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의학석사 학위논문

국소 원발성 위 MALT 림프종에서 최적의
초기 병기검사

The strategies of selective initial work-up in patients with
superficial gastric MALT lymphoma

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The strategies of selective initial work-up in
patients with superficial gastric MALT lymphoma

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이 논문을 의학석사 학위 논문으로 제출함

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English Abstract

Background and aims: Prognosis of gastric MALT lymphoma is favorable, especially when there is no lymph node (LN) metastasis. We investigated the incidence and occurrence site of LN metastasis in superficial gastric MALT lymphoma.

Methods: Retrospective analysis of gastric MALT lymphoma from February 1995 to December 2016 was performed. A total of 452 patients with gastric MALT lymphoma whose depth of tumor infiltration confined to mucosa or submucosa on EUS was enrolled. The incidence and occurrence site of LN metastasis was evaluated.

Results: Out of 452 patients, the majority of patient (n=436, 96.5%) were LN negative in initial staging work-up using CT scanning. sixteen patients (3.5%) were LN positive and there was no difference in clinical characteristics between two groups except for extent of lymphoma involvement (p=0.024) and endoscopic features (p=0.008). Among 41 patients who underwent

only abdominal/pelvic CT (APCT), LN metastasis was detected in one patient (2.4%). There were eight LN metastasis in patients who underwent both APCT and chest CT (n=238, 3.4%). Among 171 patients who underwent APCT, chest CT and neck CT all, seven LN metastasis was detected (4.1%). The detection rates for each CT were as follows: 13 out of 450 patients in Abdominal CT (2.9%), 6 out of 408 patients in chest CT (1.5%), one out of 171 patients in neck CT (0.6%).

Conclusion: The incidence of LN metastasis was low in gastric MALT lymphoma patients whose depth of tumor infiltration confined to mucosa or submucosa on EUS. The extent of lymphoma involvement and endoscopic features were statistically significant factors associated with lymph node metastasis. Except for APCT, chest CT and neck CT as initial staging work-up does not seem to have additional benefit. In superficial gastric MALT lymphoma, it might be appropriate to perform the initial staging work-up selectively considering the extent of lymphoma and endoscopic features.

Keywords: MALT-lymphoma, LN metastasis, CT, EUS

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INTRODUCTION

Malignant lymphoma of mucosa-associated lymphoid tissue (MALT) has been recognized in the early 1980s as a distinct clinical and pathological entity¹. The majority of these tumors arise in the gastrointestinal tract and within the GI tract, the stomach is the most commonly involved organ.² Gastric extranodal marginal zone B-cell MALT lymphoma accounts for 1%–7% of malignant gastric tumors and 60%–75% of gastrointestinal MALT lymphomas.³

Gastric MALT lymphomas have a limited tendency to distant spreading and to histological transformation. The majority of cases with gastric MALT lymphoma are in the early stage of disease, with lymphoma limited to the gastric mucosa or submucosa. Although disease is localized in most patients with MALT lymphomas, about a third of patients present with disseminated disease. Lymph node involvement and bone marrow involvement may also occur.

Several different staging systems have been used for gastric MALT lymphomas. Over times, modified Ann Arbor System^{4, 5} or Lugano modification of the Ann arbor classification by Musshoff⁶, which is mainly based on radiological finding is widely used. Since the introduction of EUS, Paris staging system, a modification of the existing TNM system was

implemented by EGILS.⁷As EUS is widely used for initial staging work-up regardless of various staging systems, it has been reported that a deep infiltration of the gastric wall by the lymphoma is strongly associated with spread to the regional lymph nodes.⁸Although there is no individual recommended initial work-up according to the tumor depth, it is necessary to consider whether initial work-up of superficial MALT lymphoma should be different from deep MALT lymphoma.

The treatment plan for gastric MALT lymphoma depends mainly on disease stage. Therefore, the initial staging work-up is a crucial step in newly diagnosed MALT lymphoma patients to provide the appropriate treatment and assess the prognosis. Diagnosing lymph node metastasis is very important for applying oncologic therapy which is considered following antibiotic treatment. Involvement of the regional lymph node is associated with considerably reduced response rates to either antibiotics or conventional treatment.⁹⁻¹¹

Current guidelines recommend comparatively extensive staging work-up for patients with gastric MALT lymphoma; however, the difference in the details of work-up between each guideline are causing the controversy.^{12,13} Moreover, considering the good prognosis of gastric

MALT lymphoma, there is a question as to the optimal strategy and initial staging work-up for superficial MALT lymphoma, since early stage MALT lymphoma shows good response to eradication therapy alone. In cases of early-stage MALT lymphoma, approximately 75% of patients with successful HP eradication achieved complete remission (CR).¹⁴

The aim of this study was to evaluate retrospectively the incidence and occurrence site of LN metastasis and to determine the optimal strategies and extent of the initial work-up in gastric MALT lymphoma who are considered to have superficial infiltration on EUS.

