Korean J Gastroenterol Vol. 67 No. 4, 183-188
http://dx.doi.org/10.4166/kjg.2016.67.4.183
pISSN 1598-9992 eISSN 2233-6869

ORIGINAL ARTICLE

KJG

# 위 점막 연관 림프조직 림프종에서 PET/CT의 유용성

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## Efficacy of Positron Emission Tomography/Computed Tomography in Gastric Mucosa-associated Lymphoid Tissue Lymphoma

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**Background/Aims:** This study evaluated the diagnostic efficacy of fluorine-18 fluorodeoxyglucose PET/CT (F-18 FDG PET/CT) for patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma and examined the association between FDG avidity and the clinical factors affecting lesions.
**Methods:** Among the patients diagnosed with gastric MALT lymphoma, 16 who underwent a PET/CT for gastric MALT lymphoma were semi-quantitatively and qualitatively tested for FDG avidity of lesions in the stomach. Retrospectively collected data was analyzed to investigate the clinicoradiological factors and endoscopic findings between the patients with positive F-18 FDG PET/CT scans and those with negative scans.
**Results:** Eight of the 16 patients showed FDG avidity. When comparing the size of lesions in the stomach, the patients with FDG avidity had significantly larger lesions than those without (28.8 mm *vs.* 15.0 mm, p=0.03). The FDG-avid group has a significantly higher rate of positive CT scans than the non-avid group (75% *vs.* 13%, p=0.03). According to the endoscopic finding of the lesions, FDG avidity was pronounced with 75% of the protruding tumors, and 100% of the erosive-ulcerative types, which are a type of depressed tumors.
**Conclusions:** When gastric MALT lymphoma is large, when lesions are found using abdominal CT scans, and the macroscopic appearance of a lesion is that of a protruding tumor or erosive-ulcerative type of depressed tumor, there is a high probability that such patients may have a positive F-18 FDG PET/CT scan. **(Korean J Gastroenterol 2016;67:183-188)**

**Key Words:** Positron emission tomography; Stomach; Lymphoma, B-cell, marginal zone

## INTRODUCTION

Gastric mucosa-associated lymphoid tissue (MALT) lymphoma represents nearly 35% of all gastric lymphomas and the stomach is the most common site of extranodal MALT lymphoma.[1-3] It is possible to diagnose a gastric MALT lymphoma by endoscopy and biopsy, but more tests are always needed.[4,5] EUS-guided fine needle aspiration can be helpful[6,7] and EUS can reduce the false negative error rate of endoscopy and biopsy.[8,9] When a patient is diagnosed with gastric MALT lymphoma, a variety of tests are needed to determine the stage of lymphoma. CT is useful to examine lymph nodes above and below the diaphragm but is not as useful in detecting lymph nodes near the stomach.[10] Fluorine-18 fluorodeoxyglucose PET (F-18 FDG PET) is widely used in determining the stage of lymphoma and in evaluating

**Received** February 22, 2016. **Revised** March 25, 2016. **Accepted** March 31, 2016.


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Financial support: None. Conflict of interest: None.

treatment responses and recurrence.[11-14] Little research using F-18 FDG PET has been conducted on MATL lymphoma; although there have been some studies on the clinical use of F-18 FDG PET for MALT lymphoma, most investigated the characteristics of MALT lymphoma in various non-gastrointestinal sites and only a few investigated the clinical validity of F-18 FDG PET for gastric MALT lymphoma.[15-21] Unlike the F-18 FDG PET, F-18 FDG PET/CT evaluates the glucose metabolism of a tumor and the anatomical changes of a lesion, thereby facilitating the differentiation of physiological activities and lesions on a PET scan. As a result, it can help localize lesions from the physiological activities of F-18 FDG in the stomach. This study examines clinical differences in the PET/CT findings of patients who underwent an F-18 FDG PET/CT after being diagnosed with gastric MALT lymphoma to determine the stage of lymphoma and to evaluate the efficacy of a PET/CT scan in diagnosing gastric MALT lymphoma.

