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ORIGINAL ARTICLE

Diagnostic role of 18F-fluorodeoxyglucose positron emission tomography for follicular lymphoma with gastrointestinal involvement

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Abstract

AIM: To investigate the capacity for 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) to evaluate patients with gastrointestinal lesions of follicular lymphoma.

METHODS: This retrospective case series consisted of 41 patients with follicular lymphoma and gastrointestinal involvement who underwent 18F-FDG-PET and endoscopic evaluations at ten different institutions between November 1996 and October 2011. Data for endoscopic, radiological, and biological examinations performed were retrospectively reviewed from clinical records. A semi-quantitative analysis of 18F-FDG uptake was performed for each involved area by calculating the maximum standardized uptake value (SUVmax). Based on the positivity of 18F-FDG uptake in the gastrointestinal lesions analyzed, patients were subdivided into two groups. To identify potential predictive factors for 18F-FDG positivity, these two groups were compared with respect to gender, age at diagnosis of lymphoma, histopathological grade, pattern of follicular dendritic cells, mitotic rate, clinical stage, soluble interleukin-2 receptor levels detected by 18F-FDG-PET, lactate dehydrogenase (LDH) levels, hemoglobin levels,

bone marrow involvement, detectability of gastrointestinal lesions by computed tomography (CT) scanning, and follicular lymphoma international prognostic index (FLIPI) risk.

RESULTS: Involvement of follicular lymphoma in the stomach, duodenum, jejunum, ileum, cecum, colon, and rectum was identified in 1, 34, 6, 3, 2, 3, and 6 patients, respectively. No patient had esophageal involvement. In total, 19/41 (46.3%) patients exhibited true-positive 18F-FDG uptake in the lesions present in their gastrointestinal tract. In contrast, false-negative 18F-FDG uptake was detected in 24 patients (58.5%), while false-positive 18F-FDG uptake was detected in 5 patients (12.2%). In the former case, 2/19 patients had both 18F-FDG-positive lesions and 18F-FDG-negative lesions in the gastrointestinal tract. In patients with 18F-FDG avidity, the SUVmax value of the involved gastrointestinal tract ranged from 2.6 to 17.4 (median: 4.7). For the 18F-FDG-negative (n = 22) and -positive (n = 19) groups, there were no differences in the male to female ratios (10/12 *vs* 4/15, P = 0.186), patient age (63.6 ± 2.4 years *vs* 60.1 ± 2.6 years, P = 0.323), presence of histopathological grade 1 *vs* 2 (20/2 and 17/2, P = 1.000), follicular dendritic cell pattern (duodenal/nodal: 13/5 *vs* 10/3, P = 1.000), mitotic rate (low/partly high, 14/1 *vs* 10/3, P = 0.311), clinical stage according to the Ann Arbor system (stages Ⅰ E and Ⅱ E/other, 15/7 *vs* 15/4, P = 0.499), clinical stage according to the Lugano system (stages Ⅰ and Ⅱ-1/other, 14/8 *vs* 14/5, P = 0.489), soluble interleukin-2 receptor levels (495 ± 78 *vs* 402 ± 83, P = 0.884), LDH levels (188 ± 7 *vs* 183 ± 8, P = 0.749), hemoglobin levels (13.5 ± 0.3 *vs* 12.8 ± 0.4, P = 0.197), bone marrow involvement (positive/negative, 1/8 *vs* 1/10, P = 1.000), detectability by CT scanning (positive/negative, 1/16 *vs* 4/13, P = 0.335), and FLIPI risk (low risk/other, 16/6 *vs* 13/6, P = 0.763), respectively in each case.

CONCLUSION: These findings indicate that it is not feasible to predict 18F-FDG-avidity. Therefore, 18F-FDG-PET scans represent a complementary modality for the detection of gastrointestinal involvements in follicular lymphoma patients, and surveillance of the entire gastrointestinal tract by endoscopic examinations is required.

Key words: Follicular lymphoma; Gastrointestinal endoscopy; 18F-fluorodeoxyglucose positron emission tomography; Gastrointestinal lymphoma; Duodenal neoplasm

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INTRODUCTION

To date, 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) has been widely used for the initial staging of various malignant diseases, as well as for the evaluation of therapeutic responses[1-5]. Similar to other types of lymphomas[6-10], follicular lymphoma exhibits a high avidity for 18F-FDG[11-15]. Correspondingly, the percentage of patients with 18F-FDG-avid follicular lymphoma has been reported to range from 91% to 100%[16-20]. Furthermore, nodal and extranodal lesions not detected by other modalities have been identified using 18F-FDG-PET, thereby resulting in a significant advance in lesion management[18-22]. The usefulness of post-treatment 18F-FDG-PET during the follow-up period in cases of follicular lymphoma has also been noted, with positive 18F-FDG accumulation suggesting an adverse outcome[23-25]. Consequently, 18F-FDG-PET is considered a valuable tool for the management of nodal follicular lymphoma.