MATERIALS AND METHODS

Patients

Gastric MALT lymphoma was defined as MALT lymphoma that primarily developed in stomach that could be evaluated by endoscopy. From February 1995 and December 2016, 885 patients who were newly diagnosed with gastric MALT lymphoma at Asan Medical Center were eligible to be included in this study. Patients were excluded from the study subjects if 1)

they underwent treatment for gastric MALT lymphoma before visiting our hospital; 2) they had another malignancy at the time of diagnosis; or 3) Patient who did not undergo EUS were also excluded because the precise depth of infiltration could not be determined.

Among the 885 patients (Figure 1), the patients who had other malignancies (n=60), previous history of treatment for MALT lymphoma (n=129), or patients who did not undergo EUS (n=107) were excluded. Of the remaining 589 patients, 112 patients were lost to follow-up during the study period, and 25 patients who were found to have lesion beyond submucosal layer on EUS were excluded. After exclusion, a total of 452 patients of 885 (51.1%) who had superficial disease confined to mucosa or submucosa on EUS were finally included in this study. The medical records of the enrolled patients were retrospectively reviewed.

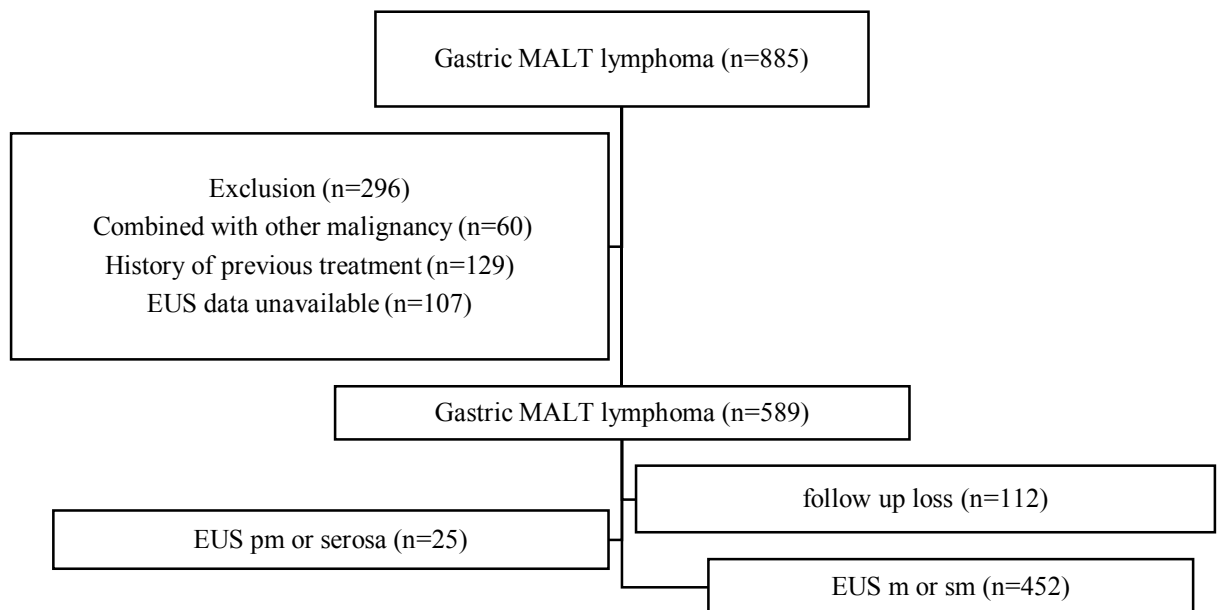


Figure 1. Flowchart of this study.

MALT, mucosa-associated lymphoid tissue; EUS, endoscopic ultrasonography; pm, proper muscle; m, mucosa; sm, submucosa.

