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Nutritional Status of Patients with Nasopharyngeal Carcinoma

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Abstract

BACKGROUND: Nasopharyngeal carcinoma (NPC) is one head and neck malignancy that often occur, especially in the field of ORL-HNS. Malnutrition is a common problem among cancer patients.

AIM: The objective of the study was to determine the relationship between NPC stage and nutritional status.

METHODS: Data were obtained retrospectively through medical records of NPC patients at Hasan Sadikin Hospital Bandung and Santosa Hospital Bandung Kopo, who were examined in the first examination between 2016 and 2020. Data collection included age, gender, NPC stage, and BMI of all patients. This study used Mann–Whitney, Chi-square test statistical analysis with Kolmogorov–Smirnov test alternative, Fisher's Exact for categorical data, and Multivariate Analysis with Binary logistic regression to analyze the association among variables.

RESULTS: Patients included in this study found 554 people, mostly malnourished. There was a significant difference between the NPC stage and the level of malnutrition with a p = 0.0001. Still, there was no meaningful significance found between the NPC stage and age (p = 0.353), the NPC stage and gender (p = 0.074), BMI, and age only (p = 0.194), early-stage only (p = 0.464), and advanced-stage only (p = 0.368); BMI and gender in early and advanced-stage (p = 0.411), early-stage only (p = 0.583), and advanced-stage only (p = 0.731).

CONCLUSION: For the advanced stage of NPC, the BMI value is lower.

Introduction

Nasopharyngeal carcinoma, cancer of the nasopharyngeal epithelial cells, is a less common malignancy [1]. Nasopharyngeal carcinoma is highly prevalent in Indonesia, Malay, Southeast Asia, and Southern China. The incidence rate varies from 1 per 100.000 individuals per year in non-endemic areas up to 25–30 per 100.000 individuals per year in endemic areas [1]. Nasopharyngeal carcinoma patients at the ORL-HNS Department Hasan Sadikin Hospital Bandung Indonesia were 3.8% in 2010–2017 [2]. There was a higher in middle age with significant histopathology finding was undifferentiated carcinoma [1].

Nutrition is an essential factor in cancer therapy. It determines the patient's functional status, management, and prognosis [3]. Malnutrition is when food intake is not by energy needs for the body caused by increased metabolism, malabsorption, or insufficient food intake. Malignant cell transformation alters its metabolism to support the metabolic needs of the tumor, an inefficient process involving mitochondrial oxidative phosphorylation to aerobic glycolysis [4]. Causing a rapid depletion of glucose stores and a change toward gluconeogenesis of fat and protein stores in muscle. Metabolic and immunological responses to cancer promote malnutrition through anorexia [1].

Malnutrition and wasting in cancer are common conditions, and their incidence ranges from 30 to 80% [1]. Malnutrition exacerbated by odynophagia, dysphagia, pain, and depressed mood in head and neck malignancies [1]. Malnutrition increases the risk of health care costs, infection, and treatment toxicity. It also adversely affects the quality of life, prognosis, or overall survival rate [1].

Several factors may be associated with NPC's treatment, including malnutrition and cachexia. Cachexia and malnutrition are problems among cancer patients. This condition can affect prognosis and the quality of life. Both conditions can occur because bombesin and serotonin secreted by tumors can suppress appetite and increase psychological factors; anxiety or depression [5]. Side effects of the management for cancer itself, such as chemoradiation, radiation, chemotherapy, or surgery alone, can lead to malnutrition. Inadequate oral intake, the immune system will decrease and eventually result in weight loss and increased secondary infection risk. About 50% of cancer patients experience weight loss and decreased nutritional status at diagnosis. Therefore, the patient's initial dietary status and needs at this stage are significant. Body mass index (BMI) is one indicator determining a person's nutritional status. Body mass index has calculated on the weight (kilograms) formula divided by height (meters) square. According to the Asia Pacific, the classification of nutritional status is divided into several categories; poor nutrition BMI < 18.5, average if 18.5–22.9, overweight ≥23, risk if 23–24.9, obese type 1 if BMI 25–29.9, and obese type 2 if BMI ≥ 30 [6].

