Original article

Association between standardized uptake value and survival in patients with locally advanced or metastatic squamous cell head and neck cancer

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ABSTRACT

Introduction and objective: The present study aimed to evaluate the association between tumor Standard Uptake Value (SUVmax) values obtained by PET/CT, and survival in patients with locally advanced or metastatic squamous cell head and neck cancer.
Method: The present study included 38 patients with locally advanced or metastatic squamous cell head and neck cancer, who were staged using PET/CT at diagnosis. PET/CT imaging findings were evaluated retrospectively. The effect of SUVmax value by PET/CT on overall survival was analyzed.
Results: The most common tumor localization was laryngeal cancer among 38 patients included in the study (n = 25, 65.8%). The study group consisted of mostly male patients (n = 33, 86.8%), and the median age was 58 (range: 24–77). The median SUVmax value was 11 (range: 3–58). Median survival was 32.7 months in patients with SUVmax ≤11 compared to 16.5 months in patients with SUVmax >11 (p = 0.019).

1. Introduction

The TNM stage is the most important prognostic factor in patients with head and neck cancer. This staging system is based on imaging methods such as Computerized Tomography (CT) or Magnetic Resonance Imaging (MRI). Conventional imaging methods remain incapable of differentiating metastatic and non-metastatic lymph nodes and identifying residual or recurrent masses due to the treatment-related changes in the tissues.[1–4] Positron Emission Tomography/CT (PET/CT) is commonly used to identify regional lymph node metastases, and to establish post-treatment residual tumor and loco-regional recurrence since it can metabolically display active lesions in patients with head and neck cancer.

PET/CT 2-18F-fluoro -2-deoxy-ᴅ-glucose (18F-FDG) is a useful imaging technique for pre-treatment staging, radiotherapy planning, evaluation of treatment response, and post-treatment follow-up in head and neck cancer as it is in many cancer types. As measured by PET/CT, the standard uptake value (SUVmax value) (18F-FDG tumor uptake) is associated with vitality and proliferative activity of the tumor.[5,6] Therefore, a high SUVmax value may indicate tumor aggressiveness. Several retrospective studies have investigated the prognostic significance of SUVmax value. There are many studies that have suggested poorer post-treatment outcomes in patients with higher SUVmax values on PET/CT.[7–9] Despite several studies, the prognostic value of SUVmax value of the primary tumor is still controversial in patients with head and neck cancer. The present study aimed to evaluate the association between SUVmax value as a prognostic marker and survival in patients with head and neck cancer.

2. Materials and methods

The study included patients with locally advanced or metastatic squamous cell head and neck cancer receiving palliative treatment who were staged by PET/CT at the diagnosis at our clinic between January 2007 and June 2013. They had an ECOG (Eastern

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Cooperative Oncology Group) performance status of 0–2. The tumor localization of the patients with head and neck cancer, ECOG performance score, tumor grade, and whether the tumor was locally advanced or metastatic were recorded initially. The patients' clinical and the tumor's pathological characteristics are presented in Table 1.

All whole-body PET/CT images were obtained using a PET/CT scanner (Biograph Six LSO; Siemens Medical Solutions) consisting of a PET scanner and a 6-section CT scanner. After ensuring that the peripheral blood glucose level was <150 mg/dL, patients received an intravenous injection of 3 MBq/kg of FDG. PET/CT scanning was performed from the center of the skull to the upper thigh 60 min after the injection and additional regional PET/CT scanning was performed. CT was performed with the following settings: 110 kV; 30 mA; tube rotation time, 0.8 s/rotation; pitch, 2; and section thickness, 2.5 mm (whole body CT had 307 or 356 slices). The PET scans were performed immediately after the CT scans in the identical transverse field of view. All 18F-FDG PET-CT images were interpreted qualitatively by 2 nuclear medicine physicians with prior knowledge of the clinical history. SUVmax within the region of interest (ROI) chosen by a nuclear medicine specialist were used as standard values.

OS (overall survival) was defined as the time from diagnosis to death. The median SUVmax value of the primary tumor was calculated. The median SUVmax value of the primary tumor was 11. The evaluated patients were analyzed for survival by classifying into two groups with SUVmax value ≤ 11 and SUVmax value > 11.