Diagnosis and staging

Diagnosis of gastric MALT lymphoma was made on endoscopic examinations and on histological analysis of endoscopic biopsies and were classified according to the World Health Organization (WHO) classification.¹⁵ The Ann Arbor classification modified according to Musshoff⁴ and Radaszkiewicz⁵ was used for clinical staging. Initial staging work-up included physical examination, imaging studies including CT scans of the chest, abdomen and

pelvis, endoscopic ultrasonography (EUS), and bone marrow aspiration and biopsy. In addition, 163 patients (36.1%) underwent neck CT and 151 (33.4%) underwent positron-emission tomography (PET). Bone marrow biopsy was performed in 441 patients (97.6%).

Superficial gastric MALT lymphoma was defined as a gastric MALT lymphoma that is confined to the mucosa or submucosa, irrespective lymph node metastasis. Depth of tumor infiltration was assessed by EUS and was mostly performed simultaneously with biopsy.

Lymph nodes with a short-axis diameter of more than 1 cm were considered pathological.

Determination of extranodal involvement was defined as organomegaly, abnormal mass or structural changes in a normal-sized organ, and abnormal contrast enhancement.

Helicobacter pylori infection status was determined by histology, rapid urease test and noninvasive test like urea breath test or serologic test. *H. pylori* infection was regarded as positive if any of these test's result was positive; as negative only when all of the test's results were negative. Eradication was confirmed by histology, a urea breath test, or rapid urease test.

Endoscopic classification

The main endoscopic finding and the site of the lesions were reviewed retrospectively. The endoscopic images were broadly classified into two types; mass-forming type and superficial type. On EGD, MALT lymphoma lesions with Subepithelial tumor like appearance, cobblestone mucosa, fold thickening, polypoid or mass were considered to be of the mass forming type, whereas lesions appearing as Ilc like ulcer, erosions, discoloration were categorized as superficial type.

Gastric localization was categorized as: upper third, mid third, lower third, or diffuse (more than one involved part). A 12-point scale was used to determine the extent of involvement of MALT lymphoma. The scale divided stomach into twelve sections, sum four dimensions (anterior wall, lesser curvature, posterior wall, greater curvature) of each upper third, mid third and lower third.

Statistical analysis

Continuous and categorical variables are presented as medians (range), interquartile ranges (IQR) and numbers (%), respectively. The characteristics and clinicopathological features of

the patients were compared using chi-square tests, Fisher's exact tests, and t-tests, as appropriate. The McNemar test was used to assess the difference in detection rates for LN metastasis. All statistical analyses were performed using SPSS software version 21.0 (SPSS Inc., Chicago, IL), and a p Value <0.05 was considered statistically significant.

RESULTS

Patient characteristics

The baseline characteristics of the patients are summarized in Table 1. The median age at diagnosis was 53 years (range: 45-61 years) and 196 patients (43.4%) were male. *H. pylori* infection was present in 403 patients (89.2%). The most frequent involved location was the mid third of the stomach (n=158, 35.0%), followed by the lower third (n=115, 25.4%), and upper third (n=100, 22.1%). The diffuse involvement, involving more than one part, was the least (n=79) but it accounted for 17.5%. Superficial type was the most frequent endoscopic lesion, and the mean value of 12-point scale which shows the extent of lymphoma involvement was 1.86 (range 1-8). In the initial staging work-up including CT and PET/CT, lymph node metastasis was confirmed in 16 patients (3.5%) based on clinical staging. Considering staging work-up focusing only on CT, APCT scan was performed for all of the included patients except for two patients who underwent PET/CT instead of APCT. 41 patients underwent only APCT, 283 patients both APCT and chest CT, 171 patients underwent additional neck CT, respectively.

Table 1. Clinical characteristics of patients

	Mucosa or Submucosa (<i>n</i> =452)
Age, years	53 (45–61)
Sex	452
Male	196 (43.4%)
Female	256 (56.6%)
<i>H. pylori</i> positivity	403 (89.2%)
Location	
Upper third	100 (22.1%)
Mid third	158 (35.0%)
Lower third	115 (25.4%)
Diffuse	79 (17.5%)
Involvement extent (12-point scale)	1.86 (1-8)
Median follow up (IQR)	53.9 (25.9-81.9)
CR rate	384 (85.0%)
Time to CR (IQR)	14 (7.5-16.6)
Recurrence after CR during follow up	52 (13.3%)
Bone marrow involvement	24 (5.8%)
CT work-up ^a	
APCT only	41
APCT, chest CT	238
APCT, chest CT, neck CT	171
none	2
LN metastasis	16 (3.5%)

^a Two patients underwent PET/CT instead of APCT.