## SUBJECTS AND METHODS

### 1. Patients

The retrospective data of 71 patients diagnosed with gastric MALT lymphoma between September 2008 and October 2014 at Inje University Busan Paik Hospital (Busan, Korea) was analyzed. For this study, clinical data and radiological outcomes obtained from the medical records of the patients who underwent PET/CT scans were analyzed. The study excluded patients who were under 18 years of age, did not have an endoscopic diagnosis and biopsy results, did not have PET/CT scans before gastric MALT lymphoma treatment, and those whose post-treatment observation period was less than six months or whose clinical data was missing.

This study was carried out in compliance with The World Medical Association Declaration of Helsinki and ethical principles for medical research involving human subjects. We analyzed treatment records and clinical outcomes of the patients' medical data by adhering to the deliberation requirements of the Inje University Busan Paik Hospital's clinical ethics committee (IRB No. INJE 15-0088).

### 2. Clinicoradiological factors

The study examined the following factors: age, gender, blood test results, infection status, and eradication rate of *Helicobacter pylori*, treatment modalities other than eradication, improvement with gastric MALT lymphoma treatment, Ann Arbor stage, positive CT findings of lesions in the stomach, bone marrow invasion, extragastric lesions, and endoscopic and radiological diagnoses of gastric MALT lymphoma. The endoscopic macroscopic findings were categorized as chronic gastritis-like tumors, depressed tumors, or protruding tumors according to the classification of lesions by Hirose et al.[22] In addition, the number, location, and size of gastric lesions were investigated by endoscopy.

Associations between the aforementioned clinical factors and positive F-18 FDG PET/CT results were studied, as was the connection between the lesions' maximum standardized uptake value ($SUV_{max}$) among the patients with positive findings and their clinical factors.

### 3. FDG PET/CT imaging procedure

All patients fasted for at least six hours and had a blood glucose level of less than 120 mg/dL before receiving an intravenous injection of 481 MBq (13 mCi) of FDG. PET and CT images from the skull base to the proximal thigh were obtained using a dedicated PET/CT scanner (Discovery STE; GE Healthcare, Milwaukee, WI, USA) 60 minutes post-injection. Just before taking the PET/CT images, all patients were encouraged to drink at least 500 mL of water to ensure stomach dilation. CT images were first acquired with acquisition parameters of 140 Kvp, 80 mA, 0.8 sec per CT rotation and a pitch of 6, followed by torso emission scans for 2.5 to 3 minutes per bed position. The acquired PET data were reconstructed to volumetric images using a 2D-OSEM algorithm with two iterations and 16 subsets.

### 4. Analysis of F-18 FDG PET/CT image

The PET/CT images of every patient were first examined by nuclear medicine physicians, after which the $SUV_{max}$ of tumors seen on the images was measured. In order to differentiate physiological activity from a lesion, we had to locate the gastric lesion discovered by endoscopy using PET/CT scans. The lesions are considered as follows; 1) the FDG uptake in the stomach can be macroscopically detected when compared to normal physiological activities, 2) the diffuse uptake in a dilated stomach is greater than the liver uptake. Therefore, the $SUV_{max}$ of tumors was measured. The $SUV_{max}$ was defined as decay-corrected FDG tissue concentration (Bq/g)/(injected dose of F-18 FDG [Bq]/patient's body weight [g]).

### 5. Statistical analysis

A statistical analysis was conducted using IBM SPSS Statistics software version 20.0 (IBM Co., Armonk, NY, USA). Based on the F-18 FDG uptake in PET/CT scan, a Mann-Whitney test was used for continuous variables, whereas a Fisher's exact test was used in categorical variables. Null hypotheses of no difference were rejected if p-values were less than 0.05.

## RESULTS

Of the 71 patients who received gastric MALT lymphoma treatments from September 2008 to October 2014, 55 patients were excluded from the study. Thus, 16 patients were enrolled (Fig. 1). Of these, eight had lesions with positive F-18 FDG uptake, while the rest had lesions with negative F-18 FDG uptake. The average $SUV_{max}$ of the lesions with positive F-18 FDG uptake when scanned by PET/CT was 4.9 (range, 2.3-8.7).

