



ASSOCIATION BETWEEN ENTERAL NUTRITION AVAILABILITY WITH NUTRITIONAL FULFILLMENT AND NUTRITIONAL STATUS IN HEAD AND NECK CANCER PATIENTS

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Abstract

Background: The availability of enteral nutrition is one of nutritional intervention that can be given to prevent a decrease in nutritional intake and nutritional status in head and neck cancer (HNC) patient.

Research objective: This study aims to see the correlation between the availability of enteral nutrition with nutritional fulfillment and nutritional status.

Methodology: A cross sectional study was conducted on adult subjects with HNC after radiation therapy at the RSCM radiotherapy outpatient clinic. Nutritional fulfillment was assessed by semi-quantitative FFQ while nutritional status was measured by calculating body mass index (BMI).

Research results: Forty-one HNC subjects mean age of 51 years, with oral or enteral nutrition route, participated in the study. The mean BMI of subjects with enteral nutrition was lower than those on oral nutrition, $18,2 \pm 2,6$ kg/m² compared to $21,2 \pm 3,5$ kg/m² respectively. The mean total energy intake of subjects with enteral nutrition route was higher, which was $1498,1 \pm 430,6$ Kcal/day compared to $1291,4 \pm 393,3$ Kcal/day. There was a moderate negative correlation between the availability of enteral nutrition and nutritional status ($r = -0,346$, $p = 0,027$), meanwhile there was a weak positive correlation with nutritional fulfillment ($r = 0,216$, $p = 0,174$). However, in this study we found that the proportion of subjects with enteral nutrition who experienced a decrease in BMI was less than the proportion of subjects on the oral route, which was 22,2% compared to 43,8% respectively.

Conclusion: There is a moderate negative correlation between the availability of enteral nutrition with nutritional status and a weak positive correlation with nutritional fulfillment which is still influenced by confounding factors.

Keywords: enteral nutrition availability, head and neck cancer, nutritional status, nutritional fulfillment, semi quantitative FFQ.

Introduction

Cancer has become one of the highest mortality diseases in the world.¹ Head and Neck Cancer (HNC) is the seventh most common cancer in the world.² The incidence of HNC is high in Southeast Asia, the Western Pacific, and Western Europe.^{3,4} Men

are more likely to get HNC than women.^{3,5}

Nasopharyngeal cancer, which is a type of HNC, based on the Global Cancer Observatory (Globocan) 2020 has become the fifth highest new cases in Indonesia followed by thyroid cancer.⁶ Nasopharyngeal cancer cases based on the

2014 RSCM Cancer Registry Report were 9,5% of all cancer cases and ranked in the top ten most cancer cases.⁷

Treatment of HNC patients often causes side effects, especially when given in the form of chemoradiation. Side effects of therapy can appear in the form of oral mucositis, dysphagia, and dermatitis.^{2,3,8} Side effects of HNC treatment can cause patients to have difficulty meeting their nutritional needs, thereby increasing morbidity.^{9,10} Impaired nutritional intake of HNC patients can be seen through weight loss and malnutrition that occur during radiation and chemoradiation.^{3,11} The main nutritional problem of HNC patients is disruption of the nutritional pathways due to complications of both the cancer itself and side effects of therapy.^{2,3,9,10}

Head and neck cancer patients who suffered from side effects of cancer therapy and complications from tumors often require enteral nutrition to meet their nutritional needs, but the role of enteral nutrition in HNC patients undergoing radiation therapy has not been clearly studied. There are no studies regarding the optimal timing of enteral nutrition administration.¹² Further research on enteral nutrition in patients with HNC is still needed.⁹ Sheth, et al.¹³, found that patients with HNC, required enteral nutrition support up to six months before patients could return to oral nutrition.¹³ Another study

revealed that giving prophylactic feeding tube to HNC patients undergoing chemoradiation had a better impact on preventing weight loss, dehydration, hospitalization, and therapy interruptions.¹¹

The existing studies have not investigate the correlation of enteral nutrition availability to nutritional fulfillment and nutritional status of HNC patients undergoing radiotherapy. No studies have investigated the relationship between the availability of the enteral nutrition route and its effect on the patient's ability to meet nutritional needs and maintain or improve nutritional status. This study aimed to examine the correlation between availability of enteral nutrition route with nutritional fulfillment and nutritional status in outpatient HNC cancer patients undergoing radiotherapy.