Characteristics and treatment outcome of patients according to LN metastasis status

Table 2 summarized clinical characteristics and treatment outcomes with superficial gastric MALT lymphoma according to LN metastasis status. A comparison of the characteristics of patients according to LN metastasis status did show that there were no statistically significant differences in age, sex, *H. pylori* status and depth of infiltration. The distribution of gastric lesions did not also differ between the two groups, although LN negative group tended to be more frequently confined in the upper and mid third. There was significant difference in endoscopic features between two groups, which mass-forming type was significantly more frequent in LN metastasis group (21.6% vs. 50%, $p=0.008$). Details of sixteen patients with LN metastasis in superficial gastric MALT lymphoma are shown in Table 3.

LN positive group tended to involve more extensively gastric mucosa as compared with LN negative group. 12-point scale was significantly higher in LN positive group (1.8 vs. 2.8, $p=0.024$). As the 12-point scale increased, the proportion of patients with LN positivity increased ($p=0.001$, table 4).

Table 2. Clinical characteristics and treatment outcomes according to LN metastasis status

	LN negative (n =436)	LN positive (n = 16)	p value
Age, years	53 (45–60)	52 (42.25-65.75)	0.803
Sex			0.443
Male	191 (43.8%)	5 (31.3%)	
Female	245 (56.2%)	11 (68.8%)	
<i>H. pylori</i> positivity	390 (89.4%)	13 (81.3%)	0.400
Location			0.464
Upper third	98 (22.5%)	2 (12.5%)	
Mid third	153 (35.1%)	5 (31.3%)	
Lower third	111 (25.5%)	4 (25.0%)	
Diffuse	74 (17.0%)	5 (31.5%)	
Endoscopic feature*			0.008
Mass-forming	94 (21.6%)	8 (50%)	
Superficial	341 (78.4%)	8 (50%)	
Median follow up	55.1 (27.6-83.1)	62.5 (30.7-91.9)	0.748
Depth on EUS			0.185
Mucosa	288 (66.1%)	8 (50%)	
Submucosa	148 (33.9%)	8 (50%)	
Involvement extent (12-point scale)	1.8 (0.7-3.0)	2.8	0.024
CR rate	374 (85.8%)	10 (62.5%)	0.022
Time to CR	10.8(7.5-16.5)	10.6 (6.6-25.1)	0.095
Recurrence after CR during follow up	47 (12.4%)	5 (41.7%)	0.013
Bone marrow involvement	21 (5.3%)	3 (20.0%)	0.05
Bone marrow involvement	21 (5.3%)	3 (20.0%)	0.05

*One patient was diagnosed through surgery and had no description of endoscopic findings.

Table 3. Details of patients with LN metastasis (N=16)

Case	Sex	Age	<i>H. pylori</i> infection	Abdomen- pelvis CT	Chest CT	Neck CT	BM involvement	Stage	EUS depth
1	F	49	Positive	LN(+)	Negative	Not done	No	2E1	sm
2	F	54	Positive	LN(+)	LN(+)	Not done	Yes	4	m
3	F	67	Positive	LN(+)	Lung	Not done	No	4	sm
4	F	66	Positive	Negative	LN(+)	Negative	No	3E	sm
5	F	65	Positive	LN(+)	Negative	Not done	No	2E1	sm
6	F	69	Positive	LN(+)	Negative	Not done	No	2E1	sm
7	M	43	Positive	LN(+)	Negative	Not done	No	2E2	m
8	M	36	Positive	LN(+)	Negative	LN(+)	No	3E	sm
9	F	42	Positive	LN(+)	Negative	Negative	Yes	4	m
10	F	39	Negative	LN(+)	LN(+)	Negative	No	4	m
11	F	58	Positive	LN(+)	Negative	Negative	No	2E1	sm
12	F	71	Positive	LN(+)	Not done	Not done	Not done	2E1	m
13	F	50	Negative	Negative	LN(+)	Not done	No	4	m
14	M	25	Positive	LN(+)	Negative	Negative	No	2E1	m
15	M	48	Positive	Negative	LN(+)	Negative	No	4	m
16	M	62	Negative	LN(+)	Negative	Not done	Yes	4	sm

Table 4. Lymph node status according to involved extent (12-point scale)

LN	Section (12-point scale)								P value
	1	2	3	4	5	6	7	8	
Negative	229	113	58	23	4	4	3	1	
Positive	4 (1.7%)	4 (3.4%)	2 (3.3%)	4 (14.8%)	1 (20%)	1 (20%)	0	0	0.001
Total	233	117	60	27	5	5	3	1	

The CR rate were 85.8% for LN positive group and 62.5% for LN negative group, and there was statistically difference between two groups ($p=0.022$). The median time to CR did not differ significantly between LN negative and LN positive group (10.8 vs 10.6, $p=0.095$). The recurrence after CR was higher in LN positive group (12.4 vs. 41.7%, $p=0.013$) than LN negative group during median follow up period of 55.1 and 62.5 months. The presence of bone marrow involvement was significantly more frequent in LN positive group than LN negative group (5.3% vs. 20.0%, $p=0.05$).

