



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

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Received 2 September 2019,  
Accepted 3 February 2020

Link to DOI:  
10.25220/WNJ.V03.i2.0005

Journal Website:  
[www.worldnutrijournal.org](http://www.worldnutrijournal.org)

### 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<sup>®</sup>, Scopus<sup>®</sup>, and Pubmed<sup>®</sup>. 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

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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.<sup>1</sup> 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.<sup>1</sup>

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.<sup>2,3</sup> 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.<sup>3</sup>

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.<sup>4</sup>

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.<sup>5</sup> 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.<sup>6</sup> Some studies have found the relationship between BMI and survival

rate of NPC patients but the results remain inconsistent.<sup>7</sup> 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<sup>®</sup>, Cochrane<sup>®</sup>, and Scopus<sup>®</sup> on October 9<sup>th</sup> 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  $\geq 18$  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.<sup>8</sup>

### Results

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

Those 41 articles were screened for duplication using endnote X7. Eleven out of 41 articles have duplication, thus only 30 articles used

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

Table 1. Resources and search strategy

Database	Search Strategy	Hits
Pubmed	(((nasopharyngeal cancer[MeSH Terms]) OR nasopharyngeal neoplasm[Title/Abstract])) AND (((body mass index[MeSH Terms]) OR "body mass index"[Title/Abstract]) OR "BMI"[Title/Abstract])) AND (((survival rate[MeSH Terms]) OR "survival rate"[Title/Abstract]) OR prognosis[Title/Abstract])	19
Cochrane Library	<p>#1 ("body mass index"):ti,ab,kw OR ("BMI"):ti,ab,kw in Cochrane Reviews (Word variations have been searched) N: 93</p> <p>#2 MeSH descriptor: [Body Mass Index] explode all trees N:9240</p> <p>#3 #1 OR #2 N:9307</p> <p>#4 ("survival rate"):ti,ab,kw OR ("prognosis"):ti,ab,kw in Cochrane Reviews (Word variations have been searched) N:230</p> <p>#5 MeSH descriptor: [Survival Rate] explode all trees N:9443</p> <p>#6 #4 OR #5 N:9661</p> <p>#7 #3 AND #6 N:45</p> <p>#8 (nasopharyngeal cancer):ti,ab,kw OR (nasopharyngeal neoplasm):ti,ab,kw in Cochrane Reviews (Word variations have been searched) N:2</p> <p>#9 MeSH descriptor: [Nasopharyngeal Neoplasms] explode all trees N:332</p> <p>#10 #8 OR #9 N:332</p> <p>#11 #3 AND #6 AND #10 N:0</p>	0
Scopus	(TITLE-ABS-KEY(nasopharyngeal AND cancer) OR TITLE-ABS-KEY(nasopharyngeal AND neoplasm) AND TITLE-ABS-KEY("body mass index") OR TITLE-ABS-KEY("BMI") AND TITLE-ABS-KEY(survival AND rate) OR TITLE-ABS-KEY(prognosis) AND LANGUAGE(english)) AND DOCTYPE(ar OR re) AND PUBYEAR > 2012	22

for the next step. There were only 2 articles that met the eligibility criteria, meanwhile 28 articles excluded. Among 28 articles excluded, 25 articles

an accurate method yet expensive, and a specific tool must be used. Meanwhile, BMI is the simple and inexpensive method.<sup>6</sup>