Materials and Methods

Research location

This study was a cross-sectional study that conducted to HNC patients in Radiotherapy Outpatient Clinic Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia from January 2021 to November 2021.

Population and sample

Recruitment of research participants through the consecutive sampling method of subjects with HNC who completed radiation therapy, are over 18 years of age, and are willing to participate in the study. Exclusion criteria in this study were non-ambulatory,



subjects with HNC originating from brain, orbital, or skin cancer, and subjects diagnosed with chronic disease other than HNC.

Data collection

Interviews conducted on the subjects contained questions about inclusion criteria, exclusion criteria, age, gender, education level, and occupation. Subjects will also be asked if they have had or are currently having an enteral feeding tube and for how long. Semi quantitative food frequency questionnaire (SQ-FFQ) was used to analyze nutritional intake in the last one month. Food models were used to give aid in determining the portion size of food intake. The nutritional intake interview results were put to *nutrisurvey 2007*[®] program to get the average total daily energy intake. Nutritional fulfillment was obtained by comparing the average total daily intake with basal energy requirements. Data related to stage and location of cancer were obtained from medical records. Anthropometric measurement was conducted during the visit. The body weight of research subjects was measured using OMRON HBF 375[®] with precision of 0.1 kg, while the height was measured using a microtoise. Nutritional status represented by body mass index (BMI) was obtained by dividing weight in kilograms by the square of height in meters.

Data analysis

Statistical Package for the Social Sciences (SPSS) version 20[®] was used for data analysis. Kolmogorov-Smirnov test was used to assess the normality of data distribution. Correlations between variables were analyzed using the Pearson or Spearman correlation test, with *p*-value <0.05 was considered significant.

Ethical approval

Ethical permission was granted by Committee for Ethics in Research, Faculty of Medicine Universitas Indonesia (No. KET-901/UN2.F1/ETIK/PPM.00.02/2020 and protocol number 20-08-0928).

Research Results

A total of 41 participants were enrolled in this study. Most research subjects were around 50 years old, male gender, middle educational level, unemployed, and underweight until normal body mass index criteria. Majority participants diagnosed at stage IV and located in nasopharynx region. The proportion of subjects using enteral route was 22% with a range of duration enteral route from 0 to 47 days. Table 1 describe the characteristics of research subjects.

Nutritional status of participant can be seen in table 2. Mean BMI of participants with enteral route was significantly lower than oral route. Underweight BMI category

was higher in enteral route compare to normal weight category in oral route.

Mean nutritional intake of enteral route was higher than oral route. Resting energy expenditure was not statistically different. Nutritional fulfillment of enteral route subject was higher than oral route, although not statistically significant. Nutritional fulfillment of study participants can be seen in table 3.

Correlation between enteral nutrition route availability and nutritional status is presented on table 4. There was a moderate negative correlation using Spearman correlation test that statistically significant.

There was a weak correlation using Spearman correlation test between nutrition route availability and nutritional fulfillment, although not statistically significant. Correlation between enteral nutrition route availability and nutritional fulfillment is presented on table 5.

Discussion

A total of 41 participants out of the target 50 participants were enrolled in this study due to the limited number of prospective research subjects during corona virus disease 19 pandemic. Research conducted by Chen, et al.¹⁴ found that the *corona virus disease 19* pandemic caused interruption of radiation therapy, chemotherapy, and chemoradiation in 60,7% HNC patients. Interruption of HNC therapy causes disease progression or death in 31%.¹⁴

This is a limitation in this study with criteria of subjects who have completed radiation therapy.

