



Impact of obesity on outcomes for patients with head and neck cancer

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ABSTRACT

Objectives: The prognostic role of obesity in head and neck squamous cell carcinoma (HNSCC) is not well defined. This study aims to determine its effect on disease-specific outcomes such as recurrence-free survival (RFS), locoregional recurrence-free survival (LRRFS), and distant metastasis-free survival (DMFS) in addition to overall survival (OS).

Methods: For patients with newly diagnosed HNSCC undergoing radiation therapy (RT) at a single institution, body mass index (BMI) at diagnosis was categorized as normal (18.5 to 24.9 kg/m²), overweight (25 to 29.9 kg/m²) and obese (≥ 30 kg/m²). Outcomes were compared by BMI group using Cox regression.

Results: 341 patients of median age 59 (range, 20–93) who underwent curative RT from 2010 to 2017 were included. 58% had oropharynx cancer, 17% larynx and 15% oral cavity. 72% had stage IVA/B disease and 28% stage I-III. At diagnosis, 33% had normal BMI, 40% overweight, and 28% obese. 59% had definitive RT and 41% had postoperative RT. Alcoholic/smoking status, advanced tumor stage, hypopharynx/larynx tumors, and feeding tube placement were more common in patients with lower BMI ($P < .05$ for each). Median follow-up was 30 months (range, 3–91). Higher BMI was associated with improved OS ($P < .05$) and obesity was associated with longer RFS ($P < .05$) and DMFS ($P < .05$), but not LRRFS ($P = .07$) after adjusting for confounding variables.

Conclusion: Being overweight/obese at the time of HNSCC diagnosis is an independent prognostic factor conferring better survival, while obesity is independently associated with longer time to recurrence, primarily by improving distant control.

Introduction

Obesity rates have dramatically increased in the United States over the past two decades [1], and its relationship to cancer has been well documented. Higher body mass index (BMI) has been shown to increase the incidence of many types of cancer [2] and overall cancer mortality in healthy adults [3]. Obesity has also been shown to affect cancer prognosis, decreasing survival in patients diagnosed with cancers of the breast [4,5], colon [6], lung [7] and pancreas [8], among others.

However, the effect of obesity in head and neck cancer is less clear. Like obesity, head and neck cancer is becoming more common in the United States [9]. Squamous cell carcinoma of the head/neck (HNSCC) is most commonly caused by tobacco, alcohol and/or human

papillomavirus (HPV). These factors are also known to affect patient prognosis [10], as do age, gender, and disease stage [11]. Obesity, however, has not been shown to increase risk or worsen prognosis in HNSCC. In fact, lower BMI is associated with increased incidence of HNSCC, independent of tobacco and alcohol use [12–15]. The existing data has also suggested that high BMI is associated with improved prognosis in HNSCC patients [16–18], with the exception of one study of oral tongue SCC showing lower survival rates in obese patients [19].

While this positive association has been suggested in different populations, more granular investigation is required to determine the true prognostic effect of BMI in HNSCC patients. First, many studies [20–24] have only categorized BMI as normal or overweight by World Health Organization (WHO) standards with a cutoff of 25 kg/m². This study

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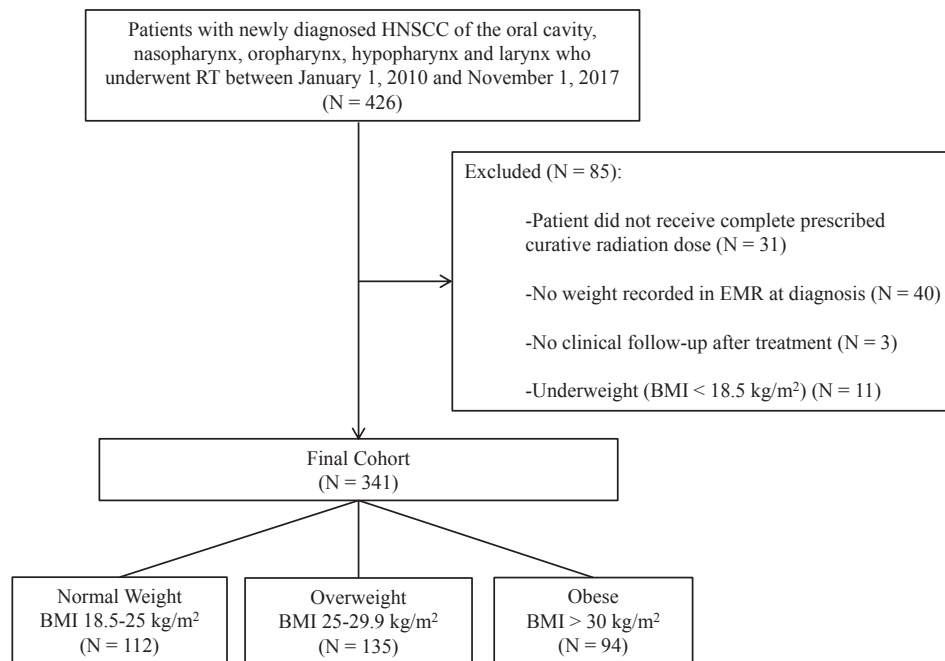


Fig. 1. Flow diagram of the selection of patients for the current study. Abbreviations: HNSCC; head and neck squamous cell carcinoma; RT; radiation therapy; EMR; electronic medical record; BMI; body mass index.

will compare survival outcomes between overweight and obese patients, a particularly important distinction in the western world where the majority of the population is now overweight [25]. Second, the confounding factors accounted for in previous studies have been general and variable. Most correct for demographic and known prognostic factors such as age, alcohol consumption, smoking status, and cancer stage. In addition to these clinical variables, this study will include important treatment characteristics like radiation dose and neck volume, chemotherapy, and the placement of a percutaneous endoscopic gastrostomy (PEG) tube as well as important pathologic factors such as lymph node (LN) involvement and extra-capsular extension (ECE). Third, very few studies have distinguished between locoregional recurrence and distant metastasis in their survival analysis. In nasopharyngeal carcinoma, Huang et al. showed improved distant failure-free survival for obese patients, but no association with locoregional failure-free survival [26]. Given such a finding, further delineation in the context of other HNSCC sites is warranted to both determine the type of disease failure for which BMI can be prognostic and to spur further investigation into the inner mechanisms of BMI and region of recurrence.

Our study will seek to assess the association between BMI, categorized as obese, overweight and normal, and survival outcomes, including the distinction between locoregional recurrence and distant metastasis, and will adjust for known prognostic factors including important treatment and pathologic characteristics.

Methods

Study cohort

The Institutional Review Board at our institution approved this retrospective study. Adult patients with newly diagnosed HNSCC of the oral cavity, nasopharynx, oropharynx, hypopharynx and larynx at any tumor stage who underwent radiation therapy (RT) at our institution between January 1, 2010 and November 1, 2017 were included. These patients were selected from a retrospective database of head and neck cancer patients consecutively treated by the Radiation Oncology Department at our institution. Height (inches) and weight (lbs) at the

earliest time point between pathologic diagnosis and the start of treatment were extracted from the electronic medical record (EMR) and BMI was calculated using the formula, weight (lbs) / [height (inches)]² x 703. There were 426 patients who met initial inclusion criteria. 31 patients were excluded because they were not prescribed or did not complete a full curative radiation dose, 40 were excluded because weight had not been recorded in the EMR at the time of diagnosis, and 3 were excluded for lack of any clinical follow up after treatment. 11 patients who were underweight according to WHO standards (BMI < 18.5 kg/m²) were excluded from analysis. The final cohort included 341 patients after exclusions (Fig. 1).

Collection of clinical data

Demographic and clinicopathologic data including age at diagnosis, gender, race, alcohol and tobacco use, diabetes mellitus, disease site, tumor (T) stage, prognostic stage, HPV status, LN involvement, ECE, perineural invasion (PNI), lymphovascular invasion (LVI), and surgical margins were recorded where appropriate. Also, treatment characteristics including adjuvant or definitive RT, radiation dose and target (primary site only, unilateral neck or bilateral neck), chemotherapy, and the use of prophylactic or reactive PEG tube for nutritional support were recorded. All data was reviewed for accuracy. Follow-up data including locoregional and distant control as well as survival data were obtained from the EMR. When unavailable in the EMR, the date of the death was obtained from the Social Security Death Index or the United States Find A Grave Index.

Clinical end points and statistical analysis

The primary endpoint of the study was overall survival (OS), defined as the time from diagnosis to all-cause mortality. Data was censored at the date of last follow-up for patients still alive. Secondary outcomes included recurrence-free survival (RFS), defined as the time from diagnosis to any recurrence, locoregional recurrence-free survival (LRRFS), defined as the time from diagnosis to first locoregional recurrence of the primary cancer, and distant metastasis-free survival (DMFS), defined as the time from diagnosis to first distant metastasis of

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