

Prognostic Significance of Standardized Uptake Value on ¹⁸F-Fluorine-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Patients with Nasopharyngeal Carcinoma

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Abstract

The aim of this study was to investigate the prognostic significance of standardized uptake value (SUV) on 18 fluorine-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography/computed tomography (PET/CT) in patients with nasopharyngeal carcinoma (NPC). Thirty-four patients who have histologically proven NPC and underwent ¹⁸F-FDG PET/CT were included in this study. After ¹⁸F-FDG PET/CT, all the patients received radiation therapy and 32 of them received concomitant weekly chemotherapy. The maximum SUV (SUV_{max}) at the primary tumor and the SUV_{max} of the highest neck nodes were determined. The SUV_{max}-T ranged from 5.00 to 30.80 (mean: 15.37 ± 6.10) and there was no difference between SUV_{max}-T values for early and late stages ($P = 0.99$). The SUV_{max}-N ranged from 3.10 to 23.80 (mean: 13.23 ± 5.76). There was no correlation between SUV_{max}-T and SUV_{max}-N ($r = 0.111$, $P = 0.532$). There was no difference between the SUV_{max}-T and the positivity of neck lymph nodes ($P = 0.169$). The ability of SUV_{max}-N to predict stage was obtained by a receiver operating characteristic (ROC) analysis. The area under the curve is 0.856 and the best cut-off value is 7.88. There was a good correlation between SUV_{max}-N and stage. While the mean SUV_{max}-T for the alive patients was slightly lower than that for the dead (14.65 ± 5.58 vs. 20.30 ± 7.92, $P = 0.061$), the difference between the groups was not statistically significant. Furthermore, there was no statistically significant difference for SUV_{max}-N between these two groups ($P = 0.494$). Cox-regression analysis showed that an increase in SUV_{max}-T and SUV_{max}-N was associated with death risk (relative risk [RR]: 1.13, $P = 0.078$ and RR: 1.052, $P = 0.456$, respectively). SUV_{max}-T and SUV_{max}-N were independent prognostic factors for survival in NPC patients. This will help the clinicians in choosing suitable candidates for more aggressive treatment modalities.

Keywords: Maximum standardized uptake value, nasopharyngeal cancer, prognostic significance

Introduction

Nasopharyngeal carcinoma (NPC) is one of the most common types of head and neck cancer with the greatest

incidence of neck node and/or distant metastases.^[1-3] NPC is radiosensitive, and 5-year overall survival, and disease-free survival rates of up to 70% can be obtained by the use of concurrent chemoradiotherapy.^[4,5] However, some disease recurrence may develop after treatment.^[5,6] For these reasons, identification of prognostic factors that

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more accurately predict treatment outcome may help in determining which NPC patients might benefit from more aggressive treatment.

Eighteen fluorine-fluorodeoxyglucose (F-18 FDG) positron emission tomography/computed tomography (PET/CT) has been widely used in the initial diagnosis and staging of newly diagnosed NPC patients. F-18 FDG PET/CT can be used to assess glucose metabolic activity of tumors.^[7-11] It provides useful information that cannot be obtained with other conventional imaging techniques.^[9-11] The standardized uptake value (SUV) of F-18 FDG-PET is a quantified index of FDG uptake. Recent studies have focused on the relationship between F-18 FDG uptake and survival outcome in a variety of tumors.^[12-16] SUV is an important prognostic factor for the head- and neck-cancer patients also.^[12,17,18] In this study, we aimed to investigate the prognostic value of F-18 FDG PET/CT in patients with NPC.

Materials and Methods

A total of 34 patients (23 men [67.6%] and 11 women [32.4%]; median age: 46.76 ± 14.48 range: 16-73) were analyzed. Patients were evaluated with a complete medical history and physical examination, complete blood count, baseline serum biochemistry, fiberoptic nasopharyngoscopy with nasopharyngeal biopsy, chest radiography, magnetic resonance imaging (MRI) of the head and neck, abdominal ultrasonography and F-18 FDG PET/CT imaging. Tumors were staged according to the American Joint Committee on Cancer, 2010 staging system. During the follow-up period, patients were clinically assessed every 3-6 months by blood tests, physical examination and head- and neck-MRI.