Staging is a significant indicator in decision-making for treatment management and predicting prognosis. The more advanced cancer, the more complex the treatment, and the worse the prognosis. Unfortunately, nutritional status is found more frequently in advanced stages [7], [8]. Several questions related to these facts, including the correlation of stage and nutritional status. We analyzed the independent effect of nutritional status on the NPC stage.

Materials and Methods

Subject

The Research Ethics Committee Universitas Padjadjaran approved this study in June 2020. The number of ethical exemptions is 542/UN6.KEP/EC/2020. Patients who had been diagnosed with NPC were included in the study. The study analyzed the relationships between different variable data. Data collection was conducted through a retrospective medical record on all NPC patients at Hasan Sadikin Hospital and Santosa Hospital Kopo Bandung Indonesia. The medical history for this study was taken from 2016 to 2020.

Methods

We have collected some data from medical records, including the age, gender, NPC stage, and BMI status, across all subjects. The NPC stage would be categorized according to the 8th edition of NCCN. BMI values have been calculated based on body weight (kg) and height (m) data and classified based on Asia Pacific Standard used in Indonesia. A Shapiro Wilcoxon dan Kolmogorov–Smirnov test was used to know the normality distribution of the data. The unpaired T-test was used to analyze the comparison between the variable if usually distribution data; if it was not normally distributed, we performed the Mann–Whitney test Chi-square test with alternative Fisher's Exact for categorical data. Multivariate analysis with binary logistic regression was carried out to find the relationship between variables.

Results

In the early-stage patient group, the patient's age was 48.42 ± 12.105, consisting of 60 male patients or 56.1% and 47 female patients or 43.9%, for BMI Patients have an average of 21.81±2.166. In the advanced-stage patient group, the patient's age had an average of 49.37 ± 13,359, consisting of 292 male patients or 65.3% and 155 female patients or 34.7%. For BMI, patients have an average of 19.49 ± 2.957.

The analysis of numerical data was tested using the Mann–Whitney test, the variables of age and BMI. The statistical test results above obtained information on the p-value of the age variable greater than 0.05 (p > 0.05); it is statistically insignificant; it can be explained that there is no statistically significant mean difference between the age variable in early and advanced-stage.

For the categorical data analysis, gender in the Table 1 was tested using the Chi-square test. The p-value of the gender variable is greater than 0.05 (p > 0.05), which means it is statistically insignificant. Thus, it can be explained that there was an insignificant difference in percentage between variables of gender in the early and advanced-stage.

Table 1: Comparison between characteristics of patient npc in early and advanced-stage

Variable	Group		p-value
	Early-stage	Advanced-stage	
	n = 107	n = 447	
Age (year)			0.353
Mean ± SD	48.42 ± 12.105	49.37 ± 13.359	
Median	49.00	51.00	
Range (min-max)	18.00–78.00	13.00–83.00	
Gender			0.074
Man	60 (56.1%)	292 (65.3%)	
Woman	47 (43.9%)	155 (34.7%)	
BMI			0.0001**
Mean ± SD	21.81 ± 2.166	19.49 ± 2.957	
Median	21.47	19.10	
Range (min-max)	16.65–33.67	11.20–30.63	

For numerical data, the P value is tested by unpaired T-test if the data are usually distributed with the alternative of Mann–Whitney test if the information is not normally distributed. Categorical data P value is calculated based on the Chi-Square test with the alternative Kolmogorov–Smirnov test and Fisher's Exact if the Chi-Square requirements are not met. The significance value is based on the p < 0.05. The sign * indicates p < 0.05 with significant statistically.

