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Research Article

CORRELATION BETWEEN DIETARY SELENIUM INTAKE AND CHANGES IN FAT-FREE MASS INDEX AND HANDGRIP STRENGTH IN HEAD-AND-NECK CANCER PATIENTS UNDERGOING CHEMORADIATION THERAPY

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ABSTRACT

Objectives: The purpose of this study was to analyze the correlation between dietary selenium intake in fat-free mass index (FFMI) and handgrip strength among head-and-neck cancer patients undergoing chemoradiation therapy.

Methods: A 2-week prospective cohort study was conducted at the Radiotherapy Unit of Dr. Cipto Mangunkusumo National General Hospital. Dietary selenium intake was estimated using the semi-quantitative food frequency questionnaire. FFMI was measured using bioelectrical impedance analysis (seca mBCA 525) and handgrip strength (HGS) using a Jamar dynamometer.

Results: Fifty-three patients (median age 49 years) were included. Median dietary selenium intake was 81.3 μg/day. No significant correlation was observed between dietary selenium intake and changes in FFMI or HGS after adjustment for confounders. A weak correlation was found in the non-active hand (p=0.045), which should be interpreted with caution due to the short duration of observation and possible confounding.

Conclusion: Within this short 2-week observation, dietary selenium intake was not significantly associated with changes in FFMI or HGS. The borderline finding in the non-active hand is likely an anomalous result and should be interpreted with caution. Longer-term studies with biomarker assessments are warranted.

Keywords: Head-and-neck cancer, Chemoradiation, Dietary selenium intake, Handgrip strength, Fat-free mass index.

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INTRODUCTION

Head-and-neck cancer (HNC) is predominantly squamous cell carcinoma originating from the mucosal epithelium of the oral cavity, pharynx, larynx, vocal cords, salivary glands, or paranasal sinuses and may also involve muscles or nerves within the head-and-neck region [1]. Globally, HNC was reported as the seventh most common cancer in 2018, with around 890,000 new cases and 450,000 deaths [2,3]. HNC in Indonesia in 2020 originated from the type of nasopharyngeal cancer in men, around 8.4% [4].

In HNC, metabolic changes occur that support cancer cell growth. Cancer cells can stimulate the innate immune system (macrophages and dendritic cells) and stimulate the release of proinflammatory cytokines, especially tumor necrosis factor alpha (TNF-α). TNF-α triggers the release of proteolysis-inducing factor, which can induce proteolysis so that cancer patients are more susceptible to malnutrition characterized by a decrease in fat-free mass [5,6]. From research by Lapornik *et al*., [7] the main nutritional problems in cancer are decreased muscle mass, weight loss, and fat-free mass. Decreased muscle mass will lead to decreased functional capacity, a higher incidence of chemoradiation toxicity, increased hospitalization and complication rates, and mortality. According to research by Cosway *et al*., [8] 77 HNC patients had a low handgrip strength (HGS). In addition to disease factors, cancer therapy also contributes to an increased risk of malnutrition. Chemoradiotherapy can cause mucositis, dysphagia, odynophagia, dysgeusia, xerostomia, thick saliva, nausea, and vomiting, which can reduce energy, protein, and selenium intake [9,10]. According to research by Löser *et al*., [10] malnutrition occurs in HNC with chemoradiotherapy and decreases at the end of radiotherapy (p<0.001). A decrease in fat-free mass index (FFMI) can be observed within 2 weeks, according to research by Ding *et al*., [11] in nasopharyngeal cancer patients undergoing chemoradiotherapy.

Selenium functions through selenoproteins that incorporate the amino acid selenocysteine. These proteins, including glutathione peroxidase, play a vital role in protecting cells from oxidative stress and supporting musculoskeletal integrity. Evidence suggests that inadequate selenium intake is associated with impaired muscle strength and sarcopenia, whereas sufficient intake may contribute to the preservation of muscle mass and function [13-15].

Despite this, research on selenium intake and its relationship with body composition and muscle strength in cancer patients undergoing (chemo)radiotherapy remains limited. This study therefore aimed to investigate the correlation between dietary selenium intake, FFMI, and HGS among patients with HNC receiving chemoradiation therapy.