Despite these advantages, few studies have addressed the use of 18F-FDG-PET for gastrointestinal involvement of follicular lymphoma. In 2004, Hoffmann *et al*[26] reported eight cases of follicular lymphoma localized in the duodenum, and 18F-FDG did not accumulate in any of those patients. Subsequently, several authors described follicular lymphoma patients with positive 18F-FDG uptake in the gastrointestinal tract, including the stomach, duodenum, jejunum, ileum, cecum, and colon[27-30]. However, a limited number of these cases have been reported Therefore, the sensitivity of 18F-FDG-PET for gastrointestinal lesions of follicular lymphoma has not been sufficiently evaluated.

In this study, 18F-FDG-PET results and clinical characteristics of 41 follicular lymphoma patients with gastrointestinal involvement were retrospectively examined. Based on these results, the role of 18F-FDG-PET in the management of these cases was evaluated.

MATERIALS AND METHODS

A database search performed at the Department of Pathology of Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences identified follicular lymphoma patients with gastrointestinal involvement (n = 80) treated at ten collaborating institutions between November 1996 and October 2011. The diagnosis of follicular lymphoma was made according to World Health Organization (WHO) classifications[31,32].

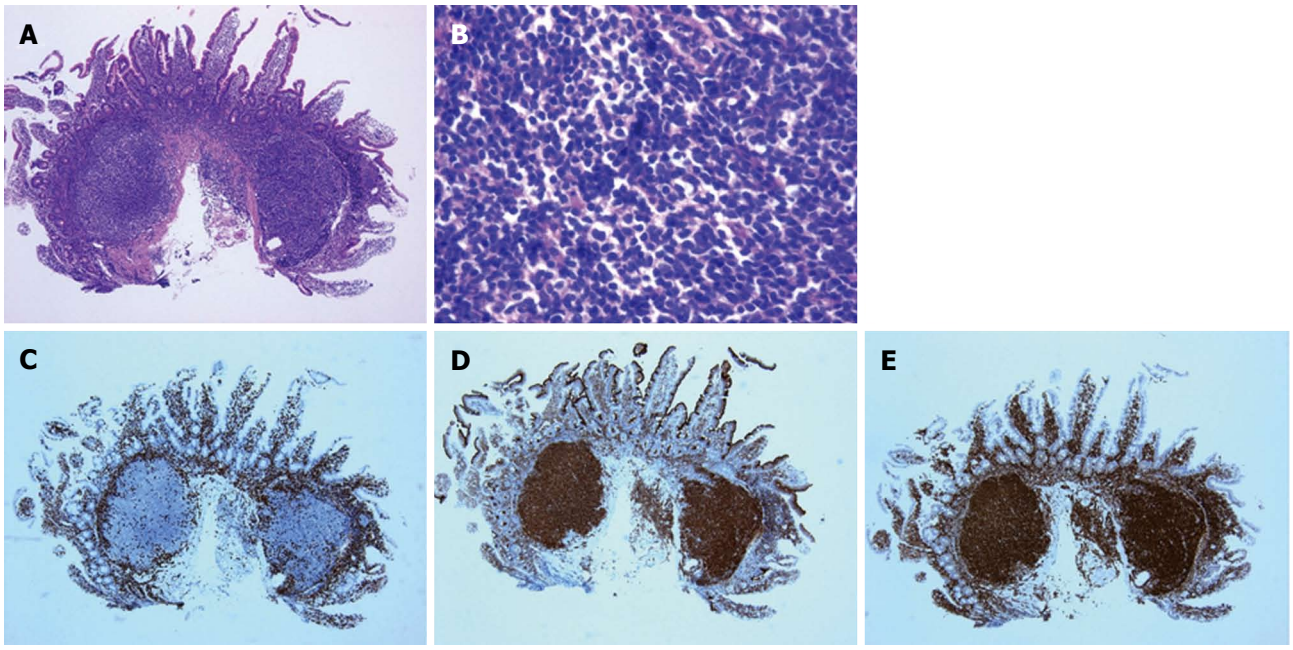

Figure 1 Typical histological features of follicular lymphoma. A, B: Small cleaved cells that infiltrated the duodenal mucosa and formed lymphoid follicles are present (hematoxylin and eosin staining); C: Representative immunohistochemical staining of lymphoma cells negative for CD3; D: Lymphoma cells positive for CD10; E: Lymphoma cells positive for BCL-2. All of the images shown are at 40 × magnification, except for panel B which is at 400 × magnification.

A histological diagnosis was based on morphologic and immunophenotypic analyses of endoscopically biopsied specimens or surgically resected specimens (Figure 1). Histopathological grading was also determined according to WHO criteria[31]. Patients with grade 3 follicular lymphoma were excluded from this study since these cases are typically managed as diffuse large B cell lymphoma[31]. A subset of the 80 patients examined were also subjects of our previous studies[33-36].

