Article published online: 2022-05-18

Original article

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

Şeyda Türkölmez, Sabire Yılmaz Aksoy[1], Elif Özdemir[1], Zuhal Kandemir[1], Nilüfer Yıldırım[1], Atiye Yılmaz Özsavran[2], Mehmet Faik Çetindağ[2], Kenan Köse[3]

Department of Nuclear Medicine, Ankara Ataturk Training and Research Hospital, Yıldırım Beyazıt University, Departments of [1]Nuclear Medicine and [2]Radiation Oncology, Ankara Ataturk Training and Research Hospital, [3]Department of Biostatistics, Ankara University Medical School, Ankara, Turkey

Abstract

The aim of this study was to investigate the prognostic significance of standardized uptake value (SUV) on 18 fluorine-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) in patients with nasopharyngeal carcinoma (NPC). Thirty-four patients who have histologically proven NPC and underwent ^{18}F-FDG PET/CT were included in this study. After ^{18}F-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_{maks}-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 reason, identification of prognostic factors that

Address for correspondence:
Dr. Şeyda Türkölmez, Department of Nuclear Medicine, Ankara Ataturk Training and Research Hospital, Yıldırım Beyazıt University, Ankara, Turkey.
E-mail: sturkolmez@yahoo.com

Access this article online

Quick Response Code:

Website: www.wjnm.org

DOI: 10.4103/1450-1147.181151

How to cite this article: Türkölmez S, Aksoy SY, Özdemir E, Kandemir Z, Yildirim N, Özsavran AY, *et al.* Prognostic significance of standardized uptake value on ^{18}fluorine-fluorodeoxyglucose positron emission tomography/computed tomography in patients with nasopharyngeal carcinoma. World J Nucl Med 2017;16:33-8.

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/m^2 in 29 patients, or intravenous infusion of weekly carboplatin 30 mg/m^2 plus intravenous infusion of weekly docetaxel 30 mg/m^2 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

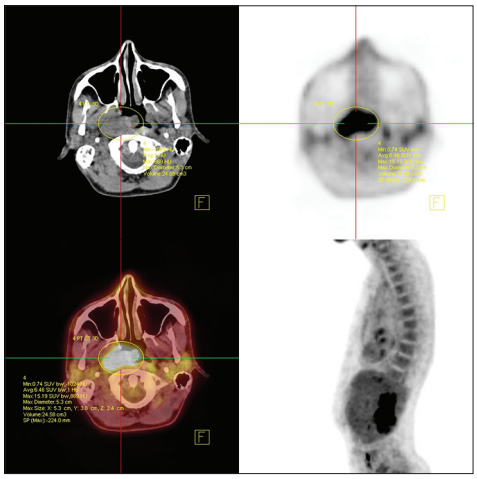

Figure 1: A 46-year-old male patient with nasopharyngeal cancer. The maximum standardized uptake value were determined by drawing a region of interest around the primary tumor on the transaxial slices

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 NFC 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 SUVmaks-N to predict stage was obtained by an ROC analysis. The area under the curve is 0.856 and the best cut-off value is 7.88 [Figure 3]. There was a good correlation between SUV_{max}-N and stage [Table 3].

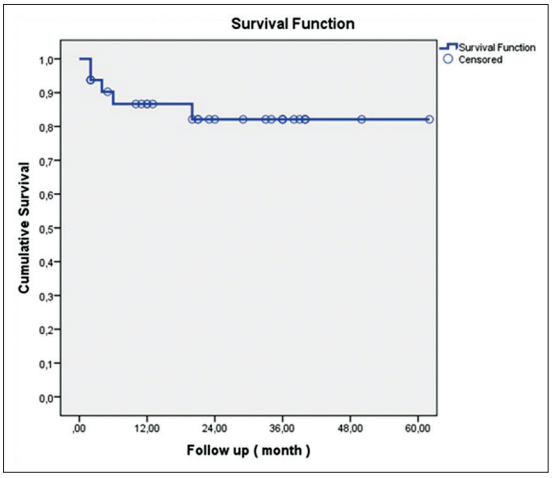

Figure 2: Survival function of nasopharingeal cancer patients

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).

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

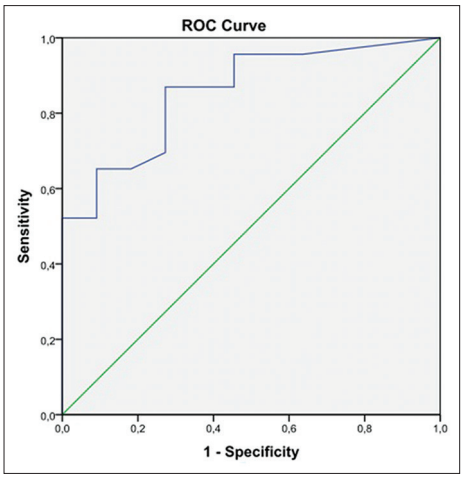

Figure 3: The ability of maximum standardized uptake value-N to predict stage was obtained by a receiver operating characteristic curve. Area under the curve is 0.856 and the best cut off value is 7.88

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 deads. 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 SUVmean-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 deads, 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.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. Tang SG, Lin FJ, Chen MS, Liaw CC, Leung WM, Hong JH. Prognostic factors of nasopharyngeal carcinoma: A multivariate

analysis. Int J Radiat Oncol Biol Phys 1990;19:1143-9.

2. Teo PM, Kwan WH, Lee WY, Leung SF, Johnson PJ. Prognosticators determining survival subsequent to distant metastasis from nasopharyngeal carcinoma. Cancer 1996;77:2423-31.
3. Lee AW, Poon YF, Foo W, Law SC, Cheung FK, Chan DK, *et al.* Retrospective analysis of 5037 patients with nasopharyngeal carcinoma treated during 1976-1985: Overall survival and patterns of failure. Int J Radiat Oncol Biol Phys 1992;23:261-70.
4. Al-Sarraf M, LeBlanc M, Giri PG, Fu KK, Cooper J, Vuong T, *et al.* Chemoradiotherapy versus radiotherapy in patients with advanced nasopharyngeal cancer: Phase III randomized Intergroup study 0099. J Clin Oncol 1998;16:1310-7.
5. Lin JC, Jan JS, Hsu CY, Liang WM, Jiang RS, Wang WY. Phase III study of concurrent chemoradiotherapy versus radiotherapy alone for advanced nasopharyngeal carcinoma: Positive effect on overall and progression-free survival. J Clin Oncol 2003;21:631-7.
6. Lee AW, Sze WM, Au JS, Leung SF, Leung TW, Chua DT, *et al.* Treatment results for nasopharyngeal carcinoma in the modern era: The Hong Kong experience. Int J Radiat Oncol Biol Phys 2005;61:1107-16.
7. Yen TC, Chang JT, Ng SH, Chang YC, Chan SC, Lin KJ, *et al.* The value of 18F-FDG PET in the detection of stage M0 carcinoma of the nasopharynx. J Nucl Med 2005;46:405-10.
8. Liu FY, Chang JT, Wang HM, Liao CT, Kang CJ, Ng SH, *et al.* [18F] fluorodeoxyglucose positron emission tomography is more sensitive than skeletal scintigraphy for detecting bone metastasis in endemic nasopharyngeal carcinoma at initial staging. J Clin Oncol 2006;24:599-604.
9. Liu FY, Lin CY, Chang JT, Ng SH, Chin SC, Wang HM, *et al.* 18F-FDG PET can replace conventional work-up in primary M staging of nonkeratinizing nasopharyngeal carcinoma. J Nucl Med 2007;48:1614-9.
10. Chan SC, Ng SH, Chang JT, Lin CY, Chen YC, Chang YC, *et al.* Advantages and pitfalls of 18 F-fluoro-2-deoxy-D-glucose positron emission tomography in detecting locally residual or recurrent nasopharyngeal carcinoma: Comparison with magnetic resonance imaging. Eur J Nucl Med Mol Imaging 2006;33:1032-40.
11. Chan SC, Yen TC, Ng SH, Lin CY, Wang HM, Liao CT, *et al.* Differential roles of 18F-FDG PET in patients with locoregional advanced nasopharyngeal carcinoma after primary curative therapy: Response evaluation and impact on management. J Nucl Med 2006;47:1447-54.
12. Liao CT, Chang JT, Wang HM, Ng SH, Hsueh C, Lee LY, *et al.* Preoperative [18F]fluorodeoxyglucose positron emission tomography standardized uptake value of neck lymph nodes predicts neck cancer control and survival rates in patients with oral cavity squamous cell carcinoma and pathologically positive lymph nodes. Int J Radiat Oncol Biol Phys 2009;74:1054-61.
13. Takeda A, Sanuki N, Fujii H, Yokosuka N, Nishimura S, Aoki Y, *et al.* Maximum standardized uptake value on FDG-PET is a strong predictor of overall and disease-free survival for non-small-cell lung cancer patients after stereotactic body radiotherapy. J Thorac Oncol 2014;9:65-73.
14. Imsande HM, Davison JM, Truong MT, Devaiah AK, Mercier GA, Ozonoff AJ, *et al.* Use of 18F-FDG PET/CT as a predictive biomarker of outcome in patients with head-and-neck non-squamous cell carcinoma. AJR Am J Roentgenol 2011;197:976-80.
15. Moon SY, Joo KR, So YR, Lim JU, Cha JM, Shin HP, *et al.* Predictive value of maximum standardized uptake value (SUVmax) on 18F-FDG PET/CT in patients with locally advanced or metastatic pancreatic cancer. Clin Nucl Med 2013;38:778-83.
16. Zhang J, Jia Z, Zhou M, Ragaz J, Zhang YP, Wang BY, *et al.* The SUVmax for (18) F-FDG correlates with molecular subtype and survival of previously untreated metastatic breast cancer. Clin Nucl Med 2013;38:256-62.
