Efficacy of Different Inflammatory Markers for the Prognosis of Patients with Malignant Tumors. J Inflamm Res. 2021;14:5769-85.
16. Wang XB, Wu DJ, Chen WP, Liu J, Ju YJ. Impact of radiotherapy on immunological parameters, levels of inflammatory factors, and clinical prognosis in patients with esophageal cancer. J Radiat Res 2019;60:353-63.
17. Serón-Arbeloa C, Labarta-Monzón L, Puzo-Foncillas J, et al. Malnutrition Screening and Assessment. Nutrients. 2022;14:2392.
18. Cederholm T, Bosaeus I, Barazzoni R, et al. Diagnostic criteria for malnutrition e An ESPEN Consensus Statement. Clin Nutr. 2015;34:335-40.

19. Gorenc M, Kozjek NR, Strojan P. Malnutrition and cachexia in patients with head and neck cancer treated with (chemo) radiotherapy. Rep Pract Oncol Radiother. 2015;20:249-58.
20. Silander E, Nyman J, Hammerlid E. An exploration of factors predicting malnutrition in patients with advanced head and neck cancer. Laryngoscope. 2013;123:2428-34.
21. Mantzorou M, Koutelidakis A, Theocharis S, Giaginis C. Clinical Value of Nutritional Status in Cancer: What is its Impact and how it Affects Disease Progression and Prognosis? Nutr Cancer. 2017;69:1151-76. http://dx.doi.org/10.1080/01635581.2017.1367947
22. Couch ME, Dittus K, Toth MJ, et al. Cancer cachexia update in head and neck cancer: Definitions and diagnostic features. Head Neck. 2015;37:594-604.
23. Braga M, Wischmeyer PE, Drover J, Heyland DK. Clinical evidence for pharmaconutrition in major elective surgery. JPEN J Parenter Enteral Nutr. 2013;37(5 Suppl):66-72.
24. Kim DH. Nutritional issues in patients with cancer. Intest Res. 2019;17:455-62.
25. Deng LH, Chi K, Zong Y, Li Y, Chen MG, Chen P. Malnutrition in patients with head and neck cancer undergoing radiotherapy: A cross-sectional study. Eur J Oncol Nurs. 2023;66:102387.
26. Zeidler J, Kutschan S, Dörfler J, Büntzel J, Huebner J. Impact of nutrition counseling on nutrition status in patients with head and neck cancer undergoing radio- or radiochemotherapy: a systematic review. Eur Arch Otorhinolaryngol. 2024.
27. Bach HV, Thao NT, Thi N, et al. Nutritional status and diet of preoperative and 7 days postoperative patients with colorectal cancer at National Cancer Hospital 2018-2019 . J Public Heal Nutr. 2020;3.235-40.
28. Mulasi U, Vock DM, Kuchnia AJ, et al. Malnutrition Identified by the Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition Consensus Criteria and Other Bedside Tools Is Highly Prevalent in a Sample of Individuals Undergoing Treatment for Head and Neck Cancer. JPEN J Parenter Enteral Nutr 2018;42:139-47.
29. Viana ECRM, Oliveira IDS, Rechinelli AB, et al. Malnutrition and nutrition impact symptoms (NIS) in surgical patients with cancer. PLoS One. 2020;15:e0241305.
30. Susetyowati S, Sarasati RM, Rizqi F, Sanubari NDG, Nuraini A. Determining the Valid Tools to Screen Malnutrition in Cancer Patients: A Comparison to Patient Generated-Subjective Global Assessment (PG-SGA). J Gizi Indones (The Indones J Nutr). 2022;11:49-56.
31. Sarkar D, Shettigar P, Prahlad HY. Effect of diet counseling on anthropometric indices and dietary intake of the head and neck cancer patients undergoing chemo-radiotherapy. Int J Innov Technol Explor Eng. 2019;8(11 Suppl 2):400-5.
32. Alkan ŞB, Artaç M, Rakıcıoğlu N. The relationship between nutritional status and handgrip strength in adult cancer patients: a cross-sectional study. Support Care Cancer. 2018;26:2441-51.
33. Agustsson T, Wikrantz P, Rydén M, Brismar T, Isaksson B. Adipose tissue volume is decreased in recently diagnosed cancer patients with cachexia. Nutrition. 2012;28:851-5.
34. Van Soom T, El Bakkali S, Gebruers N, Verbelen H, Tjalma W, van Breda E. The effects of chemotherapy on energy metabolic aspects in cancer patients: A systematic review. Clin Nutr. 2020;39:1863-77.
35. Schofield KL, Thorpe H, Sims ST. Resting metabolic rate prediction equations and the validity to assess energy deficiency in the athlete population. Exp Physiol. 2019;104:469-75.
36. Unal D, Orhan O, Eroglu C, Kaplan B. Prealbumin is a more sensitive marker than albumin to assess the nutritional status in patients undergoing radiotherapy for head and neck cancer. Contemp Oncol (Pozn). 2013;17:276-80.
37. Bharadwaj S, Ginoya S, Tandon P, et al. Malnutrition: Laboratory markers vs nutritional assessment. Gastroenterol Rep (Oxf). 2016;4:272-80.
38. Bullock AF, Greenley SL, McKenzie GAG, Paton LW, Johnson MJ. Relationship between markers of malnutrition and clinical outcomes in older adults with cancer: systematic review, narrative synthesis and meta-analysis. Eur J Clin Nutr. 2020;74:1519-35.
39. Enkobahry A, Sime T, Kene K, Mateos T, Dilnesa S, Zawdie B. Blood biomarkers as potential malnutrition screening alternatives among adult patients with cancer on treatment in oncology unit of jimma tertiary hospital: A cross-sectional analysis. BMC Nutr. 2023;9:38.
40. Chiabrando D, Vinchi F, Fiorito V, Mercurio S, Tolosano E. Heme in pathophysiology: a matter of scavenging, metabolism and trafficking across cell membranes. Front Pharmacol. 2014;5:61.