Of the 80 patients identified, 30 were excluded since they did not undergo 18F-FDG-PET. Nine patients were further excluded from this study, and these included: four patients that received systemic chemotherapy and remained in complete remission during their 18F-FDG-PET examination, four patients that underwent surgical resection of gastrointestinal lesions and 18F-FDG-PET scans were postoperatively performed, and one patient that underwent 18F-FDG-PET during their initial staging, and later was diagnosed with follicular lymphoma by laparotomy. In the latter case, the patient was not endoscopically evaluated preoperatively. Therefore, a total of 41 patients were enrolled in this study, and data regarding endoscopic, radiological, and biological examinations performed were retrospectively reviewed from their clinical records. Gastrointestinal involvement was defined by gross findings of endoscopic examinations which included esophagogastroduodenoscopy, colonoscopy, double-balloon enteroscopy, and/or video capsule endoscopy. Typically, small, whitish polypoid nodules up to 2 mm in diameter were observed[37,38]. In cases involving an atypical endoscopic appearance, a histopathological assessment of biopsy specimens was performed to confirm a diagnosis of gastrointestinal involvement.

For all patients, 18F-FDG-PET was performed after patients had fasted for at least 4 h, and it was confirmed that their serum glucose levels were below 150 mg/dL. Moreover, 18F-FDG-PET was preceded by a low-dose computed tomography (CT) scanning, and these scans were used to correct attenuation and to localize anatomical variations visualized in 18F-FDG-PET. The time to initiation of 18F-FDG-PET following the intravenous administration of 18F-FDG also varied according to institution (i.e., 60, 90, or 120 min). A semi-quantitative analysis of 18F-FDG uptake was then performed for each involved area by calculating the maximum standardized uptake value (SUVmax).

Based on the positivity of 18F-FDG uptake in the gastrointestinal lesions analyzed, patients were divided into two groups. To identify potential predictive factors for 18F-FDG positivity, patient gender, age at diagnosis of lymphoma, clinical stage, bone marrow involvement, histopathological grade, soluble interleukin-2 receptor (sIL-2R) levels, lactate dehydrogenase (LDH) levels, and hemoglobin levels were evaluated. CD21 and CD23 staining were also performed to characterize duodenal patterns and nodal patterns of follicular dendritic cells present, as previously described[35]. To estimate the mitotic rate, Ki-67 staining was performed. Positive staining of 0%-5% of cells was classified as a low mitotic rate, while > 5% positivity was classified as high mitotic activity. The Lugano staging system for classification of gastrointestinal lymphoma[39,40], and the classical Ann Arbor staging system for nodal lymphoma[41], were used to determine patients' clinical stages. The follicular lymphoma international prognostic index (FLIPI) was used as well[42]. Despite FLIPI-2 recently being introduced as an updated

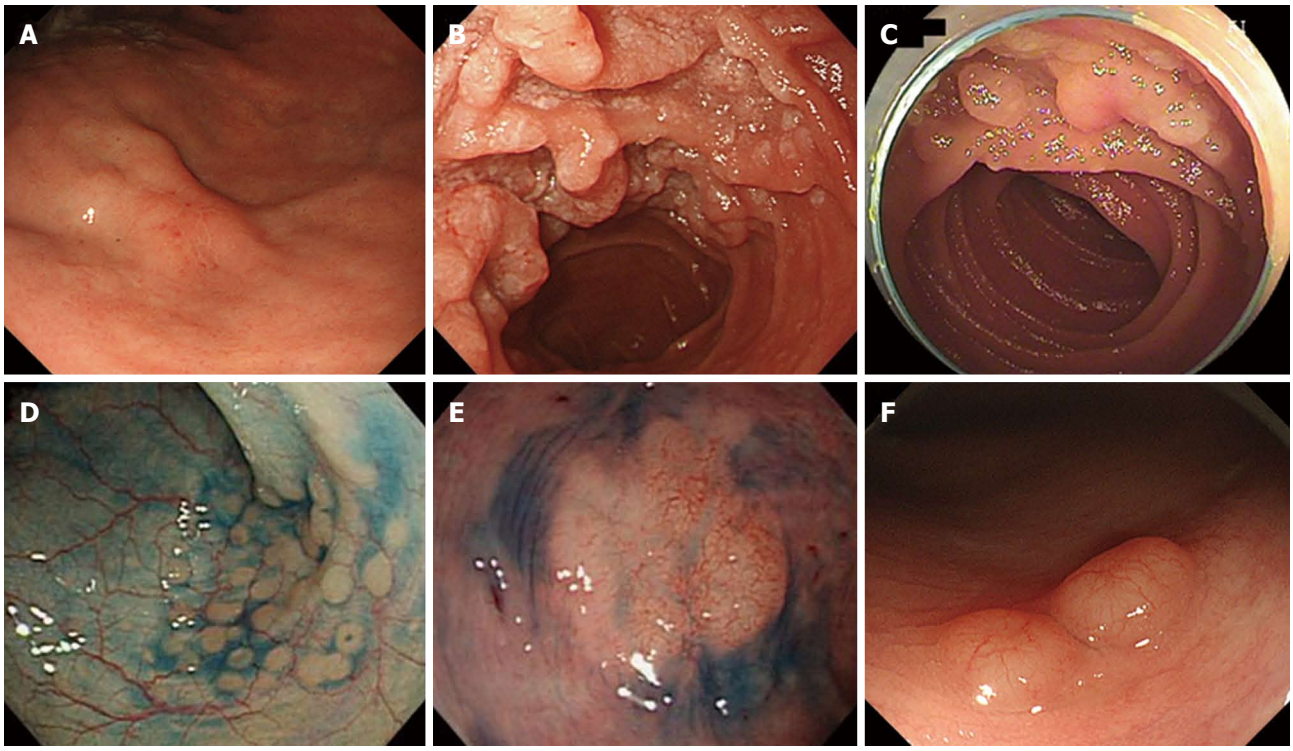

Figure 2 Endoscopic images of follicular lymphoma. A: A gastric lesion with thickened rugae exhibiting a slight redness; B: Typical features of the whitish polypoid granules observed in the duodenum; C: Whitish polypoid lesions in the jejunum; D: Indigo carmine contrast was used to emphasize the slightly elevated small polyps present in the colon; E: An elevated lesion with a flat surface and a 20 mm diameter was observed in the rectum; F: In another patient, polypoid lesions exhibiting hypervascularity on the surface were detected in the rectum.

prognostic index[43], it was not employed in this study since beta-2-microglobulin levels were not available for all of the patients. In some patients, CT scanning was separately performed from 18F-FDG-PET, and the detectability of gastrointestinal lesions by CT scanning was also analyzed.

For comparisons of the two groups, statistical analyses were performed by JMP 8.0.1 software (SAS Institute, Cary, NC, United States), which included *t*-tests, χ^2 tests, and *F*-tests. A *P*-value less than 0.05 was considered statistically significant.

RESULTS

For detection of gastrointestinal lesions, an esophagogastroduodenoscopy was performed for all 41 patients included in this study. However, for one patient with colonic follicular lymphoma, the results of the esophagogastroduodenoscopy performed at another referral center were not available. Colonoscopies were also performed for 29/41 patients. For these patients, the small intestines were evaluated by double-balloon enteroscopy (n = 7), video capsule endoscopy (n = 6), or both methods (n = 3). None of the patients had esophageal involvement. Furthermore, one patient had involvement of the stomach which manifested with thickened rugae observed to have a slight redness to its surface (Figure 2A). Involvement of the duodenum was identified in 34 patients, with the duodenal lesions present in 32 of these patients exhibiting an accumulation of small, whitish polypoid nodules (Figure 2B). For the other two patients, one presented with erosions having peripheral whitish mucosa in the duodenum, while the other had confluent whitish granules in the duodenum. These atypical macroscopic features were previously described[44,45]. Jejunal involvement was identified in six patients. Ileal lesions were found in three patients. In the jejunum and ileum, small whitish polypoid nodules, or ulcerative tumors, were observed (Figure 2C). The cecum was found to be involved in two cases, the colon in three patients, and the rectum in six patients. For cases involving the cecum and the colon, multiple polypoid lesions of various sizes were identified (Figure 2D). Moreover, rectal involvement varied in morphology, with nodules, polyps, submucosal tumors, and laterally spreading tumors observed (Figures 2E, F).

Representative images of 18F-FDG-PET performed are shown in Figures 3-6. In addition, the results of 18F-FDG accumulation in the gastrointestinal tract are summarized in Table 1. The sensitivity of 18F-FDG-PET for the detection of gastrointestinal lesions ranged from 33.3% to 100%. It is noteworthy that sensitivity for duodenal involvement was only identified in 35.3% of cases, while the duodenum was the most frequently affected site[41]. In total, 19 of the 41 patients (46.3%) exhibited true-positive 18F-FDG uptake in the involved gastrointestinal tract. Furthermore, two of these cases had both 18F-FDG-positive lesions and 18F-FDG-negative lesions present in the same gastrointestinal tract. In one patient,

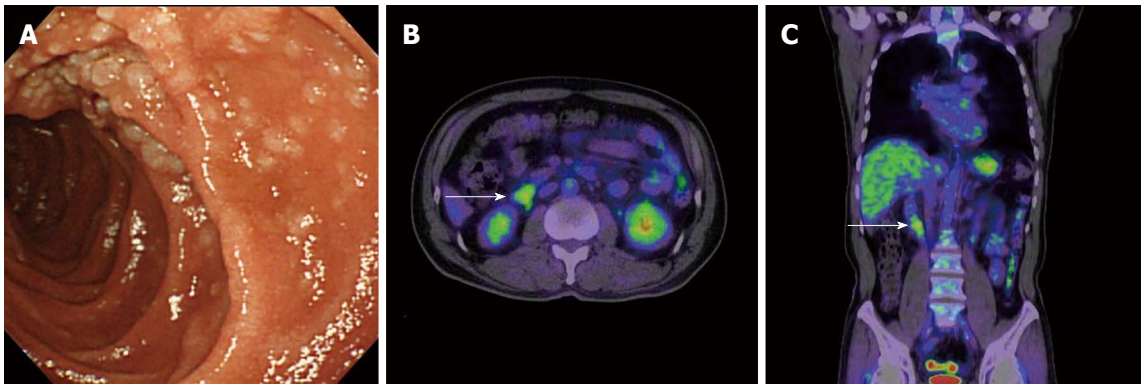

Figure 3 A 60-year-old male patient with duodenal follicular lymphoma without nodal lesions (Lugano system stage Ⅰ, grade 1). A: An esophagogastroduodenoscopy detected features typical of primary duodenal follicular lymphoma, including small whitish nodules; B, C: 18F-fluorodeoxyglucose positron emission tomography detected tracer uptake in the duodenal second portion (indicated with arrows).