METHODS

Research design and population

This study used a prospective cohort design in adult HNC subjects undergoing chemoradiation at the Radiotherapy Outpatient Clinic of Dr. Cipto Mangunkusumo National Hospital, Jakarta, Indonesia, from March 2025 to May 2025. Subjects were recruited using a consecutive sampling method, with the inclusion criteria being aged over 18 years and undergoing chemoradiation. The primary outcome of this study was the correlation between selenium intake and changes in HGS and FFMI.

Data collection

Subjects were interviewed based on age and gender. Selenium intake was assessed using a semi-quantitative food frequency questionnaire (SFFQ), and energy and protein intake were obtained from a 24-h recall. HGS was assessed using a hand grip ®Jamar, and FFMI was assessed using bioelectrical impedance analysis (BIA)® seca mBCA 525. Food photo books (Food photo book for portion size estimation) were used to visualize estimated portion sizes. Cancer stage and cancer location were obtained from medical records.

Ethical approval

The study protocol was reviewed and approved by the Institutional Ethics Committee (Approval No: KET-240/UN2.F1/ETIK/PPM 00.02/2025). Ethical standards were maintained throughout the study in accordance with the Declaration of Helsinki.

Statistical analysis

Data analysis was performed using the Statistical Package for the Social Sciences version 26. Normal data distribution was assessed based on a p>0.05 using the Kolmogorov–Smirnov test. The mean and standard deviation were used to describe normally distributed data, while the median with minimum-maximum values was used for non-normally distributed data. Bivariate analysis was performed to assess the correlation between selenium intake and changes in FFMI and HGS. The analysis was performed using the Spearman rank correlation test. The analysis used a 95% confidence interval with a significance limit of p<0.05.

RESULTS

A total of 53 participants enrolled in this study. Participants ranged in age from 20 to 59 years, with a median of 49 years. Most participants were male, had normal nutritional status, were diagnosed at stage IV, had cancer in the nasopharynx, and had histopathological features of squamous cell carcinoma. The FFMI was still categorized as adequate at 47.2%.

The subjects' FFMI was assessed using the BIA seca mBCA 525 measuring instrument. The results of the subjects' FFMI assessment can be seen in Table 2. The changes in the subjects' FFMI had a median value of 0.5 (0.1–3.5) kg/m^2.

The subjects' HGS was assessed using the Jamar handgrip. The results of the subjects' HGS assessment can be seen in Table 3. The change in the subjects' HGS on the active hand in this study was 1.7 (0.2–9.6) kg, while the change in the subjects' HGS on the non-active hand was 1 (0.1–6.2) kg.

DISCUSSION

The results of this study indicate that of the 53 research subjects, the median age of HNC subjects was 49 years, with the youngest being 20 years old. The characteristics of the subjects are presented in Table 1. The research subjects were mostly male (67.9%). Based on RISKESDAS 2018 data, the highest prevalence of cancer sufferers was at the age of 55–64 years, and based on GLOBOCAN 2018 data, the ratio of male and female subjects who experienced HNC was 2:1 [16,17]. The increase in HNC incidence in men is related to smoking and drinking habits, which are higher in men than in women, which are risk factors for HNC [18]. In this research subject, the most common cancer location was in the nasopharynx (62.3%), then in second place was laryngeal cancer (13.2%), while the rest were in the oral cavity (11.3%), oropharyngeal (7.5%), and sinonasal (5.7%). Based on GLOBOCAN 2020 data showing the prevalence of HNC, the incidence of nasopharyngeal cancer in 2018 was around 0.7% (around 129.079 out of 18.1 million new cases) [19]. Based on research at Sanglah General Hospital, Bali (RSUP), the dominant incidence of HNC was nasopharyngeal cancer, with 25 subjects (55.6%). Based on the body mass index (BMI), the average BMI of the subjects was 21.1±4.5 kg/m^2, with 50.9% of subjects classified as normal weight, 24.5% classified as underweight, 7.5% classified as overweight, and 16.9% classified as obese [20].