Positron emission tomography/computed tomography imaging

All patients were fasted for at least 6 h before F-18 FDG PET/CT imaging. All patients had glucose concentrations <150 mg/dL. Imaging was performed at 1 h after injection of 259-777 MBq (7-21 mCi) FDG using a dedicated full-ring PET/CT scanner (Biograph 6; Siemens Medical Systems, Erlangen, Germany). Nonenhanced CT images with a section width of 5 mm were acquired at 130 kV and 90 mA (mean). The PET scan was obtained immediately after the CT scan and 5-7 bed positions with an acquisition time of 4 min for each were used. CT-based attenuation corrections were performed.

For the PET images and reconstruction was carried out using an iterative reconstruction algorithm. After the standard PET/CT scan, additional images of the neck region were acquired with the patient's arms positioned alongside the body. PET/CT images were reviewed

visually and semi-quantitatively with SUV by two experienced nuclear medicine physicians.

The maximal SUV in each region of interest was determined using the whole body attenuation corrected image [Figure 1]. The maximum SUV (SUV_{max}) was defined as the highest activity concentration per injected dose per body weight after a correction for radioactive decay. The SUV_{max}-T and SUV_{max}-N were the SUV_{max} at the primary tumor and the SUV_{max} of the highest neck nodes, respectively.

Treatment modality

After F-18 FDG PET/CT, all the patients underwent radiation therapy (RT) within 1 week period. For each patient, planning target volumes (PTV) 70, 60, 66, 54 were delineated according to International Commission of Radiologic Units 50-62. The median dose for PTV 70 (range 60-82) was given in 33 fractions (range 31-35). Simultaneous integrated boost technique was applied by helicaltomotherapy one fraction daily over 5 days/week.

Thirty-two of 34 patients received concomitant weekly chemotherapy between 3 and 7 cycles (median 6). CCRT was given by intravenous infusion of weekly cisplatin 40 mg/m² in 29 patients, or intravenous infusion of weekly carboplatin 30 mg/m² plus intravenous infusion of weekly docetaxel 30 mg/m² in 5 patients.

Statistical analysis

The results are expressed as the mean values ± standard deviations. We used SPSS statistical software, version 11.5, (SPSS Inc., Chicago, Illinois, USA) for statistical analysis. T-test for independent samples was used to compare two situation categorical groups for a continuous date, Chi-square test for categorical data. Pearson's correlation

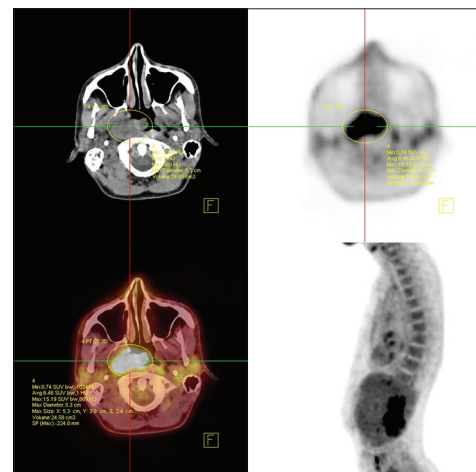


Figure 1: A 46-year-old male patient with nasopharyngeal cancer. The maximum standardized uptake value were determined by drawing a region of interest around the primary tumor on the transaxial slices

analysis was used to analyze the correlations between SUV_{max}-T and SUV_{max}-N. The associations between SUV_{max}-T and SUV_{max}-N and risk of death were assessed with a Cox-regression analysis. Receiver operator curves were determined to assess the area under the curve and the optimal cutoff value for predicting stage. A $P < 0.05$ was considered statistically significant.

Results

Between March 2011 and August 2014, 34 patients with NPC diagnosis were included in the study. The characteristics of the patients are described in Table 1. Of the 34 patients, 29 (85.3%) were still alive and 5 (14.7%) died. The median survival of the patients was 52.29 ± 3.96 (range: 44.53–60.06) months [Figure 2].

