

# Pretreatment body mass index and head and neck cancer outcome: A review of the literature

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## Abstract

**Background:** The prevalence of overweight and obesity defined as BMI  $\geq 25$  kg/m<sup>2</sup> is increasing, also among head and neck cancer patients. It is unknown whether the presence of high BMI influences disease-related mortality, overall survival and recurrence in these patients.

**Methods:** We reviewed available literature using Pubmed and Web of Science. Human observational studies were included if they reported the impact of high BMI on mortality, recurrence or survival for head and neck cancer.

**Results:** Eleven full articles and two abstracts met the inclusion criteria: six prospective and seven retrospective cohort studies, which comprised 8.306 patients. Patients with higher BMI had increased overall survival and decreased disease-related mortality and recurrence rate compared with underweight and normal weight patients. Most studies were adjusted for potentially confounding variables, such as stage of disease and smoking habits.

**Conclusion:** High BMI is associated with a better outcome in head and neck cancer.

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**Keywords:** Body mass index; Head neck cancer; Outcome; Survival; Mortality

## 1. Introduction

Most commonly head and neck squamous cell carcinoma (HNSCC) are located in the oral cavity, oropharynx,

hypopharynx or larynx. Nasopharyngeal carcinoma (NPC) is considered as a separate tumor because of pathology (squamous cell carcinoma or undifferentiated carcinoma), treatment and prognosis. Worldwide the estimated number of HNSCC cases was 599,000 and of NPC 87,000 in 2012, which together comprised 4.8% of all cancer incidences making HNSCC and NPC the seventh most frequent

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cancer site. Worldwide the estimated number of cancer deaths from HNSCC was 325,000 and from NPC 51,000 in 2012, which accounted for 4.6% of all cancer deaths [1].

More than 50% of HNSCC patients have significant weight loss at the time of diagnosis and just before starting treatment [2]. This weight loss is due to cancer induced dysphagia, odynophagia, anorexia or cancer cachexia, and it has a negative effect on survival [3,4].

High BMI is an increasing health problem around the world. In Western countries it is defined as a body mass index of 25 or more kg per square meter [5] with BMI between 25 and 29.9 kg/m<sup>2</sup> categorized as overweight and BMI  $\geq$  30 kg/m<sup>2</sup> as obesity, while in Asian populations, BMI  $\geq$  25 kg/m<sup>2</sup> is considered as obese, BMI between 23 and 24.9 kg/m<sup>2</sup> as overweight and  $<$ 23 kg/m<sup>2</sup> as normal weight [6]. The prevalence of high BMI among adults has risen from 46.0% in 1982–1984 to 69.2% in 2009–2010 in USA [7] and in Europe prevalence of overweight was 56.8% and of obesity was 23% in 2014 [8]. In Southeast Asia prevalence of overweight was 22.2% and of obesity was 5% in 2014 [8].

High BMI is associated with an increased incidence and mortality in several cancers, such as esophageal adenocarcinoma [9], breast cancer [10] and colon cancer [11]. There is no association between head neck cancer risk and BMI [12]. High BMI may cause problems with regard to HNSCC diagnostics as well as treatment. It is more difficult to perform endoscopies in obese patients and to stage cervical lymphadenopathy due to excessive neck fat. In some cases treatment needs to be modified: surgery cannot be performed because of high anesthetic risks or open surgery is performed when endoscopic techniques are not possible. The rate of postoperative complications is higher in obese patients [13]. These problems could negatively affect HNSCC survival, mortality and recurrence. In contrast, excessive neck fat may have a protective effect against radiotherapy side effects [14]. This could lead to better outcome in patients with high BMI.

In this review, the impact of high BMI on outcome of head neck cancer, in terms of survival, mortality and recurrence, is investigated. By systematically searching and reviewing all available data, for the first time evidence was collected on BMI and outcome in head neck cancer.

## 2. Materials and methods

### 2.1. Search strategy

Full texts and abstracts that reported on the association between BMI and outcome of HNSCC and NPC were searched. Head neck cancer was defined as oral cancer, tongue neoplasms and otorhinolaryngologic cancer.

In Medline, through PubMed, and Web of Science, Medical subject headings or key words were used for the search. These included Tongue neoplasms[Mesh], Otorhinolaryngologic neoplasms[Mesh] and Mouth neoplasms[Mesh]. Otorhinolaryngologic neoplasms included laryngeal,

hypopharyngeal, nasopharyngeal and oropharyngeal tumors. They were used separately or combined with 'OR', then combined using AND with recurrence, survival, prognosis as Mesh-terms and outcome as key word. Finally (obesity [Mesh] OR overweight [Mesh] OR body mass index [Mesh] OR anthropometry [Mesh]) with body weight as key word were added. Only articles in English were included.

Reference lists of the studies included in our analyses were also searched.

### 2.2. Study selection

One reviewer analyzed the yielded hits. The first selection was made by including only human observational studies (retrospective and prospective cohort studies). After that, studies were selected based on title, then further selection was made after reading the abstract and finally after reading the full text, studies were included. They were included if they reported: (1) diagnosis of head and neck squamous cell carcinoma or only one of the head and neck localizations, (2) data on body mass index (BMI) and (3) data on survival in percentage or months, mortality in percentage or hazard ratio and local or regional recurrence or distant metastases in hazard ratio or relative risk. Studies that combined the data with esophageal cancer, salivary gland cancer and/or thyroid cancer were excluded.

## 3. Results

Eleven articles and two abstracts met the inclusion criteria after a review of 37 abstracts and 23 full articles. The excluded articles consisted of studies that did not provide data on body mass index, outcome-measures or that reported on other localizations of tumors. Fig. 1 shows the searching and selection process.

Of the thirteen included studies in this review, six were prospective cohort studies [12,15,16,18,21,23] and seven retrospective cohort studies [13,14,17,19,20,22,24]. Other study characteristics such as study population, BMI assessment, comparison between BMI groups, analysis, outcome and time of follow-up are described in Table 1. Seven studies [12,15–19,22], three with only NPC patients, two with only HNSCC patients and two with all HNC subsites, together reported 2092 overweight and 689 obese patients in their population at baseline, the other six studies did not report data on numbers of patients in different BMI categories. Seven of the included studies also distinguished between overweight and obese patients and their survival and recurrence rates [12,15–17,19,21,22]. There were differences in duration of follow-up with medians ranging from 2.2 years [14] to 8.6 years [20] (Table 1).

The studies of Huang et al. [15] and Hu et al. [17] found that overweight and obese NPC patients had a significantly higher OS-rate than normal weight patients (Table 2). Huang et al. reported that obese patients had a worse OS than overweight patients, since more patients died of obesity-related

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