The mean age of research participants was 51 years old and the highest gender was male. The study results are in accordance with the data on the prevalence of HNC which is more in men than women.^{3,5} Research conducted by Dittberner, et al.¹⁵ found that the incidence of HNC in men was higher than in women with the highest age being in the range of 50 until 64 years.¹⁵ Another study from Gupta, et al.¹⁶ found that nasopharyngeal cancer was most commonly found in Asia Pacific and North Africa regions.¹⁶ According to this study, our study found that the most common type of HNC was nasopharyngeal cancer, which was found in 59% of study participants.

Most of the study participants were at the middle level of education and unemployed. This finding is in accordance with the study of Conway, et al.¹⁷ which found that lower middle economic level and lower education level were associated with twofold increased risk of HNC. This is associated with differences in lifestyle, especially in terms of alcohol consumption and smoking habit.¹⁷

The mean BMI of participants in our study is 20,5 kg/m². Body mass index is one of prognostic factors in HNC. Gama, et al.¹⁸ conducted a study to correlated BMI with



prognosis in HNC patients, found that being underweight was a poor prognostic factor in HNC.¹⁸ Study conducted by Langius, et al.¹⁹ found that weight loss occurred more in HNC patients who underwent radiation therapy, as many as 57% of patients.¹⁹ Most BMI categories in this study were in the normal category, namely 43,9%, followed by the underweight category as much as 34,1%. Study participants who used the enteral nutrition route had a lower median BMI compared to subjects in the oral route. Based on additional data analysis, we found that the BMI of subjects on enteral nutrition before radiation was lower than subjects on oral nutrition, namely $18,7 \pm 2,8$ kg/m² compared to $21,9 \pm 3,6$ kg/m². This condition will become a research confounder, where the BMI categories subjects before radiation therapy did not have an even distribution.

The median stage of cancer in the study participants was at stage four with a range from stage two to stage four. The study of Lee, et al.²⁰ found that more than 50% of patients with HNC were diagnosed at stage three or four.²⁰ Maria, et al.²¹ in their study also found that most HNC patients were diagnosed at stage three and four, namely more than 60% of patients.²¹ The location of the tumor in this study was found mostly in the nasopharynx, as many as 59% of the participants. The location and tumor size may

affects weight loss, in accordance with the study conducted by Jager, et al.²² who found that weight loss was more common in HNC involving the hypopharynx, oropharynx, oral cavity, and supraglottis region. This significant weight loss was associated with decreased appetite, dysphagia, and dysgeusia.²²

A food frequency questionnaire was used to calculate the estimated nutritional intake. Research conducted by Watanabe, et al.²³ found that FFQ can be used as a method to calculate energy intake estimates.²³ Study participants who received enteral nutrition had a higher mean caloric intake and nutritional fulfillment than oral route. This result is in accordance with a study conducted by Daly, et al.²⁴ on HNC patients who underwent radiation therapy, found that HNC patients fed with enteral route had a higher mean caloric intake than the oral route.²⁴

The proportion of study participants who used the enteral nutrition route was less than the oral route, with the proportion 22% and 78% respectively. The study by Cheng, et al.²⁵ found that HNC patients who underwent radiation therapy only about 14% received enteral nutrition, while the rest received nutrition through the oral route.²⁵ Another study by Maria, et al.²¹ found that 21,7% of HNC patients who underwent radiation

therapy required enteral nutrition route to fulfill their nutritional need.²¹ The need for enteral nutrition route is often not matched with patient's willingness, most of them are willing to get enteral nutrition if they have experienced nutritional problems.²⁶

There was a moderate negative correlation between the availability of enteral nutrition route and nutritional status ($r = -0,346$, $p < 0,05$). The incidence of malnutrition in HNC patients reaches 30-50%, while 30% of which have experienced severe malnutrition even before being diagnosed.^{21,25} The study of Isenring, et al.²⁷ found that 60% of HNC patients lost their weight during radiation.²⁷ Ferreira, et al.²⁸ in their study found that there was a decrease in BMI compared to before radiation.²⁸ A Study by Pai, et al.²⁹ found that a low BMI before radiation was associated with severity of HNC.²⁹ Based on additional data analysis, we found that the mean BMI of participants before radiation was $21,2 \pm 3,7$ kg/m². The mean BMI before radiation of research participants with enteral route significantly lower ($p = 0,017$) than oral route, $18,7 \pm 2,8$ kg/m² compared to $21,9 \pm 3,6$ kg/m² respectively. Differences in nutritional status and severity of disease before radiation are confounding factors that may affect nutritional status after radiation. Research conducted by Corry, dkk.³⁰ found that the majority of HNC patients who underwent