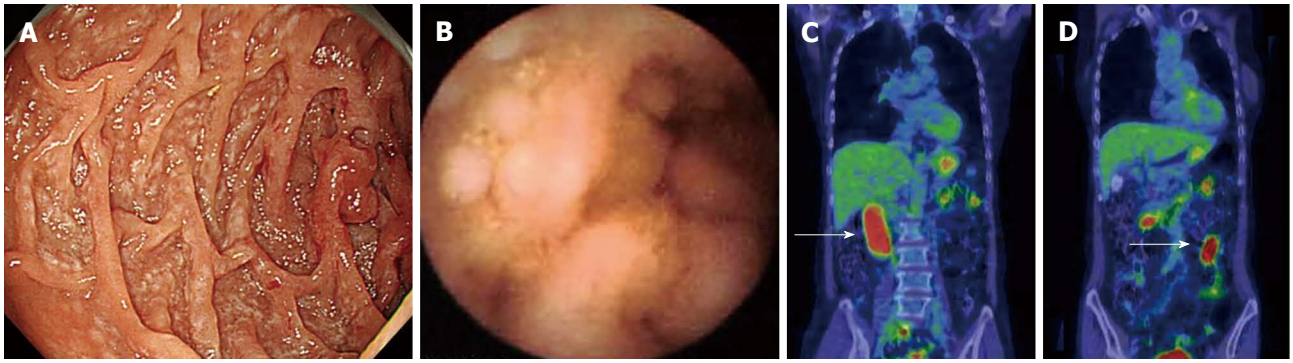

Figure 4 A 65-year-old female patient with duodenal and jejunal follicular lymphoma and intra-abdominal lymph node involvement (Lugano system stage Ⅱ-1, grade 1). A: An esophagogastroduodenoscopy revealed small whitish nodules present in the duodenum; B: Video capsule endoscopy also identified small nodules present in the jejunum; C, D: 18F-fluorodeoxyglucose positron emission tomography detected tracer uptake in the duodenum (C) and the jejunum (D).

Table 1 Accumulation of 18F-fluorodeoxyglucose detected in the gastrointestinal tract

	Positive involvement (defined by endoscopy)	True-positive 18F-FDG uptake	False-positive 18F-FDG uptake	Sensitivity (%)
Esophagus	0	0	0	NA
Stomach	1	1	1	100.0
Duodenum	34	12	0	35.3
Jejunum	6	5	0	83.3
Ileum	3	1	1	33.3
Cecum	2	2	0	100.0
Colon	3	1	1	33.3
Rectum	6	3	2	50.0

18F-FDG: 18F-fluorodeoxyglucose; NA: Not available.

the duodenum, ileum, cecum, colon, and rectum were endoscopically involved, yet 18F-FDG only accumulated in the ileum, cecum, and colon (Figure 5). Another patient had involvement of the duodenum and ileum, yet only the ileal lesion accumulated 18F-FDG. On the other hand, false-positive 18F-FDG uptake was identified in five patients (12.2%), and false-negative 18F-FDG uptake was found in 24 patients (58.5%).

Thirty-four patients underwent CT scanning separate from 18F-FDG-PET. Gastrointestinal lesions detected by CT involved the duodenum in two cases, the jejunum in one case, and the ileum in two cases. In all cases, gastrointestinal involvement was accompanied by a thickness of the intestinal wall. In 13 cases, gastrointestinal lesions that were not detected by CT scanning were identified by 18-FDG-PET. Moreover, 18F-FDG-PET detected affected extra-gastrointestinal organs that were not diagnosed by CT scanning. These included the pleura, diaphragm, and adrenal grand in one patient, the pharynx in another, and diffuse splenic invasion in a third patient. Furthermore, regarding the latter patient, the results of 18F-FDG-PET resulted in an upgrade of the Ann Arbor clinical staging from ⅡE to ⅢES, and in the Lugano system from stage Ⅱ-2 to stage Ⅳ (Figure 6). In regard to 18F-FDG-avid patients, the SUVmax value of the involved gastrointestinal tract region ranged from 2.6 to 17.4 (median: 4.7). Moreover, while one patient had a relatively high SUVmax value of 17.4, the other patients had the SUVmax values less than 10.