There is a statistically significant mean difference between the BMI variable in the early and advanced-stage with P-value on the BMI variable is <0.05 (p < 0.05)

From the comparative analysis result of the characteristics of the two groups above, both groups are the same, or there is no difference in characteristics at the beginning of the examination. It shows that both groups are the same or homogeneous except for the BMI variable.

After the bivariate analysis in the Table 2 was followed by a multivariate analysis of the association between several independent variables and stages. The independent variables included in the model are gender and BMI. The two independent variables have the most dominant influence on the stage, as shown in Table 2. From the multivariate analysis in the initial model, the p-value of gender was more significant than 0.05 (p > 0.05); this indicates that simultaneously gender does not affect the stage, but the P-value of BMI was smaller than 0.05 (p < 0.05) this shows that simultaneously BMI affects the stage. Based on the Table 3, from the 2 initial model variables after going through two stages, the best model is in the final model.

Therefore, it can be concluded that statistically, only the BMI variable is strongly related to predicting stadium.

Table 2: Analysis of gender and BMI to early and advanced model

	B	Df	p-value	OR	CI 95%	
					Lower	Upper
Early model						
Gender	–0.363	1	0.117	0.695	0.442	1.095
BMI	–0.286	1	0.000	0.751	0.690	0.818
Advanced model						
BMI	–0.287	1	0.000	0.751	0.690	0.817

Multivariate analysis with Binary logistic regression. The independent variable included in the logistic regression model is the independent variable which in the bivariate analysis has a $p < 0.25$.

The patient's BMI had an average of 19.87 ± 2.864 in the male group. In the female patient group, the patient's BMI had a mean of 20.06 ± 3.136. The analysis of numerical data was tested using the Mann–Whitney test, namely, the BMI variable. The statistical tests obtained information on the p-value of the BMI variable greater than 0.05 ($p > 0.05$), which means it is statistically insignificant between BMI and gender variables in the early and advanced stages of patients.

Table 3: Comparison of BMI according to gender inpatient with nasopharyngeal carcinoma between early and advanced stage

Variable	Gender		p-value
	Man	Woman	
	n = 352	n = 202	
BMI			0.411
Mean ± SD	19.87 ± 2.864	20.06 ± 3.136	
Median	19.97	20.54	
Range (min-max)	11.20–30.10	12.66–33.67	

For numerical data, the p value is tested by unpaired T-test if the data is typically distributed with the alternative of Mann–Whitney test if the information is not normally distributed. Categorical data P value is calculated based on the Chi-Square test with the alternative test of Kolmogorov–Smirnov and Fisher's Exact if the Chi-Square requirements are not met. The significance value is based on the $p < 0.05$.

Table 4 shows the Spearman correlation test results between the ages and BMI in the early and advanced stages. The value of the correlation coefficient (r) information is obtained that the direction of the correlation is negative with a minimal correlation strength and can be ignored. Using Spearman's statistical analysis, the r-value for the correlation value between age and BMI is –0.072; p = 0.464; there is an insignificant correlation with the negative correlation and a very small and can be ignored between Age and BMI in the early stage.

Table 4: Analysis correlation of age with BMI in the early and advanced stage

Variable	Correlation	r	p-value
Age Correlation with BMI early stage	Spearman	–0.072	0.464
Age Correlation with BMI advanced stage	Spearman	–0.043	0.368

The significance value of $p < 0.05$.

Correlation of age and BMI in late-stage using Spearman's statistical analysis, the R-value for the correlation value between Age and BMI is –0.043; p = 0.368; this shows that there is an insignificant correlation with the direction of the negative correlation and a very small and can be ignored between age and BMI.

Discussion

Nasopharyngeal carcinoma was more common in the fourth decade of life, with more men than women, especially in an advanced stage [7]. In this study, the data show men are more affected than women, but the analysis has an insignificant correlation to the staging of NPC. The male predominance in NPC may be caused by differences in some environmental risks, such as smoking and hazardous occupational exposure. It is also possible that some intrinsic vulnerability, such as sex hormones, may explain the observed male predominance with the protective effects of endogenous estrogens that are rarely examined [9]. According to age, the incidence of nasopharyngeal cancer has a peak incidence at 50–60 years. In this study, the median age value was 49 years in early-stage and 51 years in late-stage since these groups are exposed to carcinogenic agents in the early stages of life. Nasopharyngeal carcinoma takes decades to develop into malignant cells. Exposure to carcinogens early in life may significantly affect the incidence of these cancers [10].