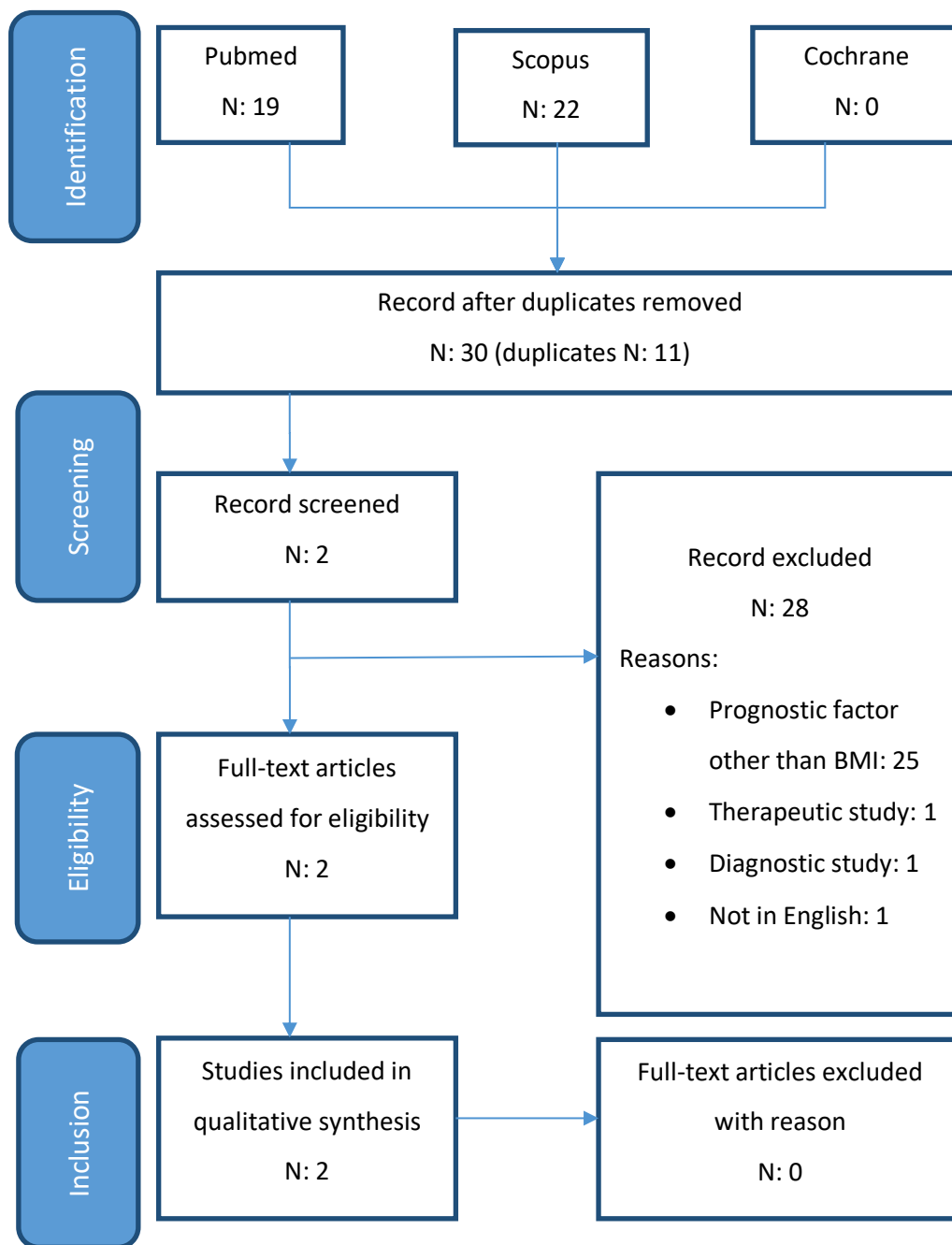


Figure 1. Flow chart of literature searching

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.<sup>11</sup>

Li W, et al.<sup>8</sup> 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 ( $p = 0.407$ ).<sup>10</sup>

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								Result	Level of Evidence <sup>9</sup>
	Common point	Follow up	Outcome	Adjustment	Outcome over time	Precision	Applicability	Clinically important		
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. Relevance 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.<sup>7</sup>

In the study of Li W, et al.<sup>8</sup>, 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.<sup>8</sup>

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.<sup>6</sup> 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.<sup>8</sup>

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.

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