Table 1: Characteristic of the subjects

Subject characteristic	Value (%)
Age (years old)	49 (20–59)‡
Sex (%)	
Male	35 (66)
Female	18 (34)
Weight (kg)	56.0±13.9†
BMI (kg/m^2)	21.1±4.5†
Nutritional status based on BMI, n (%)	
Underweight	13 (24.5)
Normal weight	27 (50.9)
Overweight	4 (7.5)
Obese	9 (16.9)
Initial FFMI (kg/m^2)	16.4±3.1
2nd week FFMI (kg/m^2)	15.9±3.1
Change FFMI (kg/m^2)	0.5 (0.1–3.5)
Initial FFMI according to sex (kg/m^2)	16.4±3.1†
Male	17.3±2.8†
Female FFMI category. n (%)	14.6±2.9†
Adequate	25 (47.2)
Low	28 (52.8)
Initial active HGS (kg)	27.9±7.9†
2nd week active HGS (kg)	25.9±7.7
Change active HGS (kg)	1.7 (0.2–9.6)
Initial inactive HGS (kg)	25.1±8.8†
2nd week inactive HGS (kg)	23.7±8.5
Changes inactive HGS (kg)	1 (0.1–6.2)
Energy intake (kcal/kgBB)/day	26 (11–65)‡
Protein intake (g/kg BB)/day	1.17 (0.35–3.8)‡
Selenium intake (μg)/day	81.3 (30–372.4)‡
Cancer location n, (%)	
Oral cavity	6 (11.3)
Larynx	7 (13.2)
Nasopharynx	33 (62.3)
Oropharynx	4 (7.5)
Sinonasal	3 (5.7)
Cancer stage	
Stage I	1 (1.9)
Stage II	7 (13.2)
Stage III	13 (24.2)
Stage IV	32 (60.4)

†: Average±standard deviation, ‡: Median (minimum-maximum), BMI: Body mass index, FFMI: Fat-free mass index, HGS: Handgrip strength

Table 2: Correlation between selenium intake and change in FFMI

Variable	FFMI change	
	r	p-value
Selenium intake	−0.168^S	0.229

r: correlation coefficient. S: Spearman correlation, FFMI: Fat-free mass index

Table 3: Correlation of selenium intake with the change in HGS

Variable	Change active HGS		Change inactive HGS	
	r	p-value	r	p-value
Selenium intake	−0.36^S	0.798	0.276^S	0.045*

r: correlation coefficient. S: Spearman correlation test. p: Significant if<0.05. *: Significant, HGS: Handgrip strength

The majority of subjects (60.4%) were classified as stage IV cancer, 24.2% were classified as stage III cancer, and 13.2% and 1.9% were classified as stage II and I cancer. These data are in accordance with research at Dharmais Cancer Hospital, which shows that the average nutritional status of HNC patients at Dharmais Hospital is in the normal weight category, namely 22.2±4.2 kg/m^2, and most patients are in stage IV, namely 69.4% [21]. Patients with HNC in the early stages usually do not have specific signs and symptoms, and they are not too disturbing, so that when they seek treatment, they are already in an advanced stage.

Lack of knowledge regarding symptoms and signs in the early stages is also a factor in delaying the diagnosis of HNC [22]. In HNC patients from this study, they still have a normal BMI even though they have been diagnosed with stage IV, because there are several influencing factors in BMI, including BMI only describing total weight, not body composition, so it does not differentiate between muscle mass, fat, fluid, or edema. In patients who have experienced loss of muscle mass (sarcopenia), but still have excess fat or fluid, so that the BMI still appears normal, and if the patient has a history of obesity or overweight, then when muscle mass decreases, the BMI still appears normal [23].