Approximately 10% of patients with non-metastatic NPC are underweight at diagnosis; overall, relapse, metastasis, and death rates, malnourished patients had worse outcomes than normal-weight patients [11]. Several factors may be associated with the management of NPC, including anemia, cachexia, and malnutrition. The independent variable that has the most dominant influence in this study is BMI or nutritional status. BMI variable has a strong correlation in predicting the NPC stage based on statistics. Malnutrition and cachexia are common problems among cancer patients.

Cachexia is a complex condition with increased energy needs and decreased metabolic dysfunction. The mechanism involves inflammatory cytokines in cancer, proteins, lipid metabolism changes, muscle protein production, and balance degradation. Dysfunction in the human inflammatory process regulation is observed in cancer. An increase in inflammatory cytokines, TNF- and interleukin-6 (IL-6), has an essential role in the metabolism of cancer patients. TNF - is a cytokine associated with cachexia that causes loss of skeletal muscle mass. Activation of TNF - is followed by activation of other cytokines that will cause cachexia, such as symptoms of anorexia. IL-6 also plays a crucial role in the development of cancer-associated cachexia. This interleukin will increase acute-phase reactants such as CRP through transducer and transcription activator 3 (STAT3) signals and muscle wasting in cancer patients. Administration of a humanized anti-IL-6 antibody in lung cancer patients effectively reduced anorexia-like symptoms but did not cause weight gain. Cancer-associated cachexia is not only associated with a single cytokine but is influenced by the interaction of various signaling substances.

Hormones and cytokines will regulate protein production and degradation through the ubiquitin-proteasome pathway, autophagy, and transformation of growth factor-beta family ligands in catabolic disease. Upregulation of the ubiquitin-proteasome pathway by catabolic stress has muscle wasting. The myofibrillar component of the protein is destroyed in the ubiquitin-proteasome path, causing a decrease in muscle strength. Stress hormones and inflammatory cytokines increase autophagy and dysfunction of the mitochondrial, causing muscle atrophy. This process is regulated by estrogens and transcription factors (NFkB) and Forkhead Box Protein O (FOXO). In cancer patients, cancer itself and malabsorption due to chemotherapy drugs can cause mucositis, reducing nutrient intake [12].

The mechanism of malnutrition is low intake of food containing macro and micronutrients, and impaired absorption will cause malnutrition. Inadequate food intake may be related to psychology, low appetite, and the effects of cancer treatment itself [13]. Cancer-associated malnutrition can result from the host response to cancer, systemic impacts of the disease, local effects of a tumor, and side effects of therapy. Alterations in nutrient metabolism and Resting Energy Expenditure (REE) are related to nutritional status. Some agents produced by the tumor cells directly or systemically respond to cancer, such as hormones or pro-inflammatory cytokines, significantly impacting the pathogenesis of malnutrition [14]. Side effects of malnutrition are decreased performance status, imbalance of immune system functions, quality of life, and muscle function. Therefore, it is logical that nutritional deficiencies will often be found in cancer patients, including NPC. However, not all patients experience malnutrition because cancer can even be triggered by obesity.

The study conducted by Hollander *et al.* showed the significance of BMI associated with increased mortality and incidence of several malignancies, such as esophageal, breast, and colon cancers. This condition causes problems in the treatment of head and neck cancer. Several studies have shown a stronger association between obesity and mortality in smokers. Smoking will trigger cancer development, increasing the risk of treatment failure and mortality in NPC patients. Adipocytes can promote tumor growth and progressivity through insulin resistance, hyperglycemia, hyperinsulinemia, and chronic inflammation [15].

