Body Mass Index and Survival Rate in Nasopharyngeal Cancer Patient: An Evidence Based Case Report

Yohannessa Wulandari¹, Metta Satyani¹, Marvin Marino¹, Nurul RM Manikam¹

¹Department of Nutrition, Faculty of Medicine, Universitas Indonesia, Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Abstract

Introduction: Nasopharyngeal cancer is the most common type of head and neck cancer with prevalence of 6.2/100000 population. Recently, study of prognostic factors for nasopharyngeal cancer still becomes one of research focuses. Several studies have tried to find the relationship between nutritional status (body mass index/BMI) and nasopharyngeal cancer patients’ survival rate, but the results are still inconsistent. This study aims to find the relationship between nutritional status represented by BMI and nasopharyngeal cancer patients’ survival rate.

Methods: Electronic literature searches were performed in Cochrane®, Scopus®, and PubMed®. Mesh term and title/abstracts were screened based on inclusion and exclusion criteria before relevant journals were reviewed.

Result: Two articles were selected based on the eligibility criteria and relevancy to the clinical question. In the study of Huang et al., the subject was nasopharyngeal cancer patient stage III and IV was included as subject of the study. In the study of Lin et al., nasopharyngeal cancer patient with metastases was also included. Patient with higher BMI has better survival rate than underweight BMI category.

Conclusions: Increasing BMI in underweight cancer patients improves nasopharyngeal cancer patients’ survival rate.

Keywords nasopharyngeal cancer, nasopharyngeal neoplasm, body mass index, BMI, survival rate, prognosis

Clinical Scenario

A 40-years-old male patient came to the outpatient clinical nutrition specialist in RSCM National Hospital. He was referred from the ear, nose, and throat (ENT) specialist for nutritional management. He has been suffering from nasopharyngeal cancer since last year. He has lost of appetite since 6 months ago. He experienced unexplained 15 kg weight-loss in one month. The ENT specialist planned to give him chemo radiotherapy. In the past 2 months, he only ate 3–4 tablespoons of porridge per day. Physical examination showed subcutaneous muscle loss. Based on his history of weight loss, BMI calculation, and physical examination, he was categorized as cancer cachexia. The clinical nutrition specialist gave medical nutrition therapy to increase his intake to overcome malnutrition condition. He asked whether improving his
nutritional status would increase his chance of survival.

Introduction

Head and neck cancer is the seventh leading cancer in the world. Head and neck cancer can occur in oral cavity, pharynx, and larynx, with squamous cell carcinoma as the most common histopathological findings. Nasopharyngeal cancer (NPC) is one of the most common cancer in South East Asia and North Africa Region. In Indonesia, NPC is one of the most frequent head and neck cancer type (28.4%) with prevalence of 6.2/100,000 population. Nasopharyngeal cancer frequently happens more in male than female.

Risk factors of NPC are smoking habit, alcohol consumption, history of Epstein-Barr virus (EBV) infection, history of human papilloma virus infection, radiation exposure, preserved food, and genetic factor. Clinical findings of patients with NPC are hoarseness, feeling of foreign body in their throat, lump at neck area, and abnormal findings in radiology imaging. Diagnosis of NPC is from histopathological findings. Management of NPC depends on the cancer stage, availability of treatment modality, and clinical experts. Treatment for NPC can be divided into surgical, non surgical, and combination therapy. Non surgical treatment consists of chemotherapy and radiotherapy.

Nasopharyngeal cancer patients often suffer from treatment complications such as normal tissue damages. The most common acute treatment complication include mucositis and dysphagia, meanwhile long term effect appears as xerostomia, loss of taste sensation, secondary malignancy, and fibrosis on neck region. Other complications are nausea and vomiting due to chemotherapy. All of these complications can disrupt patient’s food intake which result in malnutrition and dehydration.

Many studies currently have focused on the prognostic factors of NPC patients. Some known prognostic factors include cancer stage, EBV DNA findings, and nutritional status. Compared to other methods such as body composition measurement or laboratory examination, BMI measurement is an easy and inexpensive method to determine a patient’s nutritional status. Some studies have found the relationship between BMI and survival rate of NPC patients but the results remain inconsistent. For that reason, the relationship between BMI and the survival rate of cancer patients is an interesting subject as knowing it is necessary to determine the appropriate BMI target for cancer patients.