When the two groups were compared in terms of age, gender, blood test results, infection status and eradication rate of *H. pylori*, treatment modalities other than eradication, improvement with gastric MALT lymphoma treatment, Ann Arbor stage, positive CT findings of the lesions in the stomach, bone marrow invasion, and extragastric lesions, there were no significant differences in the F-18 FDG uptake between them (Table 1). Upon CT scans, the group that had lesions with positive F-18 FDG uptake was more likely to have positive CT findings in the stomach than the group that had lesions with negative F-18 FDG uptake (75% *vs.* 13%, p= 0.03).

### 1. The relationship between endoscopic findings and F–18 FDG uptake patterns

Based on the endoscopic macroscopic findings, the 16 patients were classified as having chronic gastritis-like tumors (n=5), depressed tumors (n=7), and protruding tumors (n=4). The association between F-18 FDG uptake patterns and macroscopic classifications of gastric MALT lymphoma is shown in Table 2. F-18 FDG uptake was observed in 75% (3/4) of the protruding tumors, 57% (4/7) of the depressed tumors, and 20% of the chronic gastritis-like tumors (1/5). Every patient with an erosive-ulcerative type tumor, a kind of depressed tumor, had positive F-18 FDG uptake (Fig. 2), whereas all patients with discolored-scar type tumors had negative F-18 FDG uptake (Fig. 3). There was no significant difference in F-18 FDG uptake patterns, in agreement with the number and location of MALT lymphoma. Except for four cases in which the size was difficult to measure as the lesions were diffuse, the lesions in the group with positive gastric F-18 FDG uptake (28.8±10.9 mm) were significantly larger than that of the group with negative gastric F-18 FDG uptake (15.0±7.1 mm) (p=0.03).

## DISCUSSION

The benefits of F-18 FDG PET scan are recognized in determining the stages of and treatment regimens for diffuse large B-cell lymphoma and Hodgkin's lymphoma.[11-14]

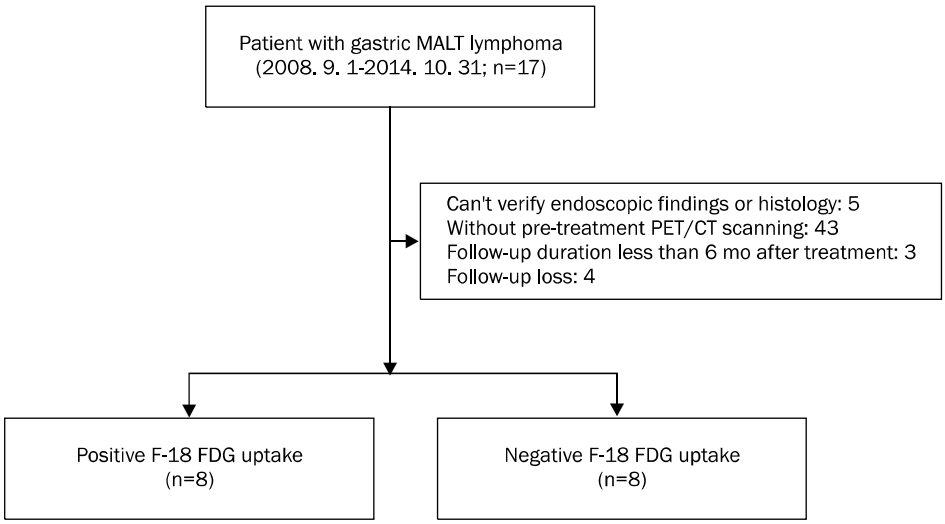


**Fig. 1.** Flowchart shows patient inclusion.
MALT, mucosa-associated lymphoid tissue; F-18 FDG, fluorine-18 fluorodeoxyglucose.