Factors associated with LN metastasis

To identify the factors affecting lymph node involvement, the associated clinicopathologic characteristics were analyzed and shown in Table 5. The results demonstrated that primary location was irrelevant to nodal involvement. Lymph node metastasis rate increased with an involved extent of lesion. logistic regression analysis showed that involvement more than three sections and mass-forming endoscopic findings were factors related to LN metastasis

Table 5. Factors associated with Lymph node metastasis

	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Location				
Upper third	1			
Mid third	1.601 (0.305-8.416)	0.578		
Lower third	1.766 (0.317-9.851)	0.517		
Multifocal	3.311 (0.625-17.541)	0.159		
Depth on EUS				
Mucosa	1			
Submucosa	1.946 (0.716-5.289)	0.192		
Involvement extent (12-point scale)				
≤3 section	1		1	
>3 section	6.857 (2.353-19.980)	0.000	8.991 (2.885-28.020)	0.000
Endoscopic feature				
Superficial	1		1	
Mass-forming	3.628 (1.326-9.923)	0.012	4.746 (1.624-13.869)	0.004

CI, confidence interval; OR, odds ratio.

Results of staging work-up

The comparisons of detection rate of CT scans for LN metastasis are summarized in Table 6.

Among 41 patients who underwent only APCT, LN metastasis was detected in one patient

Table 6. Comparisons of detection rate of computed tomography (CT) for lymph node metastasis

	LN- (n=436)	LN+ (n=16)	Detection rate	APCT only
CT work-up				
APCT only	40	1	2.4%	
APCT, chest CT	230	8	3.4%	7/238 (2.94%)
APCT, chest CT, neck CT	164	7	4.1%	5/171 (2.92%)
none	2	0	0	

(2.4%). There were eight LN metastasis in patients who underwent both APCT and chest CT (n=238, 3.4%). Among 171 patients who underwent APCT, chest CT and neck CT all, seven LN metastasis was detected (4.1%).

When analysis is restricted to patients who underwent both APCT and chest CT, among 238 patients who underwent both APCT and chest CT, APCT alone was able to detect LN metastasis in 7 of 238 patients (2.94%). However, when findings of chest CT were added to APCT, another lesion could be found in one patient and the detection rate of LN metastasis increased to 3.36%. The difference in detection rate between APCT alone and APCT plus chest CT was not statistically significant ($P=1.000$) by the McNemar test.

Of the 171 patients who underwent APCT, chest CT and neck CT all, 7 were node positive (4.1%), but only 5 of 171 patients could be detected on APCT alone (2.92%), although there was no statistically significant difference ($p=0.500$). Among these seven node positive patients, only two patients showed no evidence of LN metastasis in APCT ($n=2$, 1.17%).

Overall, only three patients turned out to be positive in chest or neck CT, who showed no evidence of LN metastasis in APCT ($n=3$, 0.7%). Endoscopic findings of these three patients are shown in Figure 2.

Table 7 shows the diagnostic performance of CT work-up for LN metastasis. The LN detection rates for each CT were as follows: 13 out of 450 patients in Abdominal CT (2.9%), 6 out of 408 patients in chest CT (1.5%), one out of 171 patients in neck CT (0.6%). APCT showed the highest detection rate for LN metastasis, although not statistically different to other two CTs (Table 7). APCT showed the highest sensitivity (13/16, 81.3%), followed by chest CT (6/15, 40%), neck CT (1/7, 14.3%), respectively.

Figure 2. Endoscopic findings of three patients with distant metastasis who showed no evidence of lymph node metastasis in APCT.

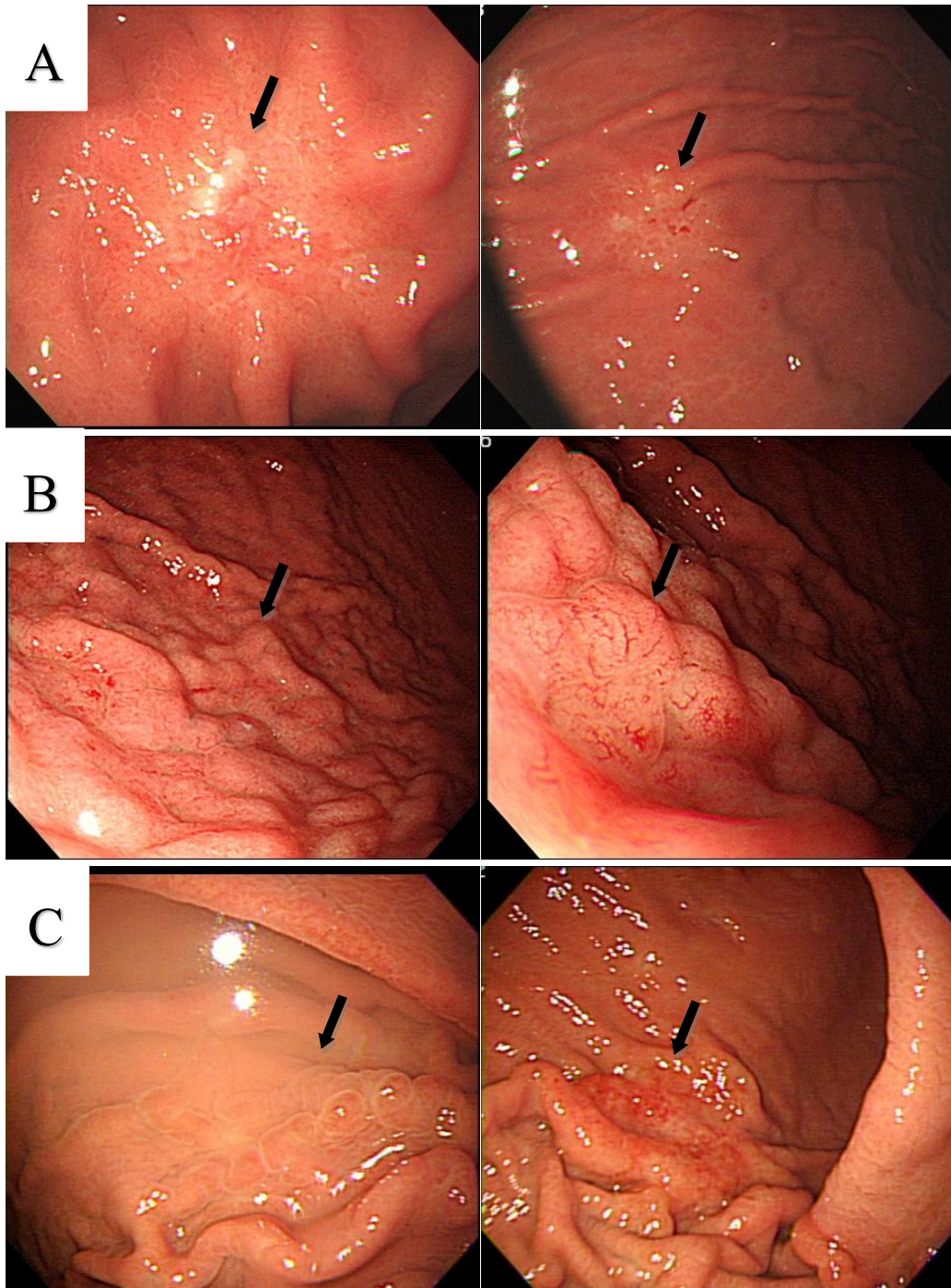


Figure 2. Lesions are indicated with black arrow. (A) in patient 1; (B) in patient 2; (C) in patient 3.

Table 7. The Sensitivity and detection rate of CT scans as initial work-up

	LN positive	Test positive	Sensitivity	Detection rate	NND ^a
CT work-up					
APCT (n=450)	16	13	13/16 (81.3%)	2.9%	34.6
chest CT (n=409)	15	6	6/15 (40%)	1.5%	68
neck CT (n=171)	7	1	1/7 (14.3%)	0.6%	171
APCT vs chest CT				0.146	
APCT vs neck CT				0.125	
Chest CT vs neck				0.625	
CT					

^aNND: number needed to diagnose

DISCUSSION

We aimed to investigate the incidence and occurrence site of LN metastasis, and the optimal initial staging work-up for staging superficial gastric MALT lymphoma by comparing APCT alone and a combination of modalities including chest CT and neck CT. According to the previous study, the depth of tumor infiltration of gastric MALT lymphoma correlates with the involvement of the regional lymph nodes¹⁶. However, those reports were not focused on superficial (T1) lesion, which is confined to mucosa or submucosa on EUS. In this study, only the gastric MALT lymphoma with a relatively low prevalence of LN metastasis whose depth of tumor infiltration confined to mucosa or submucosa were included.

The incidence of LN metastasis was low in gastric MALT lymphoma patients whose depth of tumor infiltration confined to mucosa or submucosa on EUS. In our study, there were only 16 cases (3.5%) of LN metastasis in superficial gastric MALT lymphoma patients. *H. pylori* seems to have no role in LN metastasis in this study. Lymph node metastasis rate increased with an involved extent of lesion.

We analyzed the essential predictive factors for LN metastasis in superficial gastric MALT

lymphoma. There have been several attempts at using endoscopic classification in the diagnosis of MALT lymphoma¹⁷⁻¹⁹, but endoscopic presentation of gastric MALT lymphoma are generally heterogenous. Some studies have suggested that endoscopically defined polypoid type was characterized by a longer duration to CR, with a higher likelihood of recurrence, compared to the endoscopically defined diffuse infiltration or ulceration types.²⁰ In this study, endoscopic findings seems to be relevant with LN metastasis, especially in mass-forming type rather than superficial type. As there is still some controversy in classification criteria, it is hoped that this issue should be addressed in further studies. Another significant factor was involvement extent of stomach more than three sections in 12-point scale (OR, 6.857; p=0.000).

Due to the risk of occult-disseminated disease including nodal involvement, extensive initial staging work-up is currently recommended regardless of the presentation site. Raderer et al.²¹ emphasized the importance of extensive staging in MALT lymphoma by the demonstration of multiorgan involvement in almost a quarter of patients. They, however, reported that localized disease is more frequently observed with MALT lymphoma involving the GI tract than with extra-gastrointestinal MALT lymphoma. Given this localizing nature and low prevalence of

LN metastases of gastric MALT lymphoma, extensive staging work-up may not be a reasonable option, especially who are considered to have superficial infiltration.

By current guidelines, APCT and chest CT should be performed as staging work-up for MALT lymphoma regardless of its stage^{12, 13, 22}. In this study, APCT scan was performed for all of the included patients, but 41 patients underwent only APCT, 283 patients both APCT and chest CT, 171 patients underwent additional neck CT, respectively. This abled us to recognize the benefits of each CT scans without much difficulty.

The detection rates for each CT were as follows: 13 out of 450 patients in Abdominal CT (2.9%), 6 out of 408 patients in chest CT (1.5%), one out of 171 patients in neck CT (0.6%). There was no statistically significant difference in detecting LN metastasis between APCT alone and a combination of modalities including chest CT and neck CT. Even though detection rate increased as additional work-up, number of cases with LN metastasis was too small and increasing cost caused by additional tests should be concerned.

Furthermore, gastric MALT lymphomas are significantly more frequently to localized than non-gastric MALT lymphomas.^{23, 24} The specific homing properties of lymphocytes generated

within a MALT environment contribute to the dissemination of MALT lymphoma,²⁵ with approximately half of patients with gastric origin had dissemination (often multifocal) within the GI tract. Therefore, the dissemination of gastric MALT lymphoma beyond the GI tract, which is not detected on APCT, seems to be quite rare.

In this study, we found particular cases that no lymph node metastasis was detected in APCT alone. Two patients had LN metastasis on chest CT, and one patient on neck CT. But we included only the gastric MALT lymphoma with a relatively good prognosis whose depth of tumor infiltration confined to mucosa or submucosa.

Depth of infiltration is the major prognostic factor in cases with gastric lymphoma. The remission rate is highest for mucosa-confined MALT lymphoma (approximately 70% to 90%) and then decreases markedly and progressively for tumors infiltrating the submucosa, the muscularis propria and the serosa.^{26, 27} EUS has become the most accurate imaging modality to evaluate the depth of infiltration, and useful tool in diagnosis of locoregional LN metastasis of gastric MALT lymphoma. In the evaluation of depth infiltration, the overall accuracy of EUS is reported up to 92%.^{28, 29} European Society for Medical Oncology (ESMO) guideline

for gastric MALT lymphoma recommended EUS to evaluate regional lymph nodes and gastric wall infiltration in the initial work-up whenever possible.²² Therefore, the need for extensive initial work-up is reduced when depth of infiltration is superficial on EUS which shows good treatment response.

Only 3 of 452 cases would have been missed in superficial gastric MALT lymphoma patients if would have underwent APCT alone. Considering the result of 12 section results, only one of 452 cases would have been missed. On the new era of precision medicine, selecting optimal initial staging work-up is expected to have role in reducing workload, particularly if depth of infiltration is deep or extent of involvement is extensive.

There are several limitations in this study. First, since there was few pathologic confirmation of LN metastasis through surgery or biopsy, final staging through pathologic confirmation was not available in most cases. However, it is difficult to implement invasive modality in lymphoma, especially MALT lymphoma, which shows good treatment response only with *H. pylori* eradication.

Second, a possibility of missing extra-gastrointestinal metastasis at the time of diagnosis was

not completely excluded. Chest CT, neck CT and PET/CT were performed in 90.5%, 36.1% and 33.4% of enrolled cases, respectively. But many guidelines currently recommend *H. pylori* eradication therapy as first line treatment of all gastric MALT lymphoma independent of the stage. As bone marrow biopsy is recommend when no lymphoma regression is seen after *H. pylori* eradication and before initiating oncological treatment^{12, 13, 22}, it might be beneficial to perform additional staging work-up in the case of failure of lymphoma regression.

In conclusion, the incidence of LN metastasis was low in gastric MALT lymphoma patients whose depth of tumor infiltration confined to mucosa or submucosa on EUS. It might be necessary to perform selective initial work-up with endoscopic findings and disease extent for those considered to have superficial infiltration on EUS. Performing individual and limited initial work-up in selected gastric MALT lymphoma patients without risk factors for lymph node metastasis might be more appropriate and beneficial. Chest CT and neck CT appear to be appropriate only for patients with selective risk factors, which consist of endoscopic findings and disease extent. We believe that further large-scaled studies are warranted to investigate the risk factors for LN metastasis in staging of gastric MALT lymphoma.

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국문요약

배경/목표: 위 MALT 림프종은 대개 병변이 파급되지 않고 원발부위에 국한되는 경우가 많아 좋은 예후를 보이며, 림프절 전이가 없을 경우 예후가 더 좋다고 알려져 있다. 국소 원발성 위 MALT 림프종에서 림프절 전이의 빈도와 발생부위를 확인함으로써 최적의 초기병기검사를 보고자 하였다.

방법: 1995년 2월부터 2016년 12월까지 국소 원발성 위 MALT 림프종을 진단받은 환자를 대상으로 후향적 연구를 시행하였다. 내시경초음파 (EUS)에서 병변이 점막 및 점막하층에 국한된 총 452명이 연구에 포함되었으며, 림프절 전이의 빈도와 발생부위를 비교하였다.

결과: 본 연구에서는 총 452명의 환자를 대상으로 하였다. CT를 포함한 초기병기검사에서, 림프절 전이 음성($n=436$, 96.5%)과 림프절 전이 양성($n=16$, 3.5%) 양군 간에는 림프종의 침범범위 (P value=0.024)와 내시경적 소견 (P value=0.008)에서 유의한 차이를 보였다. 초기병기검사에서 복부/골반 CT만을 시행한 41명의 환자 중에서 1명 (2.4%), 복부/골반 CT와 흉부 CT를 같이 시행한 238명 중에서 8명 (3.4%), 복부/골반 CT와 흉부 CT 및 목 CT를 시행한 171명 중 7명 (4.1%)에서 림프절 전이가 확인되었다. 각 CT 검사의 탐지율(detection rate)은 복부/골반 CT (13/450, 2.9%), 흉부 CT (6/408, 1.5%), 목 CT (1/171, 0.6%) 였으며, 각 CT간의 탐지율에서 통계적으로 유의한 차이는 없었다.

결론: EUS상 점막 및 점막하층에 국한된 국소 위 MALT 림프종에서 림프절 전이의 빈도는 낮았으며, 림프종의 침범범위와 내시경적 소견이 통계적으로 유의하게 림프절

전이와 관련된 인자였다. 복부/골반 CT를 제외하고는, 초기 병기검사로서의 흉부 CT 및 목 CT는 추가적인 이득이 크지 않아 보인다. EUS상 국소병변인 위 MALT 림프종에서 초기 병기검사는, 병변의 침범범위와 내시경적 소견을 고려하여 선택적으로 시행하는 것이 적절할 것으로 생각된다.