ORIGINAL ARTICLE

Preoperative predictive model of cervical lymph node metastasis combining fluorine-18 fluorodeoxyglucose positron-emission tomography/computerized tomography findings and clinical factors in patients with oral or oropharyngeal squamous cell carcinoma

Yumi Mochizuki, DDS, PhD,[a] Ken Omura, DDS, PhD,[b] Shin Nakamura, DDS, PhD,[c] Hiroyuki Harada, DDS, PhD,[d] Hitoshi Shibuya, MD, PhD,[e] and Toru Kurabayashi, DDS, PhD,[f] Tokyo, Japan
TOKYO MEDICAL AND DENTAL UNIVERSITY

Objective. This study aimed to construct a preoperative predictive model of cervical lymph node metastasis using fluorine-18 fluorodeoxyglucose positron-emission tomography/computerized tomography (^{18}F-FDG PET/CT) findings in patients with oral or oropharyngeal squamous cell carcinoma (SCC).
Study Design. Forty-nine such patients undergoing preoperative ^{18}F-FDG PET/CT and neck dissection or lymph node biopsy were enrolled. Retrospective comparisons with spatial correlation between PET/CT and the anatomical sites based on histopathological examinations of surgical specimens were performed. We calculated a logistic regression model, including the SUVmax-related variable.
Results. When using the optimal cutoff point criterion of probabilities calculated from the model that included either clinical factors and delayed-phase SUVmax ≥0.087 or clinical factors and maximum standardized uptake (SUV) increasing rate (SUV-IR) ≥ 0.100, it significantly increased the sensitivity, specificity, and accuracy (87.5%, 65.7%, and 75.2%, respectively).
Conclusions. The use of predictive models that include clinical factors and delayed-phase SUVmax and SUV-IR improve preoperative nodal diagnosis. (Oral Surg Oral Med Oral Pathol Oral Radiol 2012;113:274-282)

A defining characteristic of oral cavity and oropharyngeal cancer is the considerably high frequency of metastasis in lymph nodes.[1,2] Even with improved diagnostic imaging techniques, it remains difficult to reduce occult metastatic disease in oral cavity cancer to less than 20%,[3] which is why the accurate diagnosis of cervical lymph node metastasis and early treatment is so critically important for prognostic purposes.[4]

Fluorine-18 fluorodeoxyglucose positron-emission tomography/computerized tomography (^{18}F-FDG PET/CT) is increasingly being used in the preoperative staging of cancer patients.[18] F-FDG-PET has an advantage over other imaging modalities in that it detects changes in glucose metabolism, which is seen in malignant cells compared with normal cells, and is closely related to the viability of cancer cells.[3,5,6] Because metabolic changes precede structural changes, the sensitivity of ^{18}F-FDG PET/CT for early-stage disease may be higher than that of anatomical modalities.[6] ^{18}F-FDG PET/CT has been reported to be effective for the diagnosis, staging, and restaging of malignancies of the head and neck region.[7,8]

In the diagnosis of occult cervical lymph node metastasis, current radiological investigations with CT, magnetic resonance imaging (MRI), and ultrasonography (US) all suffer from limitations[3]; moreover, it has been suggested that it is difficult to select and interpret diagnostic test results correctly without making an estimate of the diagnostic probability of lymph node metastasis before offering surgery.[9,10] In efforts to resolve these problems, in recent years some studies have attempted to estimate the preoperative probability of lymph node metastasis in patients with non–small cell lung cancer or uterine cervical cancer by constructing and validating predictive compound models of metastasis-suspect lymph nodes based on ^{18}F-FDG PET/CT results and clinical factors.[9,11]

The purpose of this study was to construct a preoperative predictive model of cervical lymph node metas-