radiation or chemoradiation refused to receive enteral nutrition before having significant difficulties in fulfilling nutritional requirement and having severe weight lost.³⁰ This is consistent with our findings in this study, subjects with enteral nutrition route already had lower BMI before radiation than oral route based on our additional data analysis. The uneven distribution of BMI before radiation causes the result of this study to get a negative correlation. However, the result of additional data analysis showed that the use of enteral route was beneficial in preventing the reduction of BMI better than the oral route, 22,2% compared to 43,8% respectively. Early nutritional intervention, including adequate nutritional therapy, can improve the outcome of HNC patients receiving radiation.²¹ Guidelines issued by ESPEN explain that patients undergoing chemoradiation therapy and being given intensive dietary consultation coupled with supplementation using ONS can help to prevent weight loss and therapy interruptions.^{31,32} The Study of Isenring, et al.²⁷ found that nutritional intervention in the form of intensive nutrition consultation coupled with individual nutritional intervention provided a clinical outcome of less weight loss compared to usual care, 0,4 kg compared to 4,7 kg respectively.²⁷ Based on our additional data analysis, we found that nutritional management in this study was performed on 22,2% of participants with



enteral route compared to 25% of oral route. However, we found that the proportion of study participants who received the nutritional intervention experienced fewer interruptions of therapy than without one. Another finding based on analysis of additional data, we found that the proportion of reduction in BMI during radiation in participants with nutritional management was lower than without nutritional management, 33,3% compared to 41,4% respectively.

Cachexia conditions can occur in HNC patients due to increased catabolism associated with increased proinflammatory mediators such as TNF, IL-1, IL-6, dan IFN- γ . Nutritional management of cachexia cancer be caried out using standard nutritional management.^{33,34} However, cachexia data in this study could not be presented because not all participants received nutritional management, so that not all participants received an assessment to determine the diagnosis of cachexia.

Spearman correlation test shows weak correlation between enteral route availability and nutritional fulfillment but not statistically significant. ($r = 0,234$, $p = 0,142$). This result contradicts with a study conducted by Daly, et al.²⁴ which found that HNC patients with enteral route had higher mean caloric intake than oral route, but in this study

all patients received the same treatment in terms of nutrition consultation and ONS administration.²⁴ Nutritional consultation for patients with or without enteral route has an influence on the nutritional intake and status of HNC patients undergoing radiation therapy or chemoradiation.^{21,31,32} We found that not all research participants in this study, both subjects who received enteral route as well as oral route, receive dietary consultation. This is a confounding factor that may influence the result of this study. Based on additional data analysis, it was found that a decrease in BMI occurred in 22,2% participants on enteral route, this proportion was lower than the proportion of participants on oral route who experienced a decrease of BMI in 43,8% participants.

There were several limitations that may influence the result of this study. The small sample size due to pandemic condition that affect the research power. Baseline characteristic research participants before radiation varied in terms of nutritional status and nutritional management. The last limitations was recall bias can occur in study participants during data collection using FFQ semi quantitative.

Conclusion and Recommendation

There was a significant negative moderate correlation between enteral route

availability and nutritional status that may be influenced by several confounding factors. In head and neck cancer subjects who underwent radiation therapy. We found nonsignificant weak correlation between enteral route availability and nutritional fulfillment that may also be influenced by several confounding factors. Further study with randomized clinical trial design and larger sample size is needed to learn how early enteral nutrition availability affect nutritional status of HNC patients.

Competing Interest

The authors have no conflict of interest in this study. No educational grant is provided to the authors.