A comparison of patients with positive 18F-FDG uptake by their gastrointestinal lesions *vs* those with negative 18F-FDG uptake had no difference in their clinical backgrounds (Table 2). No differences in patient gender, age at the time of diagnosis of lymphoma, clinical stage according to the Ann Arbor and Lugano systems, bone

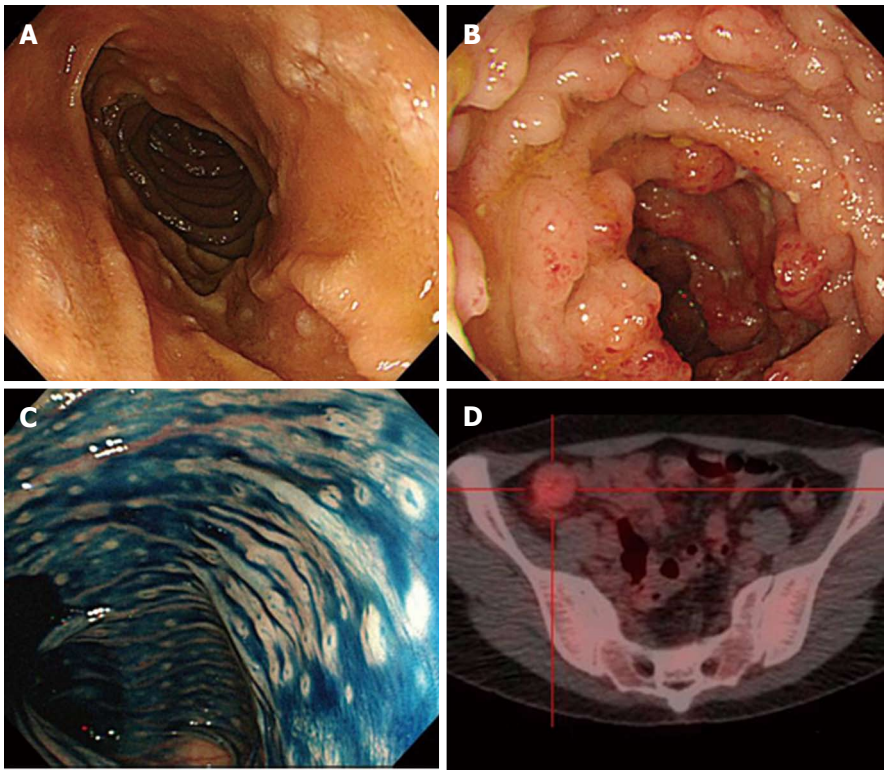

Figure 5 A 37-year-old female patient with systemic follicular lymphoma and extended gastrointestinal involvement from the duodenum to the rectum (stage Ⅳ, grade 1). A: An esophagogastroduodenoscopy detected small whitish nodules present in the duodenum; B, C: A colonoscopy revealed multiple polyps present in the ileum (B), cecum, colon (C), and rectum. Jejunal involvement was confirmed by video capsule endoscopy; D: During 18F-fluorodeoxyglucose positron emission tomography, tracer uptake was only noted in the ileum and colon.

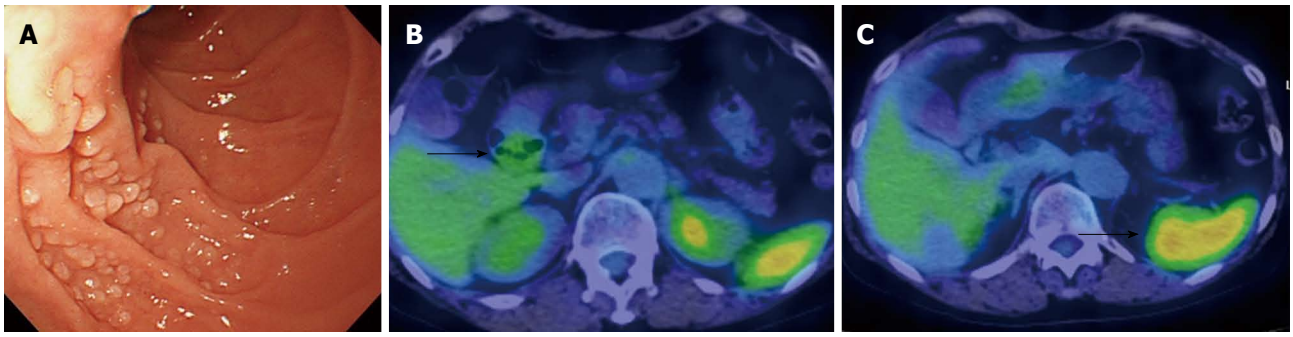

Figure 6 A 61-year-old female patient with follicular lymphoma and duodenal involvement (Lugano system stage Ⅳ, grade 1). A: In the duodenum, small whitish nodules were observed; B: 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) detected tracer uptake in the duodenum (indicated with an arrow); C: 18F-FDG-PET identified diffuse lymphoma infiltration into the spleen (indicated with an arrow), which was not detected by computed tomography scanning. In this case, these results upgraded the clinical stage.

marrow involvement, histopathological grade, pattern of follicular dendritic cells, mitotic rate, sIL-2R, LDH, hemoglobin levels, FLIPI, and detectability of gastrointestinal lesions by CT scanning were found between the two patient groups.