Statistical analysis was performed using SPSS 17.0 software. Survival was analyzed using Kaplan–Meier method and log-rank test. A univariate analysis was used to evaluate the association between age, gender, ECOG performance status, stage (locally advanced/metastatic), grade, and mortality risk. These variables were also evaluated by multivariate analysis. A p value of less than or equal to 0.05 was considered statistically significant.

3. Results

There were 33 (86.8%) males and five females among 38 patients included in the study. The median age was 58 (range: 24–77). The number of patients with locally advanced disease and metastatic disease was 33 (86.8%) and five (13.2%), respectively. Of 38 patients included in the study, 25 (65.8%) patients had laryngeal cancer. Of

the other 13 (34.2%) patients, eight patients had nasopharyngeal cancer, one patient had hypopharyngeal cancer, one patient had oropharyngeal cancer, one patient had nasal cancer, and one patient had salivary gland cancer. The number of patients with ECOG PS of 0–1 and ECOG PS of 2 was 26 (68.4%) and 12 (31.6%), respectively. The treatment strategies (surgery, RT, CT, CT + RT) administered to the patients were not specified separately in the study.

The univariate analysis of overall survival by tumor SUVmax, age, gender, performance score, stage, grade, and SUVmax is presented in Table 2. In the univariate analysis, median overall survival was 32.7 months in patients aged ≤60 compared to 17.6 months in patients aged >60 (p = 0.528). Median OS was 46.2 months in female patients compared to 17.6 months in male patients (p = 0.439). Median OS was 22.6 months in patients with ECOG performance status of 0–1 compared to 18.9 months in patients with ECOG PS > 1 (p = 0.245). Median OS was 21.4 months in patients with locally advanced disease compared to 14.2 months in metastatic patients (p = 0.111). Median OS was 34.2 months in patients of pathological tumor grade 1 compared to 46.2 months in grade 2 patients and 18.9 months in grade 3 patients (p = 0.172).

Median overall survival was lower in patients aged >60, male patients, patients with lower performance, metastatic patients, and patients with higher TM grade; however, such a difference did not reach statistical significance. The median SUVmax of the primary tumor was 11 in the present study. Median overall survival was 32.7 months in patients with SUVmax ≤11 compared to 16.5 months in patients with SUVmax >11, which was statistically significant (p = 0.019). All survival figures established by median tumor SUVmax value and p values are presented in Fig. 1.

The multivariate analysis revealed that only the SUVmax (odds ratio 3.16, 95% Cl 1.14–8.69, p = 0.026) value is an independent prognostic marker. There was no statistical significance in age, gender, ECOG performance status, and stage variables. The multivariate analysis is summarized in Table 3.

4. Discussion

Recently, PET/CT has been proven to be superior to conventional staging methods such as CT and MR in the diagnosis and staging of patients with head and neck cancer. In previous studies, PET/CT

Table 1
Characteristics of patients with head and neck cancer.

Characteristics	N = 38 (%)
Age (years)	58 (24–77)
Gender (M/F)	33/5 (86.8/13.2)
Tumor localization	
Oropharynx	1 (2.6)
Hypopharynx	2 (5.3)
Nasopharynx	8 (21)
Larynx	25 (65.8)
Nasal	1 (2.6)
Salivary gland	1 (2.6)
TNM	
Locally advanced	33 (86.8)
Metastatic	5 (13.2)
Grade	
1	4 (10.5)
2	11 (28.9)
3	4 (10.5)
Undefined	19 (50)
ECOG PS[a]	
0–1	26 (68.4)
2	12 (31.6)

[a] Eastern Cooperative Oncology Group performance status.

Table 2
Parameters affecting survival (univariate analysis).

	Median OS[a] (months)	P value
Age		0.528
≤60	32.7	
>60	17.6	
Gender		0.439
Male	17.6	
Female	46.2	
ECOG PS[b]		0.245
0–1	226	
>1	189	
Stage		0.111
Locally advanced	214	
Metastatic	142	
Grade		0.172
1	342	
2	462	
3	189	
SUVmax[c]		**0.019**
≤11	327	
>11	165	