Among the 34 NPC patients, 4 (11.8%) were Stage I, 7 (20.6%) were Stage II, 10 (29.4%) were Stage III, and 13 (38.2%) were Stage IV disease. The early stages refer to Stage I and II (32.3%) and the late III and IV (67.7%). Six of 11 patients (54.55%) with early stage and 22/23 (95.7%) of patients with late stage NPC had neck lymph node metastasis. Two of 34 patients (5.8%) presented with distant metastasis (liver and bone) at diagnosis.

The SUV_{max}-T ranged from 5.00 to 30.80 (mean: 15.37 ± 6.10) and there was no difference between SUV_{max}-T values for early and late stages ($P = 0.99$). The SUV_{max}-N ranged from 3.10 to 23.80 (mean: 13.23 ± 5.76). There was no correlation between SUV_{max}-T and SUV_{max}-N ($r = 0.111, P = 0.532$). The SUV_{max}-T of patients with and without neck lymph nodes are shown in Table 2. There was no difference between the SUV_{max}-T and the positivity of neck lymph nodes ($P = 0.169$).

The ability of SUV_{max}-N to predict stage was obtained by an ROC analysis. The area under the curve is 0.856

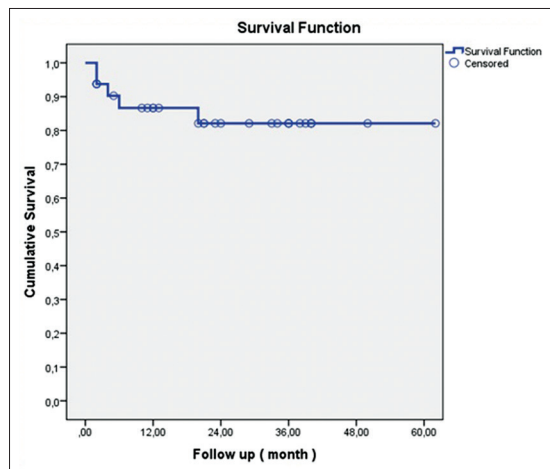


Figure 2: Survival function of nasopharyngeal cancer patients

and the best cut-off value is 7.88 [Figure 3]. There was a good correlation between SUV_{max}-N and stage [Table 3].

While the mean SUV_{max}-T for the alive patients was slightly lower than that for the dead (14.65 ± 5.58 vs. $20.30 \pm 7.92, P = 0.061$), the difference between the groups was not statistically significant. Furthermore, there was no statistically significant difference for SUV_{max}-N between these two groups ($P = 0.494$).

Cox-regression analysis showed that an increase in SUV_{max}-T and SUV_{max}-N was associated with death risk (relative risk [RR]: 1.13, $P = 0.078$ and RR: 1.052, $P = 0.456$, respectively).

Discussion

The efficacy of induction chemotherapy or dose escalation RT is investigating currently by many studies for improving survival of patients with advanced NPC. However, survival benefits of these treatments are still controversial because of their potential harms.^[19-21] Regarding these items, it's important to identify the predictors associated with poor outcomes for choosing suitable candidates for such treatment modalities.

The 3-year and 5-year distant metastases free survival (DMFS) of NPC were 88.1%^[22] and 79%.^[23] In 2002, Lee *et al.* reported the 4-year DMFS was 66%

Table 1: Patient characteristics (n=34)

Patient characteristics	Value
Median age - range (years)	46.76 (16-73)
Gender (%)	
Male	23 (67.6)
Female	11 (32.4)
Stage (%)	
Stage I	4 (11.8)
Stage II	7 (20.6)
Stage III	10 (29.4)
Stage IV	13 (38.2)

Table 2: Correlation between maximum standardized uptake value-T and neck lymph node positivity

No	SUVmax-T
Neck lymph node positive (6)	17.03 ± 8.85
Neck lymph node negative (28)	15.01 ± 5.5

$P=0.169$. SUVmax: Maximum standardized uptake value

Table 3: Comparison of stage groups categorized in terms of maximum standardized uptake value-N