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Table 1, Baseline Characteristic of Study Participants (n = 41)

Variable	Result
Age (years)	50,85 ± 13,76*
Gender, n (%)	
Male	28 (68,3)
Female	13 (31,7)
Level of Education, n (%)	
Low	5 (12,2)
Middle	24 (58,5)
High	12 (29,3)
Occupation, n (%)	
Unemployed	23 (56,1)
Employed	18 (43,9)
Nutrition route, n (%)	
Enteral	9 (22,0)
Oral	32 (78,0)
Enteral route availability (days)	0 (0-47) ‡
Daily nutritional intake (Kkal/day)	1336,7 ± 405,5*
Body mass index (kg/m ²)	20,5 ± 3,6*
Underweight, n (%)	14 (34,1)

Table 2, Baseline Characteristic of Study Participants (n = 41) (continue)

Variable	Result
Normal, n (%)	18 (43,9)
Overweight, n (%)	4 (9,8)
Obese 1, n (%)	4 (9,8)
Obese 2, n (%)	1 (2,4)
Cancer Stage	4 (2-4) ‡
1, n (%)	0 (0)
2, n (%)	6 (14,6)
3, n (%)	9 (21,9)
4, n (%)	26 (63,5)
Cancer location	
Nasal cavity, n (%)	1 (2)
Sinus, n (%)	3 (7)
Lips, n (%)	0 (0)
Oral Cavity, n (%)	2 (5)
Salivary glands, n (%)	1 (2)
Nasopharynx, n (%)	24 (59)
Oropharynx, n (%)	1 (2)
Larynx, n (%)	6 (15)
Hypopharynx, n (%)	2 (5)
Thyroid, n (%)	1 (2)

*: mean ± standard deviation, ‡: median (minimum-maximum)

Table 3, Nutritional Status of Study Participants (n = 41)

Variable	Result	p Value
Body mass index (kg/m ²)	20,5 ± 3,6*	
Enteral, (kg/m ²)	18,2 ± 2,6*	0.025 ^a
Oral, (kg/m ²)	21,2 ± 3,5*	
BMI of Enteral Route, n (%)		
Underweight	6 (66,7)	
Normal	3 (33,3)	
Overweight	0 (0)	
Obese 1	0 (0)	

Obese 2	0 (0)
BMI of Oral Route, n (%)	
Underweight	8 (25,0)
Normal	15 (46,9)
Overweight	4 (12,5)
Obese 1	4 (12,5)
Obese 2	1 (3,1)

*: mean \pm standard deviation, ‡: median (minimum-maximum), ^a: Mann-Whitney test, p: statistically significant <0,05

Table 4, Nutritional Fulfillment of Study Participants (n = 41)

Nutritional Fulfillment	Result	P Value
Total Nutritional Intake (kcal/day)	1336,7 \pm 405,5*	
Enteral Route, (kcal/day)	1498,1 \pm 430,6*	0,180
Oral Route, (kcal/day)	1291,4 \pm 393,3*	
Basal Energy Expenditure (kcal/day)	1270,0 \pm 194,9*	
Enteral Route, (kcal/day)	1230,0 \pm 177,1*	0,493
Oral Route, (kcal/day)	1281,3 \pm 200,9*	
Nutritional Fulfillment (%)	108,5 \pm 39,9*	
Enteral Route, (%)	123,8 \pm 42,0*	0,197
Oral Route, (%)	104,2 \pm 38,9*	

*: mean \pm standard deviation, ‡: median (minimum-maximum), ^a: Mann-Whitney test, p: statistically significant <0,05

Table 5, Correlation Between Enteral Nutrition Route Availability and Nutritional Status (n = 41)

Variable	Nutritional Status	
	r	P
Enteral Route Availability	-0,346*	0,027

r: correlation coefficient. P: statistically significant <0,05. *: Spearman correlation test

Table 6, Correlation Between Enteral Route Availability and Nutritional Fulfillment (n = 41)

Variable	Nutritional Fulfillment	
	r	P
Enteral Route Availability	0,216*	0,174

r: correlation coefficient. P: statistically significant <0,05. *: Spearman correlation test