[a] Overall survival.
[b] Eastern Cooperative Oncology Group performance status.
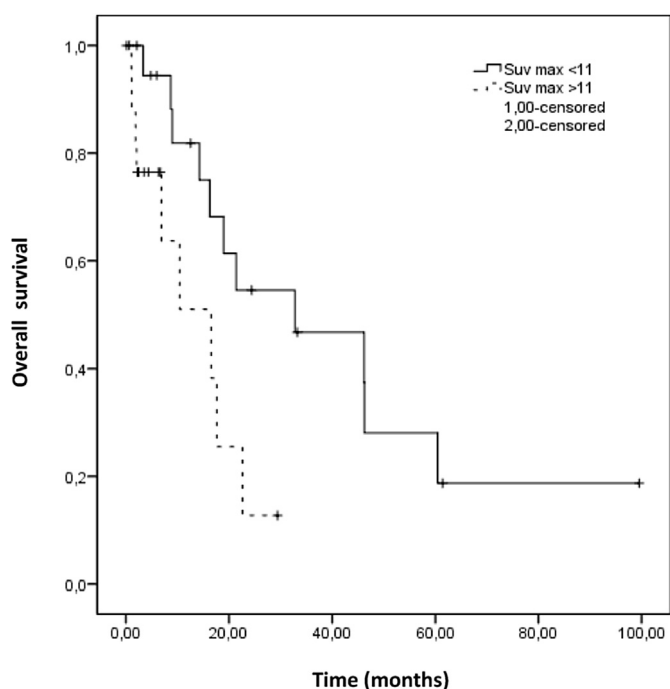[c] Standardized uptake value.

Fig. 1. Overall survival by median tumor SUVmax value.

Table 3
Multivariate analysis.

Prognostic factors	OR[a]	95% CI	p value
Age	0.805	028–2.26	0.682
ECOG PS[b]	1.50	0.57–3.92	0.411
Stage	1.34	0.35–5.1	0.670
Gender	1.87	0.42–8.32	0.374
SUVmax[c]	3.16	1.14–8.69	**0.026**

[a] Odds ratio.
[b] Eastern Cooperative Oncology Group performance status.
[c] Standardized uptake value.

caused treatment changes in approximately one-third of patients based on the change in disease stages.[10–12]

In head and neck cancer patients, clinical (stage) and pathological characteristics (tumor grade) are generally used to predict the post-treatment patient outcomes. Although there are considerable advances in approaches to the diagnosis and treatment in head and neck cancer in recent years, there may be different clinical outcomes even in the patients who have the same clinical and pathological characteristics and who receive the same treatment.[13] Identification of new prognostic factors would be useful in determining the high-risk patients and planning treatment strategies.

There are several studies reporting that FDG uptake is associated with tumor aggressiveness and poor prognosis, and may have prognostic value in head and neck cancer patients.[14–19] Some studies have found positive correlation for SUVmax value, whereas some studies have demonstrated negatively correlated SUVmax value. In a study by Querellou et al, 48 of 59 patients with head and neck cancer had locally recurrent or metastatic disease (oral cavity: 29, oropharynx: 32, hypopharynx: 5, nasopharynx: 1, and larynx: 22 patients). The claimed the study found poorer outcomes of both overall survival and progression-free survival in patients with primary tumor SUVmax >7 (cut-off value).[20] Median tumor SUVmax value was calculated in the present study and median SUVmax was 11. Median survival was 32.7 months in patients with median SUVmax ≤11 compared to 16.5 months in patients with median

SUVmax >11. Although there are marked survival differences in age, gender, PS status, tumor grade, and stage (locally advanced/ metastatic) variables, such differences reached statistical significance only in the SUVmax value.

Having the pre-treatment high SUVmax value in primary tumor, which is associated with tumor aggressiveness, the treating physician may choose a more aggressive treatment and more frequent follow-ups after treatment. However, several other studies have shown that nodal SUVmax value is specifically associated with PFS rather than the primary tumor.[21–24]

Zhang et al conducted a meta-analysis including seven clinical studies and included 674 head and neck cancer patients who had pre-treatment PET/CT. They found poorer outcomes in head and neck cancer patients with primary tumors who had higher SUVmax values.[25]

Study limitations are the small sample size, heterogeneity of primary tumor localizations, and the heterogeneity of treatment strategies administered. Of our patients, 8 had nasopharengeal cancer. Furthermore, analyzing locally advanced and metastatic patients together in the present study can make its interpretation difficult.

Nonetheless, the present study demonstrated the value of tumor FDG uptake as measured by SUV in predicting overall survival in patients with head and neck cancer. SUVmax value was an important prognostic value for overall survival, in addition to clinical and pathological parameters. However, these results should be supported by larger, prospective studies.

Conflict of interest

There is no conflict of interest.

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