The FFMI assessment of the subjects showed changes during the 2 weeks of chemoradiation. The FFMI assessment results of the subjects at the beginning of the study were 16.4±3.1 kg/m^2. The mean FFMI results of the subjects in the 2nd week of the study were 16.0±7.7 kg/m^2. From this study, there was a decrease in the subjects' FFMI by 0.5 (0.1–3.5) kg/m^2. This study did not find a significant correlation between dietary selenium intake and changes in FFMI or HGS during a 2-week observation period in HNC patients undergoing chemoradiation. The correlation between selenium intake and changes in FFMI and HGS are shown in Table 2. The absence of association is most likely related to the short duration of observation. Sarcopenia and muscle strength decline typically occur gradually over months, and a 2-week timeframe may be insufficient to detect meaningful changes. This short follow-up period therefore represents a primary limitation of the study. Several factors can influence this study, namely several other micronutrients besides selenium also affect FFMI, such as vitamin D and calcium, genetics, diet and nutrition, physical activity, hormone levels, age, and certain medical conditions such as hormonal disorders or metabolic disorders [24]. Another important limitation is the method used to assess selenium intake. The SFFQ provides an estimate of dietary intake but cannot capture the variability of selenium content in foods, which is strongly influenced by soil composition. Furthermore, no biomarkers such as plasma selenium or selenoprotein P were measured, meaning that the study reflects reported dietary intake, not actual biological selenium status. This methodological limitation must be considered when interpreting the findings. Previous studies in Int J Appl Pharm have measured plasma selenium following administration of selenium-containing formulations, highlighting the importance of assessing biological selenium status rather than relying solely on dietary recall [25].

The subjects' HGS assessment showed a decrease during the 2 weeks of radiotherapy. The results of the subjects' active hand HGS assessment at the beginning of the study were 27.9±7.9 kg. The average results of the subjects' active hand HGS at the 2nd week of the study were 25.9±7.7 kg. From this study, there was a decrease in the subjects' HGS in the active hand with a median of 1.7 (0.2–9.6) kg. The results of the subjects' inactive-hand HGS assessment at the beginning of the study were 25.1±8.8 kg. The average results of the subjects' HGS in the inactive hand at the 2nd week of the study were 23.7±8.5 kg. The change in the subjects' HGS in the inactive hand was a median of 1 (0.1–6.2) kg. The correlation between selenium intake and HGS changes in the active hand in this study did not show a significant correlation ($r=-0.360$, $p=0.798$), while the weak correlation between selenium intake and HGS changes in the non-active hand in this study showed a weak and significant correlation ($r=0.276$, $p=0.045$). Biologically, selenium would be expected to have a protective role in maintaining muscle function. Therefore, the positive association between dietary selenium intake and greater decline in HGS is implausible. The most likely explanation is confounding by disease severity, treatment-related toxicity, or nutritional support, where patients with more advanced disease or higher toxicity may have been encouraged to consume more protein-rich foods that also contain selenium.

This is contrary to previous research by Perri *et al*., [12] patients with low selenium intake had 2.72 kg lower HGS compared to those with higher selenium intake (40–74 μg). And in accordance with research by De Jong *et al*., [26] high blood selenium levels are associated with better functional capacity ($p<0.05$). HGS can be affected by cardiovascular disease, cancer, physical activity, caloric intake, arm muscle strength, aging, and body composition. Better nutrition in the 1st years of life, higher birth weight, and fetal development are the main determinants of muscle strength [27]. HGS is also affected by factors related to sarcopenia, such as physical activity level, vitamin D, energy intake, ethnicity, smoking status, and alcohol intake [28]. A total of 45.3% had sufficient HGS, and 54.7% had insufficient HGS. This is contrary to the research of Hilbert *et al*., [29] of 11 patients with HNC had a mean value of active hand HGS of 35.3±2.6 kg/m^2 and inactive hand HGS of 33.2±8 kg. Hilbert's study did not distinguish between male and female participants. The average HGS decreased along with weight loss over time for both the inactive and active hands, with an estimated average HGS loss of 0.1 kg/day [29]. This study required a more accurate HGS reference value to determine whether malnutrition was present based on the HGS value. HGS is closely related to body posture. East Asians (Chinese, Japanese, and Koreans) tend to be 5–9 cm taller than Indonesians. This is consistent with anthropometric studies showing that East Asians have larger body proportions than Indonesians. These differences in posture contribute to differences in HGS. Body size (posture and upper body dimensions) is closely related to HGS and motor function or functional capacity. The larger the dimensions (length, circumference, and width of the hand or arm), the higher the HGS and functional capacity [30,31]. The analysis revealed a significant positive correlation between selenium intake and changes in HGS in the inactive hand ($r=0.276$, $p=0.045$). Because the delta value is calculated from the difference between baseline and final values, a greater HGS change reflects a greater HGS decrease. This study, conducted on the inactive hand, showed that patients with higher selenium intake experienced a greater decrease in HGS at baseline. This is because the inactive hand is less physically active than the active hand, resulting in selenium's ability to maintain HGS reduction less optimally. Increasing selenium intake showed the opposite effect on HGS [32].

