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Original research

Clinical possibility of baseline FDG-PET SUV_{max} as a prognostic factor in patients with head and neck non-Hodgkin's lymphoma: A preliminary study☆

Kazuhito Yoshikawa[a,*], Makiko Onodera-Kyan[a,b], Yoshimasa Kitagawa[a], Akira Satoh[a], Jun Sato[a], Tetsuya Kitamura[c], Tohru Shiga[d], Shiro Watanabe[d], Nagara Tamaki[d]

[a] Department of Oral Diagnosis and Medicine, Hokkaido University Graduate School of Dental Medicine, Kita 13 Nishi 7, Kita-ku, Sapporo, 060-8586, Japan
[b] Oral and Maxillofacial Surgery, Sapporo Tokushukai Hospital, 1-1, Higashi 1, Ohyaji, Atsubetsu-ku, Sapporo, 004-0041, Japan
[c] Department of Oral Pathology, Hokkaido University Graduate School of Dental Medicine, Kita 13 Nishi 7, Kita-ku, Sapporo, 060-8586, Japan
[d] Department of Nuclear Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Japan, Kita 13 Nishi 7, Kita-ku, Sapporo, 060-8586, Japan

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ABSTRACT

Objective: FDG-PET has been shown useful in the staging of malignant lymphoma (ML) and in evaluating treatment outcomes. Serum concentration of soluble interleukin-2 receptor (sIL-2R) has also been shown prognostic in patients with MLs. This study analyzed the clinical possibility of baseline FDG-PET parameters, such as maximum standardized uptake values (SUV_{max}), metabolic tumor volume (MTV), total lesion glycolysis (TLG), and serum sIL-2R and lactate dehydrogenase (LDH) concentrations, as prognostic variables in patients with oral and neck non-Hodgkin's lymphoma (NHL).

Methods: Baseline FDG-PET parameters and serum protein concentrations were correlated with 2-year prognosis in 12 patients with oral and neck NHL. The optimal cutoff values for FDG SUV_{max}, serum sIL-2R and LDH were determined by receiver operating characteristics analyses.

Results: At 2-year follow up, seven patients remained alive (good prognosis), and five had died (poor prognosis). The median FDG SUV_{max} was significantly higher in the poor than in the good prognosis groups ($P = 0.04$), but serum sIL-2R concentrations did not differ significantly between the two groups ($P = 0.09$). Baseline MTV and TLG were significantly higher in patients with poor than with good prognosis ($P = 0.02$ each). Serum LDH levels was significantly higher in patients with poor than with good prognosis ($P = 0.01$). Univariate logistic regression analysis showed significant correlations between FDG SUV_{max} and patient prognosis ($P = 0.04$, odds ratio, 23.4).

Conclusion: Comprehensive evaluation of baseline FDG SUV_{max} may have possibility for predicting the prognosis of patients with oral and neck NHLs.

1. Introduction

Malignant lymphoma (ML), including both Hodgkin's lymphomas (HLs) and non-Hodgkin's lymphomas (NHLs), are the tenth frequent type of cancer in Japan; moreover, the prevalence of MLs is increasing [1,2]. Determination of disease extent, or staging, in patients with biopsy-proven ML is important in planning appropriate treatment and in determining prognosis [3]. Improvements in treatment outcome depend not only on new therapeutic techniques but on the development of diagnostic techniques for staging [4].

^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) is a non-invasive, reliable diagnostic imaging tool for various kinds of malignancies, including head and neck cancers, allowing for functional assessment of tumors [5–12]. The good spatial resolution and functionality of FDG-PET scans suggest that this method may be superior to computed tomography (CT) and gallium-67 and bone scintigraphy in lymphoma staging and in evaluating responses to treatment [5–9,11,12].

The serum concentration of soluble interleukin-2 receptor (sIL-2R), a truncated form of the receptor secreted by activated T cells, has been used as a marker of tumor burden and disease activity in NHL [13]. Moreover, sIL-2R concentrations have been found to be prognostic of

☆ 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.
E-mail address: kazzy@den.hokudai.ac.jp (K. Yoshikawa).

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outcomes in patients with many types of lymphomas [14–19]. Although high serum concentrations of lactate dehydrogenase (LDH) were found to be strongly predictive of ML [20], sIL-2R concentrations are considered a better marker of NHL than LDH levels [18].

CRP is an acute-phase reactant, and elevated baseline serum CRP levels have also been found to be predictive of poor prognosis in many types of cancer [21,22]. However, the relationship between pretreatment serum CRP levels and the prognosis of patients with head and neck NHL remains unclear.

Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) are newly developed FDG-PET parameters resulting from new software programs. These parameters may provide additional valuable information for evaluating tumor reaction to treatment and for assessing patient prognosis. MTV, a measure of viable tumor fraction, may better estimate tumor burden than anatomical imaging [10]. The main advantage of FDG-PET over anatomical imaging methods such as CT is the ability of FDG-PET to detect metabolic changes in tumor-associated areas [3]. However, it is not yet clear whether this complementary information affects patient prognosis [3].

The aim of this study was to investigate the clinical possibility of baseline FDG-PET parameters, including SUV_{max} and serum sIL-2R concentration, as prognostic factors in patients with oral and neck NHLs.

2. Patients and methods

2.1. Patients (Table 1)

This study retrospectively evaluated 12 patients (4 men, 8 women; age range, 47–90 years) with histopathologically proven NHLs who were referred to Hokkaido University Dental Hospital between January 2002 and September 2008. Their clinical characteristics are summarized in Table 1. Eight patients were diagnosed with diffuse large B-cell lymphoma (DLBCL), two with mucosa associated lymphoid tissue (MALT) lymphoma, and two with follicular lymphoma. Nine of the 12 patients had oral lesions. Three patients had maxillary lesions, three had tumors of the hard palate, two had lesions in submandibular lymph nodes, two had mandibular lesions, one had a malignant neck lymph node, and one had a tumor of the hard palate and parotid gland.

Tumors were clinically staged using the Ann Arbor classification [23]. The International Prognostic Index (IPI) and baseline Deauville Score (DS) were used as the prognostic model [24,25] (Table 1).

Five patients (numbers 1, 3, 6, 9, and 12) received chemotherapy alone, three (numbers 2, 4, and 5) received chemotherapy and radiotherapy, two (numbers 8 and 11) received radiotherapy alone, and one (number 10) received surgery and chemotherapy. The twelfth patient (number 7) died before treatment.

Patients were followed-up clinically for more than 2 years. The patients were divided into two groups by their prognoses. The good prognosis group included patients who were alive at the 2-years follow-up, whereas the poor prognosis consisted of patients who had died within 2-years.

2.2. Clinical examination and imaging (Table 2)

All patients were evaluated routinely with physical examination and laboratory tests, including measurement of serum sIL-2R, lactic dehydrogenase (LDH), and C-reactive protein (CRP) concentrations. Morphological imaging methods included contrast-enhanced CT, magnetic resonance imaging (MRI), and whole-body FDG-PET.

2.3. FDG-PET imaging and analysis

Pretreatment whole-body FDG-PET scanning was performed approximately 60 min after injection of 4.5 MBq/kg body weight of FDG using an ECAT EXACT 47(Siemens-Asahi, Tokyo, Japan) or ECAT EXACT HR+ (Siemens-Asahi) system. Prior to the FDG-PET examination, patients fasted for at last 6 h. None of these patients had insulin-dependent diabetes. All patients were asked to remain resting and quiet and to void just before scanning. The scanning protocol included an emission scan in the 3D mode (2 min) and a transmission scan (3 min) using rotating ^{68}Ge-^{68}Ga rod sources. To correct for attenuation, scans were reconstructed with the ordered subsets expectation maximization algorithm. FDG uptake was evaluated by specialists in nuclear medicine (TS and TN) using the SUV_{max}. Spherical regions of interests (ROIs) were placed over lesions visible on PET images. The 41% SUV_{max} threshold method was used to calculate MTV, as recommended by the European Association of Nuclear Medicine [26–29]. TLG was calculated by multiplying MTV by the SUV_{mean} of the lesion. In the present study, DS, MTV, and TLG were determined from previous databases of PET imaging. However, because data were missing for three patients (patient numbers 3, 5 and 10), only the other nine patients were evaluated.

2.4. Statistical analysis

FDG-PET parameters, serum sIL-2R, LDH, and CRP concentrations,

Table 1
Summary of clinical and histological findings of all patients.

Patient	Age/Sex	Outcome	Histology	Location (Head & Neck)	Other Lesions	Stage	IPI	DS	Treatment
1	84/M	Dead	DLBCL	Ib	Peritoneum	III <	4	5	Chemo
2	69/F	Alive	DLBCL	Maxilla		IE	1	5	Chemo + RT
3	72/M	Alive	DLBCL	Ib		IIE	2	[c]	Chemo
4	47/F	Dead	DLBCL	Mandible, Ib		IIE	0	5	Chemo + RT
5	59/M	Dead	DLBCL	Maxilla		IE	0	[c]	Chemo + RT
6	38/M	Alive	DLBCL	Mandible		IE	0	4	Chemo
7	90/F	Dead	DLBCL	II–IV	Spleen	[a]III <	3	5	[b]
8	61/F	Alive	MALT	Parotis, Hard palate		II	1	5	RT
9	71/F	Alive	Follicular	Hard palate		III <	3	4	Chemo
10	69/F	Alive	MALT	Hard palate, IIa	Chest wall	II	2	4	Ope + Chemo
11	81/F	Dead	DLBCL	Maxilla, NA		IIE	2	[c]	RT
12	67/F	Alive	Follicular	Hard palate	Axilla, Hilum of lung	II	2	4	Chemo

DLBCL: Diffuse large B-cell lymphoma, MALT: MALT lymphoma, Follicular: Follicular lymphoma.
Ib: Submandibular lymph node, II: Upper jugular lymph node, III: Middle jugular lymph node, IV: Lower jugular lymph node.
Chemo: Chemotherapy, RT: Radiotherapy, Ope: Operation.
IPI: International Prognostic Index.
DS: Baseline Deauville Score.
[a] Patient 9: Recurrent NHL.
[b] Patient 7: Died before treatment.
[c] Patient 3, 5, 11 Not available.