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Original Article

Linked color imaging can help gastric *Helicobacter pylori* infection diagnosis during endoscopy

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Abstract

Background: Esophagogastroduodenoscopy (EGD) is a standard tool for detection of mucosal and submucosal lesions. However, identification of *Helicobacter pylori* (H. P) infection using EGD alone is limited in accuracy. Linked color imaging (LCI) is a novel tool to capture real-time image with sufficient contrast to observe mucosal microstructure.

Methods: This study aims to evaluate the applicability of LCI in the identification of *H. pylori* infection. Consecutive 122 patients scheduled for EGD were included. They were examined with LCI and magnifying endoscopy. The classification of *H. pylori* was based on pathology results of biopsy and rapid urease test or urea breath test.

Results: We compared the results based on LCI or magnifying endoscopy to reference classification. Of 122 patients, 36 had *H. pylori* infection (29.51%). The level of accuracy of diagnosis of *H. pylori* infections by LCI, magnifying endoscopy, and both LCI and magnifying endoscopy was 78.38%, 81.98%, and 78.38%, respectively. The sensitivity and specificity of each group were 70.97%, 81.25%, and 80.65% and 82.5%, 83.87%, and 76.25%, respectively. The positive predictive values were 59.46%, 64.10%, and 57.78%, respectively, and the negative predictive values were 87.84%, 91.67%, and 92.42%, respectively.

Conclusion: LCI could be playing a valuable initial screen tool for real-time diagnosis of *H. pylori* infections. It has a high accuracy of diagnosis of *H. pylori* infections. Therefore, in patients suspected to have *H. pylori* infections using LCI, the infections need to be carefully diagnosed using appropriate methods because, as per the consensus, they should be eradicated as soon as possible before precancerous lesions develop.

Keywords: H. pylori infection; Image-enhanced endoscopy; Linked color imaging; White light imaging

1. Introduction

Helicobacter pylori is a major risk factor for gastric cancer which induces chronic gastritis and precancerous changes such as intestinal metaplasia.[1−3] Currently, many kinds of methods that may or may not involve endoscopy are used for investigating *H. pylori* such as the fecal antigen test, urea breath test, *H. pylori* antibody test, histology, rapid urease testing, culture, and polymerase chain reaction. These testes are cumbersome,

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time-consuming and lacking real-time information. Methods based on esophagogastroduodenoscopy (EGD) may serve as an initial guide for possible HP infection. However, it is very difficult to distinguish *H. pylori* infections in patients undergoing light EGD examinations, and a biopsy from the gastric mucosa is required for these patients, which has risks such as missing pathology and sampling errors and is expensive. Therefore, the development of real-time endoscopic assessments for the diagnosis of *H. pylori* during endoscopy has emerged.

Magnifying endoscopy improves the demonstration of mucosa details and helps the identification of HP infection. However, it is time-consuming and causes an uncomfortable sensation for the patient thus reduces patients' willingness to receive EGD. Patients with *H. pylori* infections usually present with diffuse redness of the fundic mucosa.[4] Recently, linked color imaging (LCI), which only requires the switch of one button, had been reported to be very useful in *H. pylori* and flat gastric cancers detection.[5–7] For the reason that, it can save examination time and mitigate the patient's unpleasant experience during the procedure. However, there is a lack of direct comparison of performance between LCI and current recommended modality. Therefore, we conducted this study to compare the performance of LCI with that of magnifying endoscopy with standard HP identification methods as reference.

2. Methods

2.1. Study population

This study has obtained ethical approval from the Institutional Review Board of the Chang Gung Memorial Hospital (IRB No. 201600789B0). All patients enrolled in this study were well informed and consented. We enrolled consecutive 122 patients (Table 1) who were scheduled for an EGD for various indications such as epigastric pain, anemia, gastroesophageal reflux disease, suspicion of peptic ulcer disease and liver cirrhosis by physicians at Linkou Chang Gung Memorial Hospital between January 2016 and July 2016. All the procedures were performed by an experienced endoscopist. In this study, we excluded those patients that we already knew had hallow organ perforation, gastric outlet obstruction or patients cannot tolerate the whole procedure other than *H. pylori* eradication status. 111 patients were under further analyzed who received both LCI only or combined with magnifying endoscopy.

Table 1
Patient characteristics of the study population.

Characteristics	Study population	
	No.	%
N	122	
Male	70	(57.38)
Age, years (SD)	52.35	(12.90)
NSAIDs therapy	1	(0.82)
LCI	122	(100.00)
Magnifying endoscopy	111	(90.98)
LCI and magnifying endoscopy	111	(90.98)
HP infection	36	(29.51)
s/p eradication (S)	12	(9.83)
Cumulative incidence of HF, % (95% CI)	29.51	(19.87–39.15)

LCI = linked color imaging; HP = *Helicobacter pylori*.

2.2. Process of H. pylori infection diagnosis

At first, the enrolled patients were examined with white light imaging (WLI) followed by LCI. We recorded whether the patient had an *H. pylori* infection or not according to LCI.

Second, magnifying endoscopy was performed after determining the result by LCI. According to previous reports, patients without collecting venules were considered to have a *H. pylori* infection.[8]

Third, the results of LCI and magnifying endoscopy were compared for analysis. An *H. pylori* infection was considered if either of these results was positive.

Finally, four biopsy specimens were obtained (two from the antrum and two from the body) for histology or rapid urease testing. For patients with disputed results, the urea breath test was also performed. In this study, at least two methods were used to make a definitive diagnosis of an *H. pylori* infection.

An endoscopic biopsy was performed from both the antrum and greater curvature of the corpus to avoid false negative results.[8,9]

In this study, we used the Fujifilm laser system (Fujifilm Co., Tokyo, Japan) and EG-L590ZW scope for white light and linked color imaging. LCI is a new observation mode that was recently released. By using narrowband light, high contrast images of the surface of the mucosa could be obtained.

A difference in the illumination light and signal processing emphasized the slight difference in color in infected regions that was close to the normal color of the mucosa. As a result, originally red regions appeared redder and originally white regions appeared whiter, but had natural tones. This method could be helpful in visualizing reddish and brownish areas of the mucosa and detecting inflammation and minute changes in it.

The diagnostic principle is according to Osamu Dohi et al. report, those patients with *H. pylori* infection has a diffuse, deep red color of the fundic mucosa.[7] and under LCI the collecting venules become more obvious (more reddish) as Fig. 1A shows images of no infection and Fig. 1B shows *H. pylori* infection.

2.3. Comparison between LCI and magnifying endoscopy

To compare the accuracy between LCI and magnifying endoscopy, multiple validity indexes such as sensitivity, specificity and positive predictive value were calculated by three different definition of *H. pylori* infection, one was the result of LCI indicated positive only, another was depended on magnifying endoscopy individually, the other was as positive if either of above results was positive. The *p*-value for the

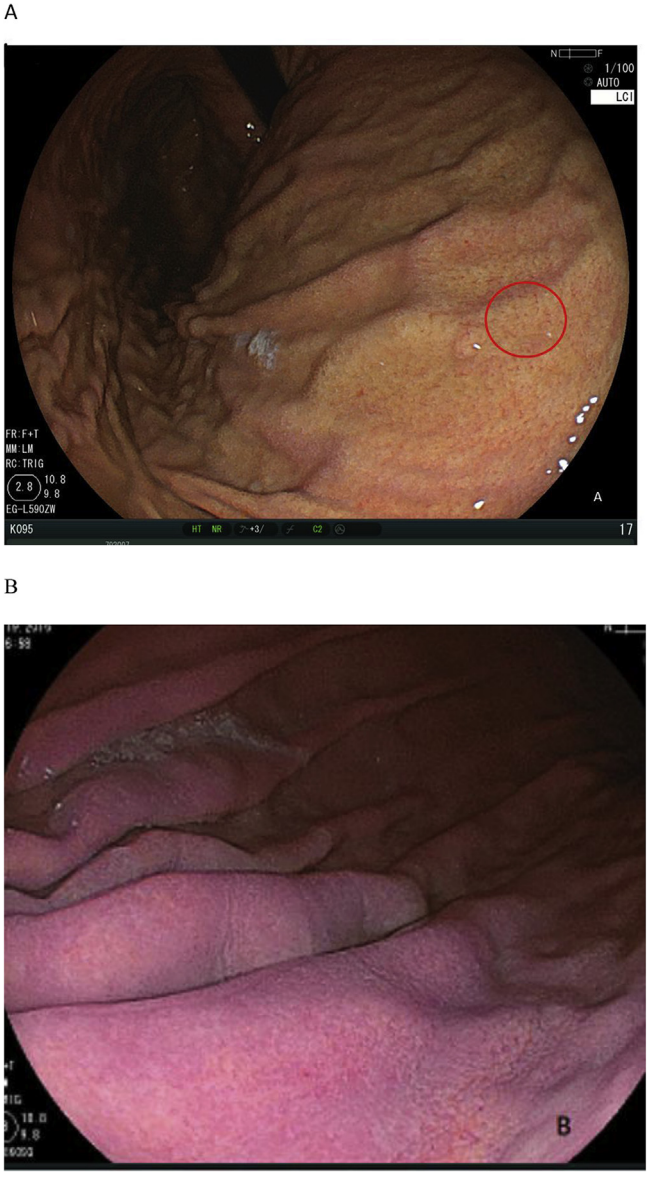

Fig. 1. A: No *H. pylori* infection and show more obvious collecting venules (red circule); B: *H. pylori* infection showing diffuse reddish to purple color under LCI.

sensitivity and specificity difference between those definitions were derived from the McNemar's Test. In addition, we conducted stratified analysis by HP eradication status because HP eradication may affect the screening consequence of *H. pylori* infection.

2.4. Statistical analysis

The statistical analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

There were 122 patients enrolled in this study (the male to female ratio was 70:52) and all of them underwent LCI. LCI and magnifying endoscopy were used for 111 patients. In our study group, patients who had taken NSAIDs were excluded to avoid the influence of NSAIDs except for one patient who had undergone COX2-inhibitor therapy. Twelve patients had undergone successful eradication previously. In our study group, 29.51% patients had an *H. pylori* infection. Patient characteristics are shown in Table 1. The *H. pylori* infection rate was 36/122 (29.51%) which comparable with our previously report.[10]

111 received LCI and LCI combined with magnifying endoscopy were enrolled for further analysis. The level of accuracy of the diagnosis of *H. pylori* infection by LCI, magnifying endoscopy, and both LCI and magnifying endoscopy was 78.38%, 81.98%, and 78.38%, respectively.

The sensitivity level for each group was 70.79%, 80.65%, and 83.87, respectively. The specificity level for each group was 81.25%, 82.5%, and 76.25%, respectively. The positive predictive values for each group were 59.64%, 64.1%, and 57.78%, respectively, and the negative predictive values were 87.84%, 91.67%, and 92.42%, respectively. The P values of sensitivity and specificity did not show significant differences. Detailed results are presented in Table 2.

In our series, 11 patients had undergone *H. pylori* eradication before. In these patients, LCI did not show better specificity than magnifying endoscopy (Table 3).

4. Discussion

Conventional EGD is generally used for *H. pylori* detection based on features of the gastric mucosa such as redness, mucosal swelling, and nodular changes, but these features are not specific enough for diagnosis.[4] Other kinds of image-enhanced endoscopy (IEE) with or without magnifying endoscopy are also used for *H. pylori* diagnosis. However, these tests are dependent on the operator, that is, they require operators to be trained by experienced supervisors and need special equipment.[11] Besides, IEE combined with magnifying endoscopy techniques are time consuming, provide variable results, and may make patients more uncomfortable. The factors mentioned above contribute to the limitation of the clinical use of magnifying endoscopy in the detection of *H. pylori* infections in routine practice.

We choose the fundus and high body for the investigation according to the previous reports that Spotty redness of the fundic gland region on histology was considered to reflect mucosal hyperemia due to inflammatory changes.[12] A strong correlation with an objective index of redness, the hemoglobin index (IHb), has been reported, suggesting that diffuse redness is the most important feature for diagnosing *H. pylori* infection.[13] As the disappearance of polymorphonucleocytes is a histologically significant change shortly after *H. pylori* eradication, spotty redness of the fundic gland region is suggested to be related to histological activity.[14]

In this study, we found that LCI has acceptable sensitivity and high specificity in *H. pylori* detection and has no significant differences from the other two groups studied. Additionally, in this study we contribute those patients who have

Table 2
Comparison of validity between LCI and Magnifying endoscopy (n = 111).

	LCI	Magnifying endoscopy	LCI and magnifying endoscopy
HP infection			
Yes	31	31	31
True positive	22	25	26
False negative	9	6	5
No	80	80	80
True negative	65	66	19
False positive	15	14	61
Sensitivity, % (95% CI)	70.97 (51.96−85.78)	80.65 (62.53−92.55)	83.87 (66.27−94.55)
Specificity, % (95% CI)	81.25 (70.97−89.11)	82.50 (72.38−90.09)	76.25 (65.42−85.05)
PPV, % (95% CI)	59.46 (42.10−75.25)	64.10 (47.18−78.80)	57.78 (42.15−72.34)
NPV, % (95% CI)	87.84 (78.16−94.29)	91.67 (82.74−96.88)	92.42 (83.20−97.49)
Accuracy, % (95% CI)	78.38 (69.56−85.63)	81.98 (73.55−88.63)	78.38 (69.56−85.63)
p value for sensitivity difference[a]		0.375	0.125
p value for specificity difference[a]		1.000	0.125

LCI = linked color imaging; HP= *Helicobacter pylori*; PPV= Positive predictive value; NPV= