Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology

journal homepage: www.elsevier.com/locate/jomsmp

Original research

A diagnosis system for detecting cervical lymph node metastasis in oral squamous cell carcinoma: Collective consideration of the results of multiple imaging modalities

Takayuki Ishida[a], Hiroshi Hijioka[a,*], Kenichi Kume[a], Takuya Yoshimura[a], Akihiko Miyawaki[b], Etsuro Nozoe[a], Shigeaki Suenaga[c], Hiroko Indo[c], Hideyuki J. Majima[c], Norifumi Nakamura[a]

[a] *Department of Oral and Maxillofacial Surgery, Graduate School of Medical and Dental Sciences, Kagoshima University, 8-35-1 Sakuragaoka Kagoshima 890-8520, Japan*
[b] *Department of Clinical Epidemiology, Institute of Industrial Ecological Sciences, University of Occupational and Environmental Health, Yahata-nishi-ku, Kitakyushu 807-8555, Japan*
[c] *Department of Maxillofacial Radiology, Graduate School of Medical and Dental Sciences, Kagoshima University, 8-35-1 Sakuragaoka Kagoshima 890-8520, Japan*

ARTICLE INFO

Article history:
Received 4 February 2016
Received in revised form
20 September 2016
Accepted 26 December 2016
Available online xxx

Keywords:
Oral squamous cell carcinoma
Metastasis
Imagings
Diagnosis

ABSTRACT

Object: The aim of this study was to assess our diagnosis system for cervical node metastasis for oral squamous carcinoma (OSCC) based on the combined results of computed tomography (CT), magnetic resonance imaging (MRI), ultrasonography (US), and 18-fluorodeoxyglucose positron emission (^{18}F-FDG-PET/CT).
Methods: 106 patients with primary OSCC who underwent surgical treatment were divided into 3 groups. In group 1, cervical node metastasis was diagnosed by disunity combinations of diagnostic devices. In groups 2 and 3, it was assessed according to a set of diagnostic criteria that included the results of the CT/MRI, US and ^{18}F-FDG-PET/CT. In group 2, node status was considered negative when the results of both CT/MRI and US were negative. In group 3, node status was considered negative when the results of both CT/MRI and US were negative and the maximum standardized uptake value determined via ^{18}F-FDG-PET/CT was <3.2.
Results: 67 patients were diagnosed as cN0. 50 cN0 patients adopted the wait and watch policy, 12 of whom (24.0%) developed cervical node metastasis without recurrence at the primary site. Metastasis rates after surgery improved 33.3%, 23.5%, and 13.3% in groups 1, 2, and 3, respectively. In contrast, positive predict value (PPV) were worst (50.0%, 40.0% and 33.3%).
Conclusions: Our diagnosis system reduces the rate of cervical lymph node metastasis after surgery.

1. Introduction

Cervical lymph node metastasis is a significant prognostic indicator in oral squamous cell carcinoma (OSCC) [1,2]. Despite the development of modern imaging techniques, the incidence of occult metastases is variable, ranging from 6 to 50% [3–7]. The ideal management strategy for OSCC patients with clinically node-negative (cN0) necks is controversial. Management options include elective neck dissection and "wait and watch"; both have proponents among head and neck surgeons in different cancer centers worldwide [8]. cN0 patients have a risk of nodal metastasis and often undergo elective neck dissection. However, approximately 70% of cN0 patients do not develop neck metastases; therefore, elective neck dissection may incur unnecessary costs and morbidities. On the other hand, 20–30% of cN-positive patients who do

Abbreviations: CT, computed tomography; ^{18}F-FDG-PET, 18-fluorodeoxyglucose positron emission; FN, false negative; FP, false positive; NPV, negative predictive value; OSCC, oral squamous cell carcinoma; PPV, positive predictive value; SUV, standardized uptake value; TP, true positive; US, ultrasonography.

☆ AsianAOMS: Asian Association of Oral and Maxillofacial Surgeons; ASOMP: Asian Society of Oral and Maxillofacial Pathology; JSOP: Japanese Society of Oral Pathology; JSOMS: Japanese Society of Oral and Maxillofacial Surgeons; JSOM: Japanese Society of Oral Medicine; JAMI: Japanese Academy of Maxillofacial Implants.

* Corresponding author at: Department of Oral and Maxillofacial Surgery, Graduate School of Medical and Dental Sciences, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima 890-8544, Japan.
E-mail address: zio@dent.kagoshima-u.ac.jp (H. Hijioka).

http://dx.doi.org/10.1016/j.ajoms.2016.12.007
2212-5558/

not undergo neck dissection develop cervical node metastases during the follow-up period [9]. Although the wait and watch policy may eliminate unnecessary surgery and associated dysfunction, it is required careful follow up to detect metastatic cervical nodes after surgery because it is not known when they will appear. In addition, subsequent metastases have a high amount of nodal extra-capsular spread that worsens outcome. Therefore, a critical goal of an imaging modality in OSCC is detection of metastatic neck disease at the time of initial treatment.

Computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonography (US) are currently used for preoperative assessment of the primary tumor and cervical node status. Diagnosis of cervical lymph node metastasis via CT and US is based on morphological imaging parameters such as nodal size, shape, and contrast enhancement pattern [10,11], but not on metabolic activity. 18-fluorodeoxyglucose positron emission tomography (^{18}F-FDG-PET) is a functional imaging modality that detects metabolic differences among tissues. It is useful for staging cervical node metastasis in head and neck cancer patients because it is more sensitive and specific than CT and MRI [12–15]. In addition to accurate staging of local and regional disease, it identifies distant metastases and synchronous malignancies and thereby avoids gratuitous treatments [16]. In the past, we did not have a unified diagnostic system; therefore, different modalities were used to detect cervical lymph node metastasis. To improve the reproducibility of diagnostic accuracy and to reduce the number of unnecessary neck dissections and the metastasis rate after tumor resection, we established a chart diagnostic criteria system based on the combined results of CT, MRI, US, and ^{18}F FDG PET. This study aimed to assess the clinical usefulness of this system in OSCC patients in terms of occult metastasis at the time of initial treatment and metastasis after tumor resection.

2. Materials and methods

2.1. Patients

Our study included 106 OSCC patients who underwent surgical treatment with providing informed consent, between October 2005 and March 2012 in the Department of Oral and Maxillofacial Surgery at Kagoshima University Hospital. All patients were evaluated via contrast-enhanced CT or MRI, US, and ^{18}F FDG-PET/CT before initial treatment. Clinical staging was based on the International Union Against Cancer TNM classifications (2002, 6th edition). Patients were grouped according to the diagnostic criteria used to assess cervical lymph node status as described below. The treatment times for the 3 groups were as follows: group 1 (45 patients), 2005 October to 2008 August; group 2 (29 patients), 2008 September to 2010 March; and group 3 (32 patients), 2010 April to 2012 March.

2.2. ^{18}F-FDG-PET/CT

^{18}F-FDG-PET/CT images were obtained using a Discovery ST system until May 2011 and a Discovery 600 system (General Electric Corporation) thereafter. Patients were instructed to refrain from ingesting processed sugar for 6 h before ^{18}F FDG-PET/CT scanning, and our exclusion criteria included diabetes mellitus. None of the patients were extremely obese. Whole body scanning was performed 1 h after ^{18}F FDG dosing, and local images were scanned 2 h later. The ^{18}F FDG dose was 3.7 MBq/kg body weight. After acquisition, 2-dimensional whole body emission images were reconstructed using an interactive reconstruction algorithm. For determination of the standardized uptake value (SUV), radiologists defined a region of interest in CT images that included the primary tumor and surrounding tissue. SUV was automatically calculated as the activity concentration [^{18}F-FDG uptake divided by the injected dose of ^{18}F FDG (dose/g body weight)]. SUVmax equals the organic radioactivity [(MBq/g)/^{18}F-FDG dose (MBq/g body weight)].

Table 1
Patient population.

n = 106	group 1	group 2	group 3	total
age	72.0 ± 12.5	69.0 ± 13.7	66.9 ± 11.5	69.9 ± 12.7
sex				
male	28	13	24	65
female	17	16	8	41
cT classification				
T1	8	7	7	22
T2	29	19	17	65
T3	2	2	5	9
T4	6	1	3	10
primary tumor site				
tongue	13	17	12	42
floor of mouth	8	3	3	14
manidble	17	4	9	30
maxilla	4	2	6	12
buccal mucosa	3	3	2	8
recurence for primary site	5	2	1	8
cN0	26	23	14	63
wait and watch policy	18	17	12	47
metastasis after surgery	6	4	2	12

2.3. Other modalities

CT images were taken using a GE Hispeed QE/i (General Electric Corporation), with slice thickness of 1 0.25 mm after immediately injection of contrast regents. MRI images were taken using a GE SIGNA (General Electric Corporation), with slice thickness of 5 mm. US images were taken ProSound 4000 (ALOKA), by 7.5 MHz linear probe.

2.4. Diagnosis of clinical nodal stage

To assess clinical node status, the results of CT/MRI, US, and ^{18}F- FDG-PET/CT were collectively considered. In group 1, the patients received various diagnostic modalities. The criteria of enhance CT/MRI and US were (Fig. 1). The diagnosis of lymph node metastasis of ^{18}FDG-PET/CT was based on subjective findings by radiologists of the Other medical institution. All patients were received ^{18}FDG-PET/CT before treatment, but the node status was determined via various combinations of some modalities.

In groups 2 and 3, node status was assessed according to the diagnostic criteria for CT/MRI (Fig. 2A) and US (Fig. 2B) and the diagnostic system outlined in Fig. 3. In group 2, a cervical node was considered positive if the results of either or both CT/MRI or US were positive. If one result was suspicious but not conclusive and the other was negative or if both results were inconclusive, the node was considered positive if its SUVmax was ≥3.2. If one result was negative and the other was inconclusive, the node was considered negative if its SUVmax was <3.2. A cervical node was considered negative if the results of both CT/MRI and US were negative, regardless of the result of PET/CT. The diagnostic criteria in group 3 were similar to those in group 2 with one exception: when the results of both CT/MRI and US were negative, the final diagnosis was based on SUVmax in group 3. US was performed by radiologists in groups 1 and 2 and by both radiologists and an oral surgeon in group 3, and the worst result was selected.

Please cite this article in press as: Ishida T, et al. A diagnosis system for detecting cervical lymph node metastasis in oral squamous cell carcinoma: Collective consideration of the results of multiple imaging modalities. J Oral Maxillofac Surg Med Pathol (2017), http://dx.doi.org/10.1016/j.ajoms.2016.12.007