17. Allal AS, Dulguerov P, Allaoua M, Haenggeli CA, El-Ghazi el A, Lehmann W, *et al.* Standardized uptake value of 2-[(18) F] fluoro-2-deoxy-D-glucose in predicting outcome in head and neck carcinomas treated by radiotherapy with or without chemotherapy. J Clin Oncol 2002;20:1398-404.
18. Allal AS, Slosman DO, Kebdani T, Allaoua M, Lehmann W, Dulguerov P. Prediction of outcome in head-and-neck cancer patients using the standardized uptake value of 2-[18F] fluoro-2-deoxy-D-glucose. Int J Radiat Oncol Biol Phys 2004;59:1295-300.
19. Yau TK, Lee AW, Wong DH, Yeung RM, Chan EW, Ng WT, *et al.* Induction chemotherapy with cisplatin and gemcitabine followed by accelerated radiotherapy and concurrent cisplatin in patients with stage IV (A-B) nasopharyngeal carcinoma. Head Neck 2006;28:880-7.
20. Lee AW, Lau KY, Hung WM, Ng WT, Lee MC, Choi CW, *et al.* Potential improvement of tumor control probability by induction chemotherapy for advanced nasopharyngeal carcinoma. Radiother Oncol 2008;87:204-10.
21. Hong RL, Ting LL, Ko JY, Hsu MM, Sheen TS, Lou PJ, *et al.* Induction chemotherapy with mitomycin, epirubicin, cisplatin, fluorouracil, and leucovorin followed by radiotherapy in the treatment of locoregionally advanced nasopharyngeal carcinoma. J Clin Oncol 2001;19:4305-13.
22. Hung TM, Wang HM, Kang CJ, Huang SF, Liao CT, Chan SC, *et al.* Pretreatment (18) F-FDG PET standardized uptake value of primary tumor and neck lymph nodes as a predictor of distant metastasis for patients with nasopharyngeal carcinoma. Oral Oncol 2013;49:169-74.
23. Kam MK, Teo PM, Chau RM, Cheung KY, Choi PH, Kwan WH, *et al.* Treatment of nasopharyngeal carcinoma with intensity-modulated radiotherapy: The Hong Kong experience. Int J Radiat Oncol Biol Phys 2004;60:1440-50.
24. Lee N, Xia P, Quivey JM, Sultanem K, Poon I, Akazawa C, *et al.* Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: An update of the UCSF experience. Int J Radiat Oncol Biol Phys 2002;53:12-22.
25. Lee SW, Nam SY, Im KC, Kim JS, Choi EK, Ahn SD, *et al.* Prediction of prognosis using standardized uptake value of 2-[(18) F] fluoro-2-deoxy-d-glucose positron emission tomography for nasopharyngeal carcinomas. Radiother Oncol 2008;87:211-6.
26. Xie P, Yue JB, Fu Z, Feng R, Yu JM. Prognostic value of 18F-FDG PET/CT before and after radiotherapy for locally advanced nasopharyngeal carcinoma. Ann Oncol 2010;21:1078-82.
27. Chan SC, Hsu CL, Yen TC, Ng SH, Liao CT, Wang HM. The role of 18F-FDG PET/CT metabolic tumour volume in predicting survival in patients with metastatic nasopharyngeal carcinoma. Oral Oncol 2013;49:71-8.
28. Chan SC, Chang JT, Lin CY, Ng SH, Wang HM, Liao CT, *et al.* Clinical utility of 18F-FDG PET parameters in patients with advanced nasopharyngeal carcinoma: Predictive role for different survival endpoints and impact on prognostic stratification. Nucl Med Commun 2011;32:989-96.
29. Eary JF, Conrad EU, Bruckner JD, Folpe A, Hunt KJ, Mankoff DA, *et al.* Quantitative [F-18]fluorodeoxyglucose positron emission tomography in pretreatment and grading of sarcoma. Clin Cancer Res 1998;4:1215-20.
30. Schulte M, Brecht-Krauss D, Heymer B, Guhlmann A, Hartwig E, Sarkar MR, *et al.* Fluorodeoxyglucose positron emission tomography of soft tissue tumours: Is a non-invasive determination of biological activity possible? Eur J Nucl Med

1999;26:599-605.

31. La TH, Filion EJ, Turnbull BB, Chu JN, Lee P, Nguyen K, *et al*. Metabolic tumor volume predicts for recurrence and death in head-and-neck cancer. Int J Radiat Oncol Biol Phys 2009;74:1335-41.
32. Lee NY, Zhang Q, Pfister DG, Kim J, Garden AS, Mechalakos J, *et al*. Addition of bevacizumab to standard chemoradiation for locoregionally advanced nasopharyngeal carcinoma (RTOG 0615): A phase 2 multi-institutional trial. Lancet Oncol 2012;13:172-80.