Clinical Question

Subjects included in this study are adult patients with nasopharyngeal cancer. The factor being analyzed is the influence of BMI to patients’ prognosis. The outcome of this study is survival rate. Therefore, this formulates a clinical question: Can BMI affect the survival rate of adult patients with nasopharyngeal cancer?

Methods

Article searching

The literature searching was performed using advanced searching from three large databases: Pubmed®, Cochrane®, and Scopus® on October 9th 2018 that screened by MesH Term and abstract/title. The keywords were “nasopharyngeal cancer”, “nasopharyngeal neoplasm”, “body mass index”, “BMI”, “survival rate”, and “prognosis”. The result of this literature searching was cleaned from duplication by EndNote application. After narrowing down literatures based on their titles and abstracts with the clinical question, the full text literatures which met the eligibility criteria were critically appraised.

Article selection

Eligibility criteria

Article selection was based on the inclusion and exclusion criteria, which addressed the clinical question. The inclusion criteria were: 1) the study subjects were diagnosed as nasopharyngeal cancer; 2) subjects were adult patients (aged ≥18 years old); 3) subject has the same characteristic; 4) BMI measurement was done before patients did chemotherapy and radiotherapy; 5) the study design was systematic review or cohort 6) study’s outcome measure was survival rate or prognosis; and 7) publication within the last 5 years. The exclusion
criteria were: 1) no available full text and 2) non-English journal.

**Critical appraisal**

Critical appraisal was done using cohort methods with BMI as prognostic factor for NPC’s survival rate. Every article was assessed by two reviewers for its validity, importance, applicability (VIA) using standardized criteria for prognostic research critical appraisal.

**Results**

Based on the inclusion and exclusion criteria, journal articles identified were 19 from Pubmed® and 22 from Scopus®. (Table 1)

Those 41 articles were screened for duplication using endnote X7. Eleven out of 41 articles have duplication, thus only 30 articles used for the next step. There were only 2 articles that met the eligibility criteria, meanwhile 28 articles excluded. Among 28 articles excluded, 25 articles used prognostic factors other than BMI, 1 article was therapeutic study, one article as diagnostic study, and 1 article used language other than English (Figure 1).

These articles were retrospective and prospective cohort studies. All studies had a level evidence of 2. The total sample is adequate to represent nasopharyngeal cancer patients. The subjects were taken from single cancer center in endemic area in China. Study characteristics are shown in Table 2. The study by Li W et al. satisfied all appraisal criteria. On the other hand, the study by Huang PY et al. lacked in one of validity criteria (Table 3, 4, and 5).

**Discussion**

Nutritional status can be assessed by measuring BMI or body composition. BMI is one of the prognostic factor for NPC. Body composition measurement is an accurate method yet expensive, and a specific tool must be used. Meanwhile, BMI is the simple and inexpensive method.
Energy Reserve of Hibernation Hypothesis explained that adipose tissue in cancer patients act as nutrient reserve in times of stress such as in patients undergoing cancer treatment. This hypothesis explained the possible mechanism of the relationship between BMI and cancer survival rate.11

Li W, et al.8 conducted a retrospective study to 819 nasopharyngeal cancer patients (median age 45 years old and age range 18–78 years old) with distant metastases whom being treated between 1998 and 2007 at Sun Yat - Sen University Cancer Center, China. During palliative chemotherapy, patients were evaluated by computed tomography or magnetic resonance imaging for response every two cycles and then every 3 months or the last follow-up (June 30, 2014) with OS and PFS as the primary outcomes. Result of this research was higher BMI patients had a significantly longer overall survival compared with underweight patients (HR 0.62; 95% CI 0.48–0.81; p<0.001) and normal-weight patients (HR 0.72; 95% CI 0.57–0.90). In contrast, PFS rates had no association with BMI (p= 0.407).10
Table 2. Study characteristics

| Articles                             | Study design            | Population                                           | Outcome                                      |
|-------------------------------------|-------------------------|------------------------------------------------------|----------------------------------------------|
| Li W, et al., (2016)                | Retrospective cohort study | 819 patients >18 years with distant metastasis NPC. Patients were classified into: underweight (n:168), normal weight (n:431), and overweight/obese (n:220) | Overall survival (OS) rates and progression-free survival (PFS). |
| Huang PY, et al., (2013)            | Prospective cohort study | 400 patients with NPC stage III and IVa. Patients were divided into: underweight (n:41), normal (n: 184), overweight (n: 83), and obese (n: 33) | Local-regional failure-free survival (LR-FFS), distant failure-free survival (D-FFS), FFS, OS |

D-FFS: distant failure-free survival; LR-FFS: local-regional failure-free survival; NPC: nasopharyngeal cancer; OS: overall survival; PFS: progression-free survival

Table 3. Validity criteria

| Articles                             | Relevance                                      |
|-------------------------------------|------------------------------------------------|
|                                     | Common point | Follow up | Outcome | Adjustment | Outcome over time | Precision | Applicability | Clinically important | Result | Level of Evidence |
| Li W, et al<sup>10</sup>            | +           | +         | +       | +          | +                  | +         | +            | +                   | A      | 2               |
| Huang PY, et al<sup>7</sup>         | +           | +         | +       | -          | +                  | +         | +            | +                   | B      | 2               |

A: Higher BMI patients had a significantly higher 5-year OS rates than underweight patients (p<0.001)<sup>10</sup>
B: Higher BMI patients had a significantly higher 5-year OS rates, FFS rates, LR-FFS rates and D-FFS rates than underweight patients (p=0.001, p=0.014, p=0.045 and p=0.037 respectively)<sup>7</sup>

Table 4. Relevancy criteria

| Articles                             | Similarity Population | Similarity Determinant | Similarity Outcome |
|-------------------------------------|-----------------------|------------------------|--------------------|
| Li W et al<sup>10</sup>             | +                     | +                      | +                  |
| Huang PY et al<sup>7</sup>          | +                     | +                      | +                  |

Table 5. Importance criteria

| Articles                             | Outcome                                          | n  | Hazard ratio | 95% CI          |
|-------------------------------------|--------------------------------------------------|----|--------------|-----------------|
| Li W, et al<sup>10</sup>            | Overall survival (OS) rates and progression-free survival (PFS) | 819 | Higher BMI compared with underweight patients: HR 0.62. | 0.48–0.81 |
| Huang PY, et al<sup>7</sup>         | 5-year OS rates in under, normal, overweight, obese group: 51%, 68%, 80%, 72%, respectively (p=0.001). 5-year FFS rates in under, normal, overweight, obese group: 44%, 61%, 68%, 73%, respectively (p=0.014) | 400 | Higher BMI compared with normal-weight patients: HR 0.57 | 0.39–0.84 |

BMI: body mass index; CI: confidence interval; FFS: failure-free survival; OS: overall survival; PFS: progression-free survival
The prospective cohort study by Huang, et al. was conducted at Sun-Yat-sen University Cancer Centre, China. Four hundred patients with stage III or IVa nasopharyngeal carcinoma were recruited for a randomized clinical trial of induction chemotherapy combined with radiotherapy or concurrent chemo radiotherapy. The mean age was 43 years (range 18–65 years). Patients with different histopathology type and distant metastases were excluded. The subjects were collected from August 2002 to April 2005 and last follow-up was in August 2011. The results showed that higher BMI patients had longer overall survival rates compared with normal weight patients (HR 0.574; 95% CI 0.391–0.845). In a multivariate analysis, whether BMI was calculated as a categorical variable or as a continuous variable, the results showed that BMI was an independent factor for the overall survival of loco regionally advanced nasopharyngeal carcinoma treated with chemoradiotherapy.

In the study of Li W, et al., there are several reasons why higher BMI patients with metastatic NPC had a better survival rate. First, higher BMI patients are less susceptible to malnutrition and/or cachexia than underweight patients with head and neck cancer. Malnutrition and cachexia are associated with reduced tolerance to cancer therapies, impaired immunity, and poor outcomes. Second, based on the preliminary data, higher BMI group received more cycles of palliative therapy after metastasis diagnosis than underweight group. Higher BMI group may prolong the patients’ tolerance to continuous treatment because they could receive more aggressive therapy rather than underweight group. However, higher BMI did not necessarily improve therapy’s efficacy.

Underweight patients in these two studies may suffer from an advanced stage of tumor. But, the study by Huang PY, et al. did not find significant differences between pre-treatment BMI and the NPC stage distribution. The BMI measurement in this study was taken on day 1 of chemotherapy while Li W, et al. measured within 14 days. In 14 days, patients might experience the therapy’s adverse effects such as nausea, vomiting, and decreased appetite so the pre-treatment BMI may be different if taken in last day.

Li W, et al. also observed that BMI level was still significant in predicting OS after analyzing it with age, metastasis onset, bone metastasis, and the number of lesions. However, further comprehensive studies are required to evaluate the relationship between the advanced stage of tumor and patients with low BMI.

Our patient is 40 years old male with NPC. He was categorized as cancer cachexia due to history of weight loss, body mass index, and physical examination. His age is similar with age characteristics in both studies. Researches show that the survival rates of higher BMI patients was better than underweight patients. In this case, we recommend giving the patient continuous medical nutrition therapy in order to increase his chance of survival. This is important because the prevalence of NPC in Indonesia is increasing. To conclude, adult NPC patients must have a better nutritional status while they received treatment.

**Conclusion**

BMI is one of independent prognostic factors that affect the overall survival of adult NPC patients. This scientific evidence can be the basis to implement nutritional support. Patients with higher BMI compared with underweight patients may have a better quality of life and therefore a higher survival chance. From this evidence-based case report, we conclude that nutritional support should be an integrated part of nasopharyngeal cancer’s management. The limitation found in this evidence based case report is the lack of research regarding BMI as a risk factor for NPC. Further studies are required so that the clinician will be able to decide the best BMI target for NPC patients.

**Conflict of Interest**

Authors declared no conflict of interest regarding this study.

**Open Access**

This article is distributed under the terms of the Creative Commons Attribution 4.0 International Licence (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give
appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

Reference

1. Thompson LDR. Head and Neck Cancers. In: Stewart BW, Wild CP, eds. World Cancer Report 2014. France: International Agency for Research on Cancer; 2014. [Google Scholar]

2. Adham M, Kurniawan AN, Muhtadi AI, Roezin A, Hermani B, Gondhowiardjo S, et al. Nasopharyngeal carcinoma in Indonesia: epidemiology, incidence, signs, and symptoms at presentation. Chinese journal of cancer 2012;31(4):185. [Google Scholar]

3. Bradley PJ. Head and Neck Cancer. In: Ludman H, Bradley PJ, eds. ABC of Ear, Nose and Throat. 6 ed. USA: Wiley-Blackwell; 2013. [Google Scholar]

4. Vokes EE. Head and Neck Cancer. In: Kasper DL, Hauser SL, Jameson JL, Fauci AS, Longo DL, Loscalzo J, eds. Harrison's Principles of Internal Medicine. 19 ed: McGraw-Hill; 2015. [Google Scholar]

5. Lin JC. Prognostic Factors in Nasopharyngeal. Berlin: Springer; 2010. [Google Scholar]

6. Huang PY, Wang CT, Cao KJ, Guo X, Guo L, Mo HY, et al. Pretreatment body mass index as an independent prognostic factor in patients with locoregionally advanced nasopharyngeal carcinoma treated with chemoradiotherapy: Findings from a randomised trial. European Journal of Cancer 2013;49:1923-31. [Google Scholar]

7. Critical Appraisal of Prognostic Studies. Centre for Evidence-Based Medicine University of Oxford. at https://www.cebm.net/wp-content/uploads/2014/04/cebm-prognosis-worksheet.pdf.)

8. 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. Chinese journal of cancer 2016;35:75. [Google Scholar]

9. Howick J, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, et al. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. Oxford Centre for Evidence-Based Medicine 2011.