The cancer stage is crucial for treatment decisions and predicting prognosis. The statistical analysis results showed a correlation between BMI and NPC stage in this study. For the advanced stage of NPC, the higher the risk of nutritional decline, but the mean value indicates that the patient has a normal BMI. The decrease in BMI in cancer patients can be caused by several things, including impaired metabolic function due to cancer and treatment in the form of chemotherapy which can damage healthy cells. Processes caused by cancer cells involve various inflammatory cytokines, lipid and protein metabolism changes, and balance in the production and degradation of muscle protein. Weight loss at the start of chemotherapy occurs in approximately 85% of patients with advanced cancer [16]. Therefore, it can be concluded that this study may be biased when a cross-sectional examination is performed. A cross-sectional study is an observational study that assesses at a particular time in the sample population. There was no prospective or retrospective examination as evidenced by no further investigation on BMI measurements; only BMI examination was carried out at the time of the patient's initial assessment. In this case, the researcher did not conduct a follow-up examination after being given treatment so that the results showed that the patient had an average BMI value. In addition, it can be caused by not assessing the history of BMI, so the researcher does not know whether the patient has experienced a decrease in BMI or not and does not know whether the patient's BMI value is included in the overweight, obese 1 or obese 2 categories. If the patient has decreased, the patient can reach average values even though the patient is experiencing changes or metabolic dysfunction, which is one of the signs of cancer. It can cause a decrease in BMI although not yet reached malnutrition.

The analysis conducted in this study showed a significant correlation between BMI and NPC stage, but for gender and age, the values were statistically insignificant. There is a negligible correlation between BMI and gender or BMI and age. Although several studies have shown a meaningful correlation between BMI and age, the most remarkable changes in BMI occur in younger generations. This young adult represents a critical period during accelerated weight gain, possible lifestyle changes involving energy expenditure, and food intake. In addition, some studies state that overweight is higher in women than men [17].

The study found no association between stage and nutritional status, but malnutrition was more common in advanced cancers [8]. This result can be explained because malnutrition occurs not only due to the stage of cancer but other factors such as tumor type, organ affected, treatment, or other diseases in later life. In addition, people with nasopharyngeal cancer may have a high BMI or obesity, one of the risk factors for NPC [15]. Further research is needed to increase the validity value of this study.

The limitations in this research are insufficient or missing information and input data collected from only two hospitals, so that not all the population. Certain variables such as smoking history, which were closely related to NPC in some of the studies mentioned, could not be studied further. In addition, the assessment of nutritional status to determine the patient had obesity, underweight or normal assessment is only through BMI. In contrast, other tests such as waist ratio, body fat proportion, skinfold thickness, and intra-abdominal fat assessment are not available.

Conclusion

There is a close relationship between BMI and NPC stage. At an advanced stage of NPC, the BMI value will be lower.

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References

1. Shah AB, Zulfiqar H, Nagalli S. Nasopharyngeal Carcinoma. [Updated 2021 Aug 11]. In: Statpearls. Treasure Island (FL): StatPearls Publishing; 2021 Jan. [Last accessed on 2022 Jan 7]; Available from: https://www.ncbi.nlm.nih.gov/books/NBK554588
2. Handayani R, Afriani Dewi Y, Madani DZ. Prevalence of Nasopharyngeal Carcinoma Patients in Departement of ORL-HNS Hasan Sadikin General Hospital 2010-2017. Int J Nasopharyngeal Carcinoma. 2020 May 3;2(01):01-3. https://doi.org/10.32734/ijnpc.v2i01.3191
3. Irungu CW, Oburra HO, Ochola B. Prevalence and Predictors of Malnutrition in Nasopharyngeal Carcinoma. Clin Med Insights Ear, Nose Throat 2015 May 26;8:19-22. Available from: http://www.journals.sagepub.com/doi/10.4137/CME6NT.S12119