**Table 1.** Comparison between Patients with Positive F-18 FDG Uptake and Patients with Negative F-18 FDG Uptake

| | Positive F-18 FDG uptake (n=8) | Negative F-18 FDG uptake (n=8) | p-value |
|---|---|---|---|
| Age (yr) | 56±9 | 59±14 | 0.51 |
| Sex (male) | 5/8 (63) | 4/8 (50) | 0.63 |
| Laboratory findings | | | |
| WBC (/mm$^3$) | 6,302±1,601 | 6,382±1,419 | 0.88 |
| PMN (%) | 57.6±6.3 | 56.3±9.0 | 0.38 |
| Hemoglobin (g/dL) | 13.4±1.6 | 14.1±1.3 | 0.33 |
| Platelet (K/mm$^3$) | 253±61 | 281±97 | 0.72 |
| LDH (U/L) | 190±51 | 186±36 | 0.84 |
| T-protein (g/dL) | 7.4±0.5 | 7.5±0.5 | 0.72 |
| Albumin (g/dL) | 4.0±0.6 | 4.3±0.5 | 0.23 |
| HP infection | 5/8 (63) | 3/8 (38) | 0.62 |
| Success of HP eradication | 3/4 (75) | 1/4 (25) | 0.74 |
| Other treatment | | | 0.51 |
| Chemotherapy | 4/8 (50) | 2/8 (25) | |
| Radiation therapy | 1/8 (12) | 1/8 (12) | |
| Operation | 1/8 (12) | 0/8 (0) | |
| Complete remission | 8/8 (100) | 6/8 (75) | 0.56 |
| Ann Arbor stage | | | 0.20 |
| Stage I | 5/8 (63) | 8/8 (100) | |
| Stage II | 2/8 (25) | 0/8 (0) | |
| Stage III | 0/8 (0) | 0/8 (0) | |
| Stage IV | 1/8 (12) | 0/8 (0) | |
| Positive CT findings | 6/8 (75) | 1/8 (13) | 0.03 |
| Bone marrow involvement | 0/5 (0) | 0/3 (0) | 1.00 |
| PET uptake sites other than stomach | 7/8 (88) | 5/8 (63) | 0.57 |
| Endoscopic findings | | | |
| Number of lesions | | | 0.07 |
| Single | 6/8 (75) | 2/8 (25) | |
| Multiple | 2/8 (25) | 2/8 (25) | |
| Diffuse | 0/8 (0) | 4/8 (50) | |
| Location of lesion | | | 0.47 |
| Upper | 1/8 (13) | 2/8 (25) | |
| Middle | 3/8 (38) | 4/8 (50) | |
| Lower | 3/8 (38) | 0/8 (0) | |
| Multiple | 1/8 (12) | 2/8 (25) | |
| Size of lesion (mm) | 28.8±10.9 | 15.0±7.1 | 0.03 |
| Endoscopic type | | | 0.71 |
| Chronic gastritis-like | 1/8 (12) | 4/8 (50) | |
| Depressed | 4/8 (50) | 3/8 (38) | |
| Protruding | 3/8 (38) | 1/8 (12) | |

Values are presented as mean±SD or n (%).
F-18 FDG, fluorine-18 fluorodeoxyglucose; WBC, white blood cell; PMN, polymorphonuclear neutrophil; HP, *Helicobacter pylori*.

**Table 2.** Endoscopic Classification of Gastric MALT Lymphoma and F-18 FDG Uptake Patterns

| Endoscopic classification | Subtype | Positive |
|---|---|---|
| Chronic gastritis-like tumors (n=5) | Atrophic type (n=4) | 1 |
| | Nodular arthritis type (n=1) | 0 |
| Depressed tumors (n=7) | Erosive-ulcerative type (n=4) | 4 |
| | Discolored-scar type (n=3) | 0 |
| Protruding tumors (n=4) | Thickened-fold type (n=3) | 2 |
| | Single-protrusion type (n=1) | 1 |
| | Multiple-protrusion type (n=0) | 0 |

MALT, mucosa-associated lymphoid tissue; F-18 FDG, fluorine-18 fluorodeoxyglucose.

However, there have been only a few studies investigating the clinical utility of F-18 FDG PET for gastric MALT lymphoma. This study's value is in its use of F-18 FDG PET/CT rather than just PET to accurately locate the lesions discovered by endoscopy on a CT image and evaluate them. Of the 16 patients confirmed to have gastric MALT lymphoma, eight patients (50%) had lesions that had higher FDG uptake compared to their normal physiological gastric activity, similar to the positivity (62.5%, 10/16) reported by Hirose et al.[22]

According to the findings of this study, a CT scan showed more positive findings for lesions among the group with positive F-18 FDG uptake than the group with negative F-18 FDG uptake. Moreover, the size of gastric MALT lymphoma was significantly larger among the group with positive F-18 FDG uptake. However, two patients were positive on FDG PET/CT scans, although no lesion was discovered on a CT scan (one protruding tumor, one depressed tumor in endoscopic finding). This indicates that not only the size of a lesion but the metabolic activity affects a positive FDG PET/CT finding. Therefore, a large population study is needed to investigate the role of F-18 FDG PET/CT for the prognostic stratification of gastric MALT lymphoma.

Hirose et al.[22] reported the benefit of F-18 FDG PET in finding the protruding type of gastric MALT lymphoma in particular after comparing gastric MALT lymphoma between 16 patients and 16 controls, despite some overlap between the patients' FDG uptake patterns and the control group's FDG uptake patterns. According to the authors, 50% of patients found to have chronic gastritis-like tumors using endoscopy had positive F-18 FDG uptake, 40% of patients with depressed tumors had positive F-18 FDG uptake and 100% of patients with protruding tumors had positive F-18 FDG uptake. In the present study, one of five patients (20%) with chronic gastritis-like tumors, four of seven patients (57%) with depressed tumors, and three of four patients (75%) with protruding tumors had positive F-18 FDG uptake. This confirmed earlier findings that F-18 FDG PET scan is more effective in diagnosing protruding tumors than in diagnosing chronic gastritis-like tumors or depressed tumors. Hirose et al.[22]

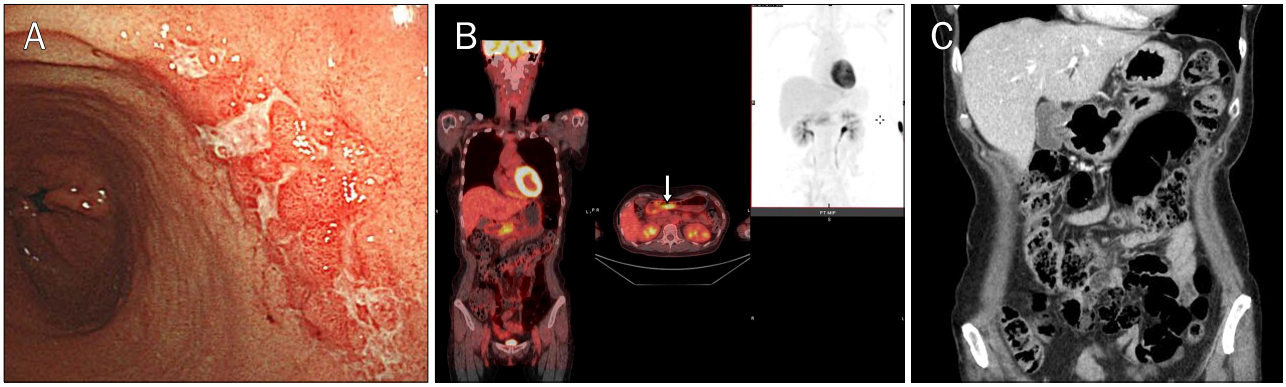


**Fig. 2.** This case shows the fluorine-18 fluorodeoxyglucose (F-18 FDG) uptake in an erosive-ulcerative type of gastric mucosa-associated lymphoid tissue lymphoma. (A) A 56-year-old female patient had an erosive-ulcerative lesion on the antral posterior wall of the stomach. (B) Maximum standardized uptake value of F-18 FDG uptake (arrow) was 6.2. (C) Abdomen CT shows irregular wall thickening at the gastric antrum.

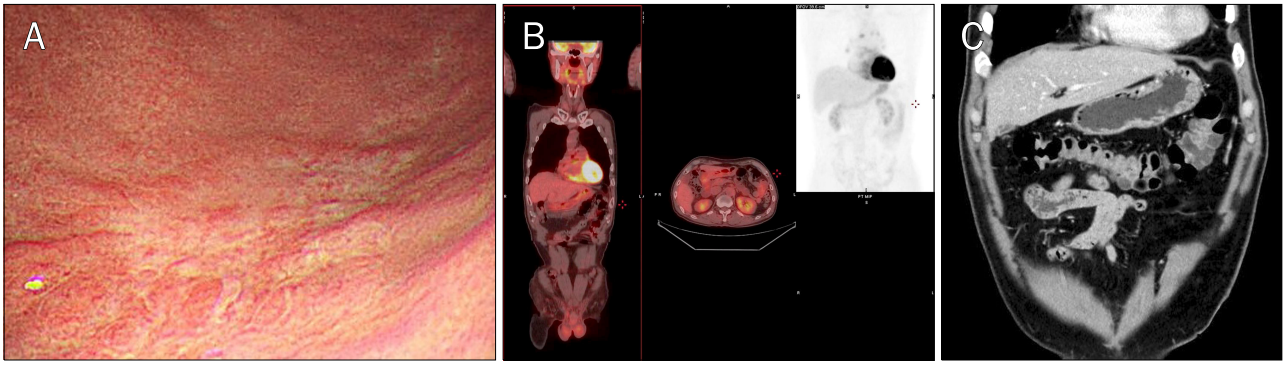


**Fig. 3.** This case shows no fluorine-18 fluorodeoxyglucose (F-18 FDG) uptake in a discolored-scar type of gastric mucosa-associated lymphoid tissue lymphoma. (A) A 53-year-old male patient had a discolored-scar lesion on the greater curvature in lower body of the stomach. (B) F-18 FDG PET revealed no significant F-18 FDG uptake in the stomach. (C) Abdomen CT shows no wall thickening at the gastric body.

found that F-18 FDG uptake was positive in nodular antritis type (100%, 1/1), a type of chronic gastritis-like tumors and in 50% (2/4) of the erosive-ulcerative type, a type of the depressed tumors. In this study, positive F-18 FDG uptake was not observed in nodular antritis type but in 100% (4/4) of the erosive-ulcerative type. This finding confirmed that a PET scan would be useful in determining the stages of gastric MALT lymphoma with erosive-ulcerative type tumors. Discolored-scar type, a form of the depressed tumors, did not have positive F-18 FDG uptake in this study or in the study by Hirose et al. Although the number of lesions did not differ significantly, there was positive F-18 FDG uptake when there was a single lesion and negative F-18 FDG uptake when lesions were diffuse. There needs to be a large population study in the future in order to investigate F-18 FDG uptake patterns of endoscopic macroscopic findings in gastric MALT lymphoma.

To allow for the endoscopist's possible subjectivity when evaluating gastric lesions, additional indices such as the association between EUS findings and F-18 FDG uptake pattern in gastric MALT lymphoma can be used. However, among 16 patients of this study, two subjects with F-18 FDG uptake16 and two subjects without F-18 FDG uptake had taken EUS. The insufficient number of the subjects did not allow statistical testing of EUS differences.

In this study, three of eight patients who had positive F-18 FDG uptake on a PET/CT scan before gastric MALT lymphoma treatment had PET/CT scans after the treatment. Because all of them showed negative FDG uptake in the PET/CT scan after the treatment, the F-18 FDG PET/CT is thought to be effective in determining the treatment effects on gastric MALT lymphoma patients who have positive F-18 FDG uptake on PET/CT scans. Perry et al.[16] reported that nine of 12 patients had a positive PET/CT scan initially at diagnosis and achieved a complete response after therapy, according to follow-up

scan. Beal et al.[17] reported that eight patients obtained post-treatment FDG-PET scans. In five of those eight, the repeated FDG-PET scan indicated a complete response, and in three there was an indeterminate or mixed response. However, additional research with more subjects is needed.

There are a few limitations of the study. Firstly, the research findings cannot be generalized due to the small scale of the research with a small number of research subjects at a single institution. Secondly, there is bias in selecting the subjects as the data were collected retrospectively from patients' medical charts and radiological diagnoses. To overcome such limitations, research involving more institutions and prospective approach is needed.

In conclusion, when gastric lesions are found on abdominal CT scans in patients with gastric MALT lymphoma, when the lesions are large by endoscopy, and their macroscopic appearance shows they are either the protruding tumors or erosive-ulcerative type, the lesions are likely to have positive F-18 FDG uptake. Therefore, PET/CT is potentially useful in diagnosing the patients with these lesions and evaluating the effects of their treatment in gastric MALT lymphoma.

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