DISCUSSION

To the best of our knowledge, this is the largest study on the sensitivity of 18F-FDG-PET for gastrointestinal involvement of follicular lymphoma. Nineteen of our 41 patients showed true 18F-FDG uptake in the involved gastrointestinal tract, resulting in a sensitivity of 46.3%. In contrast, false-negative 18F-FDG uptake was detected in 24 patients (58.5%), 22 patients (53.7%) exhibited false negative 18F-FDG uptake, and 2 patients (4.9%) showed both true positive and false negative 18F-FDG uptake in gastrointestinal lesions. These results indicate that 18F-FDG-PET is not a reliable imaging tool for evaluating the involvement of the gastrointestinal tract, since greater than half of the patients showed false-negative lesions. It is well-known that follicular lymphoma often affects multiple gastrointestinal tracts. For example, in our previous report, 46 of 54 duodenal follicular lymphoma patients (85.2%) who underwent whole gastrointestinal tract surveillance had extensive involvement within the

Table 2 Clinical backgrounds of the study subjects (mean ± SD)

	Negative FDG uptake in GI tract	Positive FDG uptake in GI tract	*P* value
No. patients (*n*)	22	19	
Male/female	10/12	4/15	0.186
Age (yr) at diagnosis of FL	63.6 ± 2.4	60.1 ± 2.6	0.323
WHO grade			1.000
Grade 1	20	17	
Grade 2	2	2	
Follicular dendritic cell pattern			
Duodenal	13	10	1.000
Nodal	5	3	
Mitotic rate			0.311
Low	14	10	
Partly high	1	3	
Ann Arbor system staging			0.499
ⅠE	12	11	
ⅡE	3	4	
ⅢES	1	0	
Ⅳ	6	4	
Lugano system staging			0.489
Ⅰ	12	10	
Ⅱ-1	2	4	
Ⅱ-2	1	1	
Ⅳ	7	4	
sIL-2R	495 ± 78	402 ± 83	0.884
LDH	188 ± 7	183 ± 8	0.749
Hb	13.5 ± 0.3	12.8 ± 0.4	0.197
Bone marrow involvement			1.000
Positive	1	1	
Negative	8	10	
Detection of GI lesions by CT			0.335
Positive	1	4	
Negative	16	13	
FLIPI risk			0.763
Low	16	13	
Intermediate	3	3	
Poor	3	3	

FDG: Fluorodeoxyglucose; GI: Gastrointestinal; FL: Follicular lymphoma; sIL-2R: Soluble interleukin-2 receptor; CT: Computed tomography; FLIPI: Follicular lymphoma international prognostic index; LDH: Lactate dehydrogenase; WHO: World Health Organization.

small intestine, predominantly in the jejunum (i.e., 40 of 54 patients, 74.1%)[44]. These data are consistent with those reported in other studies where the percentage of patients with multiple lymphoma lesions in the small intestine ranged from 66.7% to 100%[29,46-49]. Therefore, in combination, these results suggest that 18F-FDG-PET represents a complementary method for assessing gastrointestinal involvement of follicular lymphoma.

Regarding the false-negative 18F-FDG-PET results obtained in this study, there are many conditions to consider. First, some of the lymphoma lesions may have been too small to be detected by 18F-FDG-PET[28]. For example, nodes less than 1 to 1.2 cm in diameter have previously been shown to exhibit a false-negative 18F-FDG uptake[17,50]. In addition, the representative endoscopic features of gastrointestinal follicular lymphoma, especially in small intestinal cases, include the presence of small, whitish polypoid nodules up to 2 mm in diameter[37,38]. Generally, these lesions remain small and rarely form bulky tumors. In the present report, gastrointestinal lesions could not be detected by CT scanning in 29 of 34 cases (85.3%). In contrast, CT scanning was able to detect gastrointestinal lesions in five cases, four of which showed 18F-FDG uptake. Therefore, although the sensitivity of CT scanning did not statistically correlate with 18F-FDG avidity, small tumor volume appears to have contributed to the false-negative 18F-FDG uptake results obtained. Second, the intensity of 18F-FDG uptake in follicular lymphoma is relatively low compared with aggressive lymphomas[50,51]. A SUVmax value is a relative quantification of local radiotracer accumulation. Schöder *et al*[50] reported SUVmax values for nodal lesions in indolent and aggressive lymphomas to be 7.0 ± 3.1 and 19.6 ± 9.3, respectively ($P < 0.01$). They also noted that a SUVmax value > 10 excluded indolent lymphoma with a specificity of 81%. In the present study, all but one patient had a SUVmax value < 10, and the results of the present findings are in concordance with data reported in an earlier study[50]. Consequently, small tumor volume and low tracer uptake intensity represent factors that can contribute to false-negative findings.

False-positive FDG uptake by the gastrointestinal tract is another disadvantage associated with 18F-FDG-PET. In this study, five patients had a false-positive 18F-FDG uptake detected in the gastrointestinal tract. Previously it was proposed that physiological peristaltic activity, normal gastrointestinal lymphoid tissue, and granulomatous or inflammatory conditions such as enterocolitis, Crohn's disease, tuberculosis, hemorrhoids, or diverticulitis can cause false-positive 18F-FDG uptake in the gastrointestinal tract[52]. However, physiologic uptake in the gastrointestinal tract is usually diffuse and its intensity generally moderate. In contrast, intense 18F-FDG uptake can be detected under granulomatous or inflammatory conditions, and even in constipated patients[53-55]. Therefore, both false-positive, and false-negative, 18F-FDG-uptake represent potential pitfalls in evaluating possible lymphoma involvement of the gastrointestinal tract.

Despite these disadvantages, there are several benefits to the application of 18F-FDG-PET to follicular lymphoma patients with gastrointestinal involvement. First, as demonstrated in the present study, 18F-FDG-PET was able to detect a greater number of involved gastrointestinal sites than CT scanning. For example, 34 patients underwent both CT scanning and 18F-FDG-PET. Of these, 13 (38.2%) had gastrointestinal lesions that were not detected by CT scanning. Second, 18F-FDG-PET was able to detect extra-gastrointestinal sites of involvement. For example, extra-gastrointestinal sites were detected in three patients, and this resulted in an upgrade of clinical stage for one of these patients (Figure 6). Similarly, previous studies of nodal cases found that the clinical staging of follicular lymphoma patients needed to be modified in 18% to 31% of cases based on 18F-FDG-PET results[17,19,22]. This aspect is particularly

vital for stage I or stage II patients under consideration for radiotherapy as a curative treatment, since most treatment failures occur outside the involved field of radiotherapy[56]. Thirdly, 18F-FDG-PET can be used to evaluate treatment response if a patient has 18F-FDG-avid gastrointestinal lesions. In nodal follicular lymphoma, disappearance of 18F-FDG accumulation after completion of treatment has been associated with a favorable outcome[23-25]. Although the cost and benefit (e.g., sensitivity, specificity, and patient acceptability) of 18F-FDG-PET *vs* other modalities, including the combination of CT scanning and endoscopic examinations, remains to be investigated, 18F-FDG-PET represents an option for assessing the therapeutic effect in cases of gastrointestinal involvement of follicular lymphoma.

There were also several limitations associated with this study. First, not all of the patients underwent endoscopic surveillance for the entire gastrointestinal tract. In particular, the small intestine was not evaluated in 25 patients, although multiple sites, including the jejunum and ileum, were frequently involved[34]. As a result, an overestimation of 18F-FDG-PET sensitivity may have occurred. Second, 18F-FDG-PET was performed under different conditions since the patients included had been treated at various institutions. For example, the period of time between the intravenous administration of 18F-FDG and the initiation of 18F-FDG-PET varied between 60 and 120 min. It is possible that other differences in methodology among the participating institutions may have affected the positivity of 18F-FDG uptake and SUVmax values as well[57,58].

In conclusion, 19 of 41 follicular lymphoma patients (46.3%) exhibited true-positive 18F-FDG uptake in the involved gastrointestinal tract. In contrast, false-negative 18F-FDG uptake was detected in 24 patients (58.5%). There were also no differences found between the 18F-FDG-PET-positive group and the 18F-FDG-PET-negative group based on the clinical backgrounds of the patients examined, suggesting that it is not feasible to predict 18F-FDG-avidity. However, 18F-FDG-PET may facilitate the detection of gastrointestinal and extra-gastrointestinal sites of involvement. Therefore, we propose that 18F-FDG-PET represents a complementary method for the detection of gastrointestinal lesions of follicular lymphoma. However, endoscopic examinations should be performed to monitor the entire gastrointestinal tract.

COMMENTS

Background

18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) has been widely used for the initial staging of various malignant diseases. Similar to other types of lymphomas, follicular lymphoma exhibits a high avidity for 18F-FDG. The percentage of patients with 18F-FDG-avid follicular lymphoma has been reported to range from 91% to 100%. On the other hand, few studies have addressed the use of 18F-FDG-PET for gastrointestinal involvement of follicular lymphoma.

Research frontiers

Follicular lymphoma is the second most common form of non-Hodgkin's lymphoma in Western countries. Moreover, the number of patients newly diagnosed with gastrointestinal follicular lymphoma has been increasing. In the area of management of gastrointestinal follicular lymphoma, the research hotspot is what role does 18F-FDG-PET play in the initial staging.

Innovations and breakthroughs

In 2004, Hoffmann *et al* reported eight cases of follicular lymphoma localized in the duodenum, and they noted that 18F-FDG did not accumulate in any of those patients. Subsequently, several authors described follicular lymphoma patients with positive 18F-FDG uptake in the gastrointestinal tract including the stomach, duodenum, jejunum, ileum, cecum, and colon, but the number of reported cases is limited. Taken together, these inconsistent results indicate that the sensitivity of 18F-FDG-PET for gastrointestinal lesions of follicular lymphoma has not been sufficiently evaluated. Here, the authors provide the first report of the sensitivity of 18F-FDG-PET for the detection of gastrointestinal involvement in follicular lymphoma patients, 46.3%.

Applications

This study results indicates that 18F-FDG-PET may represent a complementary modality for the management of patients with gastrointestinal follicular lymphoma.

Peer review

The authors assessed 41 patients with follicular lymphoma and gastrointestinal involvement, who underwent 18F-FDG-PET and endoscopic evaluations. They demonstrated 46.3% true-positive of 18F-FDG PET in the lesions of the involved gastrointestinal tract. False-negative 18F-FDG uptake was 58.5%, and false-positive was 12.2%. They emphasized on the complementary role of 18F-FDG-PET scan in the diagnosis of gastrointestinal involvements in follicular lymphoma patients. This is a good descriptive study in this query which there is just limited available data.

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