   PMid:26056508
4. Icard P, Coquerel A, Wu Z, Gligorov J, Fuks D, Fournel L, *et al.* Understanding the Central Role of Citrate in the Metabolism of Cancer Cells and Tumors: An Update. Int J Mol Sci. 2021 Jun 19;22(12):6587. Available from: https://www.mdpi.com/1422-0067/22/12/6587
5. Ohnuma T, Ali MA, Adigun R. Anoreksia and cachexia. Statpearls.2021 Sep 21
6. Lim JU, Lee JH, Kim JS, Hwang Y II, Kim TH, Lim SY, *et al.* Comparison of World Health Organization and Asia-Pacific body mass index classifications in COPD patients. Int J Chron Obstruct Pulmon Dis. 2017;12:2465-75 https://doi.org/10.2147/COPD.S141295

   PMid:28860741
7. Kadriyan H, Sulaksana MA, Lestarini IA, Susilawati NK, Punagi AQ, Pieter NA, *et al.* Incidence and characteristics of anemia among patients with nasopharyngeal 2199 carcinoma in Lombok, Indonesia. AIP Conf Proc. 2019. P. 070015-1.
8. Trijayanti E, Probosari E. Hubungan asupan makan dan status gizi pada pasien kanker serviks post kemoterapi. J Kedokt Diponegoro. 2016;5(4):751-60. https://doi.org/10.14710/dmj.v5i4.14342
9. Hamid GA. Epidemiology and Outcomes of Nasopharyngeal Carcinoma. In: Zhou X, editor. Pharynx-Diagnosis and Treatment. India: IntechOpen; 2021 [Last accessed on 2021 May 22]. IntechOpen; 2021. Available from: https://www.intechopen.com/online-first/epidemiology-and-outcomes-of-nasopharyngeal-carcinoma
10. Salehiniya H, Mohammadian M, Mohammadian-Hafshejani A, Mahdavifar N. Nasopharyngeal cancer in the world: epidemiology, incidence, mortality, and risk factors. World Cancer Res J. 2018;5(1):e1046. https://doi.org/10.32113/wcrj_20183_1046
11. Li W, Shen LJ, Chen T, Sun XQ, Zhang Y, Wu M, *et al.* Overweight/obese status associates with favorable outcome in patients with metastatic nasopharyngeal carcinoma: A 10-year retrospective study. Chin J Cancer. 2016;35(1):75. https://doi.org/10.1186/s40880-016-0139-6

    PMid:27507261
12. Kim DH. Nutritional issues in patients with cancer. Intest Res. 2019;17(4):455-62. https://doi.org/10.5217/ir.2019.00076

    PMid:31597414
13. Perkeni. Surabaya Diabetes Workshop 7: Diabetes and Nutrition RSU Dr.Soetomo. Surabaya; 2020.
14. van de Worp WR, Schols AM, Theys J, Helvoort AV, Langen RC. Nutritional interventions in cancer cachexia: Evidence and perspectives from experimental models. Front Nutr. 2020;7:601329. Available from: https://www.frontiersin.org/articles/10.3389/fnut.2020.601329/full

    PMid:33415123
15. Efranto BH, Handoko E. Correlation of the nodule with body mass index and Karnofsky status in nasopharyngeal carcinoma chemotherapy. 2021;51(1):20-30. https://doi.org/10.32637/orli.v51i1.412
16. Kang J, Lee SH, Son JH, Lee JW, Choi YH, Choi JH, *et al.* Body mass index and weight change during the initial period of chemotherapy affect survival outcomes in advanced biliary tract cancer patients. PLoS One. 2018;13(4):e0195118. https://doi.org/10.1371/journal.pone.0195118

    PMid:29608578
17. Harbuwono DS, Pramono LA, Yunir E, Subekti I. Obesity and central obesity in Indonesia: Evidence from a national health survey. Med J Indones. 2018;27(2). https://doi.org/10.13181/mji.v27i2.1512