[a]Clinical Fellow, Department of Oral and Maxillofacial Surgery, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.
[b]Professor, Department of Oral and Maxillofacial Surgery, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.
[c]Assistant Professor, Department of Oral and Maxillofacial Radiology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.
[d]Associate Professor, Department of Oral and Maxillofacial Surgery, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.
[e]Professor, Department of Diagnostic Radiology and Oncology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.
[f]Professor, Department of Oral and Maxillofacial Radiology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.
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tasis using a combination of ^{18}F-FDG PET/CT findings and clinical factors in patients with oral or oropharyngeal squamous cell carcinoma (SCC). Previous reports of ^{18}F-FDG PET/CT for the diagnosis of cervical lymph nodes in patients with head and neck SCC evaluated nodal status from single time-point PET/CT images about 60 minutes after ^{18}F-FDG injection (early-phase PET/CT image).[12] To our knowledge, there have been few reports in which delayed-phase PET/CT imaging was used to evaluate the nodal status of patients with head and neck SCC.[12] Against this background, we constructed predictive models from ^{18}F-FDG PET/CT findings, such as early- and delayed-phase maximum standardized uptake $(SUV)_{max}$ and SUV_{max} increasing rate (SUV-IR), and we estimated the appropriate variables for the predictive models.

MATERIAL AND METHODS

Subjects

Our study was conducted with a total of 510 consecutive patients seen at the Department of Oral and Maxillofacial Surgery, Tokyo Medical and Dental University Hospital, for SCC of the oral cavity or oropharynx at some time between November 2005 and October 2010. The inclusion criteria were as follows: (1) primary SCC of the oral cavity or oropharynx, (2) had undergone dual-phase ^{18}F-FDG PET/CT scanning, (3) had undergone neck dissection or lymph node biopsy, and (4) had received no preoperative treatment. Of these 510 patients, 461 were excluded for the following reasons: 95 had undergone preoperative chemotherapy, 40 had received preoperative radiotherapy, 44 had received preoperative chemoradiotherapy after ^{18}F-FDG PET/CT scanning, 1 patient did not undergo surgery because of poor general condition, 277 underwent only tumor resection with no scanning or preoperative treatment. Four patients who underwent only single-phase ^{18}F-FDG PET/CT scanning before neck dissection with no other preoperative treatment were excluded from our analyses for a reason that the study purpose includes the construction and evaluation of predictive models based on dual-phase SUV max or SUV-IR. Thus, in total, 49 patients (31 men, 18 women) were enrolled in further analysis. Their ages ranged from 33 to 83 years, with an average age of 63.2 years. Patient characteristics are shown in Table I. The disease was controlled in 43 patients. Three patients developed neck failure, 2 patients died of uncontrolled disease because of a primary recurrence, and 1 patient died with lung metastases, despite locoregional control of the cancer during the median follow-up period, which was 915 days after surgery (range, 207-1882 days).

The Institutional Review Board of Tokyo Medical and Dental University approved this retrospective study. We obtained informed consent from all patients for performing ^{18}F-FDG PET/CT examinations and for use of the obtained data for research purposes.

Table I. Patient characteristics

Characteristic	*Case number*	*%*
Localization		
Tongue	17	34.7
Lower gingiva	16	32.7
Buccal	7	14.3
Floor of mouth	3	6.1
Mandible	4	8.2
Upper gingiva	2	4.1
T		
T1	7	14.3
T2	26	52.1
T3	7	14.3
T4	9	18.4
N		
N0	42	85.7
N1	3	6.1
N2b	3	6.1
N2c	1	2.0
Stage		
I	7	14.3
II	24	49.0
III	5	10.2
IV	13	26.5
Histologic grade of differentiation		
Well	33	67.3
Moderate	11	22.4
Poor	4	8.2

PET/CT examination

The protocol for PET/CT examination in our hospital has been described previously.[12,13] Patients received an intravenous injection of 3.7 MBq/kg ^{18}F-FDG after fasting for 4 hours. Images were obtained using a PET/CT system (Aquiduo, Toshiba Medical Systems, Tokyo, Japan), which combines a full-ring PET scanner with lutetium oxyorthosilicate crystals and a 16-row helical CT scanner. First, CT images were acquired from the head to the upper thigh. After CT,[18] F-FDG PET scanning of the same region was performed.

Attenuation correction of ^{18}F-FDG PET images was performed using CT data.[18] F-FDG PET/CT scanning was acquired twice. The early phase was scanned at a mean time of 63.0 minutes (SEM, ±6.8 minutes) and the delayed phase at a mean time of 130.4 minutes (SEM ± 14.1 minutes).

Surgical treatment and pathologic assessment

Patients were surgically treated within a median of 13 days (range, 2-36 days) after receiving their PET/CT scan. All 49 patients were operated on by 2 surgeons. We performed 10 suprahyoid neck dissections (SHND; cervical lymph node levels I and II), 17 supraomohyoid