Blood selenium levels can also be influenced by selenium intake and oxidant levels due to selenium's antioxidant properties [33]. HGS can be influenced by cardiovascular disease, cancer, physical activity, calorie intake, arm muscle strength, aging, body composition, better nutrition in the 1st years of life, higher birth weight, and fetal development, which are the main determinants of muscle strength [27]. HGS is also influenced by factors associated with sarcopenia, such as physical activity levels, vitamin D, energy intake, ethnicity, smoking status, and alcohol intake [28].

Low selenium intake can affect the formation of selenoprotein enzymes in musculoskeletal function by neutralizing reactive oxygen species such as hydrogen peroxide, thereby increasing inflammatory cytokines, causing muscle weakness and oxidative damage, which will increase interleukin-6 so that function and contraction because it interferes with the secretion of insulin-like growth factor-1, which plays a role in myogenesis and muscle mass formation [13]. In addition, low selenium can affect muscle formation and function, so that there will be a decrease in FFMI and also a decrease in HGS [34]. In HNC patients, the decrease in FFMI and HGS is caused by chemoradiation therapy, so with sufficient selenium intake, it can maintain muscle strength in the form of HGS and muscle mass in the form of FFMI.

Selenium plays a crucial role in skeletal muscle health by supporting mitochondrial function, regulating calcium balance, and modulating thyroid hormone activity. Selenoproteins such as SELENOH promote mitochondrial biogenesis by influencing key regulators such as PGC-1α, NRF1, and Tfam, which enhance mitochondrial mass and energy production. In addition, SELENON maintains calcium homeostasis, ensuring proper adenosine triphosphate synthesis and function of mitochondrial complexes. A deficiency in SELENON disrupts calcium handling and impairs mitochondrial efficiency. Selenium also acts as a deiodinase in thyroid hormone metabolism, with enzymes D2 and D3 coordinating satellite cell activity for muscle repair. D3 supports proliferation by inactivating T3/T4, while D2 enhances differentiation through T3 activation. These combined mechanisms that impact muscle mass can be measured with FFMI and muscle strength, such as HGS. Therefore, adequate selenium intake may help maintain muscle integrity and functional capacity, particularly in conditions of metabolic stress or catabolic states like cancer therapy [14,35].

The strength of this study is that it is the first to examine the correlation between selenium intake and changes in FFMI and HGS in HNC patients undergoing chemoradiation or radiation alone in Indonesia. The study to examine FFMI and HGS was conducted objectively, FFMI assessment using BIA ®secamBCA and HGS assessment using the ®Jamar handgrip. Further research is recommended, considering a larger sample size, longer observation periods, and objective biomarkers of selenium status. A limitation of the study is assessing intake with a semiquantitative FFQ. Given the large variability of selenium content in food depending on soil and processing, and the influence of overall nutrient composition (energy/protein) on muscle mass, future studies should combine dietary assessment with biochemical measures to better define selenium status and its relationship with FFMI and HGS [25,36].

CONCLUSION

Within a 2-week observation period, no significant correlation was found between dietary selenium intake and changes in FFMI or HGS among HNC patients undergoing chemoradiation. The borderline result observed in the non-dominant hand is likely spurious and should be interpreted with caution. These findings highlight the need for longer-term studies with larger sample sizes and biomarker assessments of selenium status to better clarify the potential role of selenium in maintaining muscle mass and strength during cancer therapy.

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AUTHOR'S CONTRIBUTION

Nadiyah Wijayanthie designed the study, collected data, performed the statistical analysis, and drafted the manuscript. Wiji Lestari and Diyah Eka Andayani supervised the study and critically revised the manuscript. Jerry Marat has made substantial contributions in editing, revising, and finalizing the manuscript to ensure its academic quality and completeness All authors read and approved the final version of the manuscript.

CONFLICT OF INTEREST

The authors have no conflict of interest in this research.

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