

# Differentiation of benign and malignant nasopharyngeal lesions based on FDG uptake on PET/CT: comparison with pathology

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## ABSTRACT

**Objective:** The value of incidental fluorine 18-fluorodeoxyglucose (FDG) uptake on positron emission tomography/computerized tomography (PET/CT) in patients who undergo subsequent nasopharyngeal biopsy for suspected nasopharyngeal malignancy has not been assessed. The purpose of this study was to determine the ability of FDG maximum standardized uptake value (SUVmax) on PET/CT to differentiate between benign processes and malignant nasopharyngeal lesions.

**Methods:** We retrospectively reviewed the medical records of 92 patients who underwent FDG PET/CT for diseases other than nasopharyngeal cancer with subsequent endoscopic nasopharyngeal biopsy. Receiver operating characteristic (ROC) curve analysis was used to define a cut-off for the differentiation of benign processes from malignant lesions with incidental increased FDG uptake.

**Results:** All 92 patients had incidental FDG uptake (SUVmax $\geq$ 3). Compared with routine pathological analysis, this analysis demonstrated an SUVmax cut-off of 6.5, resulting in an area under the ROC curve of 0.74 (95% confidence interval, 0.63-0.82), sensitivity of 88.8%, and specificity of 63.8% for the detection of malignant nasopharyngeal lesions.

**Conclusion:** If a nasopharyngeal lesion has intense FDG uptake on PET/CT (SUVmax $\geq$ 6.5), malignancy should be strongly suspected.

**Keywords:** Biopsy, nasopharyngeal carcinoma, PET/CT

## Introduction

Nasopharyngeal carcinoma (NPC) is a rare malignancy with an incidence of 0.5-2 per 100,000 worldwide and can occur at any age (1, 2). Imaging modalities for NPC include computed tomography (CT) and magnetic resonance imaging (MRI), although MRI has a superior ability to demonstrate the extent of soft tissue involvement (3). The advent of molecular imaging based on fluorine 18-fluorodeoxyglucose positron emission tomography/computerized tomography (FDG PET/CT) has led to a new era in the diagnosis, staging, restaging, treatment planning, and assessment of response for most cancers, including NPC (4). The standardized uptake value (SUV) is commonly used as a semi-quantitative measure of FDG uptake. Assessment of maximum SUV (SUVmax) using FDG PET/CT has been shown to have a predictive value in breast, colorectal, and lung cancers (5-7). However, the positive predictive value

of SUVmax in NPC has neither been assessed sufficiently or compared with that of pathological analyses of nasopharyngeal biopsies.

This study aimed to determine the ability of FDG SUVmax on PET/CT to differentiate between benign processes and malignant nasopharyngeal lesions. To the best of our knowledge, no data are available on the predictive value of FDG SUVmax on PET/CT in patients with incidental involvement in the nasopharynx.

## Methods

This study was approved by the Ethics Committee of our University School of Medicine (ID number: 09.2016.203, issue date: 04.03.2016). We retrospectively reviewed and analyzed the medical records of 92 patients who underwent FDG PET/

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CT at our university hospital for diseases such as non-Hodgkin lymphoma, Hodgkin lymphoma, lung adenocarcinoma, breast cancer, lung epidermoid cancer, colon cancer, hypopharyngeal cancer, prostate cancer, melanoma, multiple myeloma, asbestosis, and temporal arteritis and in whom increased nasopharyngeal FDG uptake was detected and who subsequently underwent nasopharyngeal biopsy. Informed consent was obtained from patients who participated in this study.

The exclusion criteria to avoid misinterpretation were previously suspected or documented NPC, non-diagnostic histopathological diagnosis, FDG PET/CT without assessment of physiological uptake, blood glucose >200 mg/dL at the time of intravenous FDG injection, a history of radiation therapy to the head and neck region, and clinical evidence of infection of the head and neck region at the time of FDG PET/CT. No follow-up was performed.

Recorded data included age, sex, disease, SUVmax, detailed head and neck examination notes, nasopharyngoscopy evaluation, and results of nasopharyngeal biopsy. All FDG PET/CT images were evaluated by an experienced nuclear medicine physician. On the basis of literature (8, 9), asymmetric uptake was suspected as malignant and biopsied. The primary tumor site was assessed. Punch biopsies were obtained from the masses detected during nasopharyngoscopy. Biopsy specimens were assessed as part of routine clinical care by one of the participating pathologists. Tumors were classified as benign (reactive lymphoid hyperplasia and non-specific inflammation) or ma-

lignant (squamous cell carcinoma, non-keratinizing carcinoma, or undifferentiated carcinoma).

### Statistical analysis

Data analyses were undertaken using the Statistical Package for Social Sciences, version 16.0 software (SPSS Inc.; Chicago, IL, USA). The distribution of variables was assessed using the normality test. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off point and assess the sensitivity and specificity of FDG SUVmax on PET/CT for differentiating benign processes and malignant nasopharyngeal lesions.  $p < 0.05$  was considered significant.

### Results

The cohort included 68 (73.1%) men and 24 (25.8%) women, with a mean age of 43.25 years (range, 15-77 years; standard deviation  $\pm$  1.58). Of the 92 patients already diagnosed and receiving treatment at the time of PET/CT, 36 underwent PET/CT for non-Hodgkin lymphoma (38.7%), 15 for Hodgkin lymphoma (16.1%), 12 for lung adenocarcinoma (12.9%), 7 for breast cancer (7.5%), 5 for lung epidermoid cancer (5.4%), 4 for colon cancer (4.3%), 4 for hypopharyngeal cancer (4.3%), 3 for prostate cancer (3.2%), 2 for melanoma (2.2%), 2 for multiple myeloma (2.2%), 1 for asbestosis (1.1%), and 1 for temporal arteritis (1.1%) (Table 1).

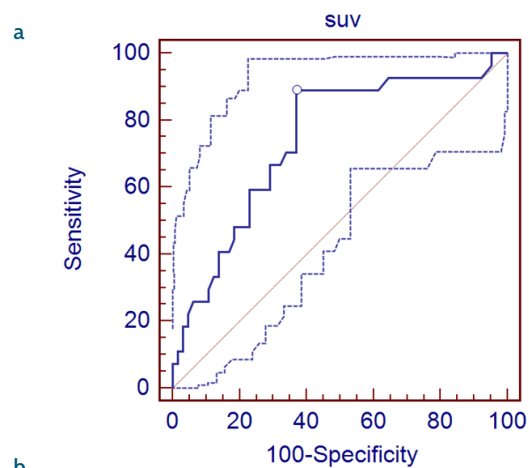
Nasopharyngoscopic examination was normal for 85/92 (92.4%) patients. Pathological analysis revealed that the re-

**Table 1. Pathological diagnoses of the 92 patients**

Condition	n	%
Non-Hodgkin's lymphoma	36	38.7
Hodgkin's lymphoma	15	16.1
Lung adenocarcinoma	12	12.9
Breast	7	7.5
Lung epidermoid cancer	5	5.4
Colon cancer	4	4.3
Hypopharyngeal carcinoma	4	4.3
Prostate cancer	3	3.2
Melanoma	2	2.2
Multiple myeloma	2	2.2
Asbestosis	1	1.1
Temporal arteritis	1	1.1

#### Main Points:

- FDG PET/CT has the potential to provide diagnostic information at an earlier stage than other imaging modalities, such as CT and MRI.
- Increased FDG uptake has a high sensitivity for diagnosis and staging in many types of malignancies, but increased FDG uptake is also observed in physiological processes and inflammatory changes.
- An SUVmax  $\geq 6.5$  may represent an appropriate cut-off for assessing suspicious nasopharyngeal lesions.



Variable	suv
Classification variable	patalogy
Positive group	
patalogy	= 1
Sample size	27
Negative group	
patalogy	= 0
Sample size	65
Disease prevalence (%)	29.3
Area under the ROC curve (AUC)	0.740
Standard Error	0.0607
95% Confidence Interval	0.638 to 0.826
z statistic	3.959
Significance level P (Area=0.5)	0.0001

**Figure 1. a, b.** ROC curve of the sensitivity and specificity of SUVmax for differentiating benign processes from malignant lesions in the nasopharynx

maining 7 (7.6%) patients had NPC: 5 (71.42%) had undifferentiated NPC and 2 (28.57%) had non-keratinizing squamous cell NPC. The optimum SUVmax cut-off for differentiating benign processes and malignant nasopharyngeal lesions was determined to be 6.5. Compared with pathological analysis, the optimum SUVmax cut-off had a sensitivity and specificity of 88.8% and 63.8%, respectively, and the area under the ROC curve was 0.74 (95% confidence interval, 0.63–0.82; Figure 1. a, b). The positive and negative predictive values of an SUVmax of 6.5 were 50.0% and 93.2%, respectively.

## Discussion

This study evaluated an approach to differentiate benign processes from malignant lesions in patients with incidental nasopharyngeal FDG uptake using PET/CT based on the SUVmax value. Compared with pathological analysis, an SUVmax cut-off of 6.5 had high sensitivity but moderate specificity for detecting malignant lesions in the nasopharynx.

The diagnostic modality FDG PET can be used for whole-body screening as well as the detection and staging of disease (10–13). Functional biological and anatomical changes occur in a tumor before overt morphological changes are detectable; thus, FDG PET/CT has the potential to provide diagnostic information at an earlier stage than other imaging modalities, such as CT and MRI (14).

Increased FDG uptake has a high sensitivity for diagnosis and staging in many types of malignancies, but increased FDG uptake is also observed in physiological processes and inflammatory changes (15). Although the utilization of PET/CT has been shown to be beneficial for diagnosis, application of this technique is limited by false-positive uptake in patients with inflammation of the nasopharynx, which is not uncommon (16). Therefore, increased FDG uptake in the palatine tonsil, lingual tonsil, or tubal tonsil may lead to a suspicion of malignancy but could be because of benign infectious or inflammatory processes in these regions. For evaluation of the potential recurrence of head and neck squamous cell carcinoma, a lesion with SUVmax>2.5–3.0 is considered suspicious of malignancy (17). However, there is no definitive diagnostic SUVmax threshold for differentiating malignant lesions and benign processes. Zhuang et al. (18) reported that a dual time point FDG imaging method appeared to be useful for distinguishing malignant and benign lesions in different tumors. However, Yen et al. (4) demonstrated no significant difference with dual-phase FDG PET scans in the diagnosis of primary tumors or loco-regional nodal metastases. Although incidental increased uptake of FDG in the nasopharynx (SUVmax≥3) was observed in all 92 patients in this study, only 7 (7.6%) of these patients were pathologically confirmed to have NPC. All 7 patients with NPC demonstrated intense nasopharyngeal uptake (SUVmax>6.5). Therefore, we propose an FDG SUVmax threshold of 6.5 to distinguish between benign and malign lesions in the nasopharynx.

Increased FDG uptake in the nasopharynx may be suspicious of malignancy but could also be because of benign infectious or inflammatory processes in these regions. We aimed to find the predictive value of FDG SUVmax on PET/CT in patients with incidental involvement in the nasopharynx. An SUVmax≥6.5

may represent an appropriate cut-off for assessing suspicious nasopharyngeal lesions.

**Ethics Committee Approval:** This study was approved by the Ethics Committee of Marmara University School of Medicine (ID number: 09.2016.203, issue date: 04.03.2016).

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – A.B.; Design – A.B.; Supervision – B.D.; Resources – B.D.; Materials – B.D.; Data Collection and/or Processing – B.D.; Analysis and/or Interpretation – Y.G.; Literature Search – Y.G.; Writing Manuscript – A.B., B.D.; Critical Review – C.B.

**Conflict of Interest:** The authors have no conflicts of interest to declare.

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