	SUVmax-N (%)	
	<7.88	>7.88
Early stage	72.7	27.3
Late stage	13.0	87.0

$P=0.001$. SUVmax: Maximum standardized uptake value

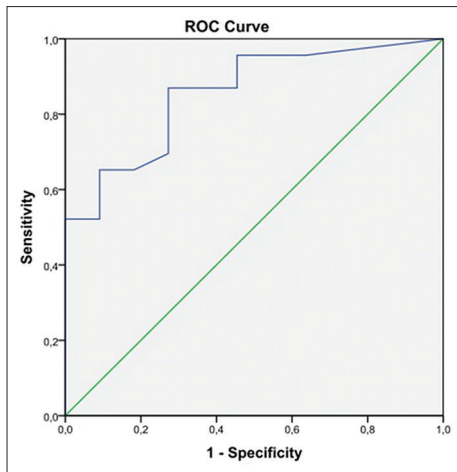


Figure 3: The ability of maximum standardized uptake value-N to predict stage was obtained by a receiver operating characteristic curve. Area under the curve is 0.856 and the best cut off value is 7.88

without using PET in the staging.^[24] Adding PET in the initial staging could reveal 10–20% of occult distant metastases.^[8,9] The better DMFS and OS in recent studies were likely because of the use of F-18 FDG PET in initial staging. Previous studies reported that the SUV of F-18 FDG PET represents a valuable prognosticator in patients with head- and neck-cancer.^[12,17,18] NPC patients with a lower SUV_{max} ($SUV_{max} < 8.0$) were found to had a significantly better disease-free survival.^[25,26] Similarly, our results showed lower SUV_{max} -T value for the alive patients compared to that of dead. Additionally, the risk of death increases with an increase in SUV_{max} -T and SUV_{max} -N. Yang *et al.* reported that SUV_{max} -T with a cut-off value of 15.6 and SUV_{mean} -T of 4.7 were associated with local control, which was higher than previous studies (SUV_{max} ranged from 6.48 to 12.0).^[22,27,28] However, in our study, statistically significant cut-off value of SUV_{max} could not be calculated.

Although high F-18 FDG uptake has been found to be related to tumor grade and aggressiveness^[29,30] and also with advanced disease stage,^[17] we did not found any difference between SUV_{max} -T values for early and late stages probably because of a limited number of the patients. However, we observed a good correlation between SUV_{max} -N and the disease stage. Chan SC *et al.* suggested that SUV_{max} value of lymph nodes is the most powerful factor in predicting regional node failure and retained its independent prognostic value in multivariable analysis.^[28] In another study, SUV_{max} of the node higher than that of the primary site was reported to be associated with poor prognosis.^[25]

The different PET parameters have specific prognostic features. Previous studies examined the prognostic

value of metabolic tumor volume (MTV) and showed that high MTV values predict an increase in recurrence and death risk in patients with head and neck cancers.^[28,31] Since total lesion glycolysis (TLG) is a combination of SUV and MTV and represents both the volumetric and metabolic component of a tumor, it is better than SUV or MTV alone in predicting prognosis.^[28] In the present study, MTV and TLG values could not be examined.

Near total of our patients were treated with both RT and CT. We observed excellent locoregional control. Among 34 patients, five were died because of toxicity ($n = 3$), disease progression ($n = 1$) and malnutrition ($n = 1$). Although combined RT and CT give excellent results, treatment toxicity is the leading cause of death in our patients. However, in literature, distant metastases are reported as the most significant reason of the treatment failure. Recently, The RT Oncology Group declared the results of a study regarding concurrent and adjuvant chemotherapy with bevacizumab. They proposed that this treatment is feasible and might delay the progression of the subclinical distant disease.^[32] Hence, it is suggested that in patients with a high risk of distant failure, more aggressive systemic treatment could be considered which could be predicted by the stage, SUV_{max} -T and SUV_{max} -N.^[22]

The major drawback of our study was the limited number of the patients. Although there were studies with similar patient number concerning prognostic factors of NPC patients in literature, further studies are needed with the larger patient population.

Conclusion

We demonstrated that SUV_{max} -T value of the alive patients was lower than that of dead, and an increase in SUV_{max} -T and SUV_{max} -N was associated with death risk.

These data suggest that SUV_{max} -T and SUV_{max} -N were independent prognostic factors for survival in NPC patients. This will help the clinicians in choosing suitable candidates for more aggressive treatment modalities.

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Conflicts of interest

There are no conflicts of interest.

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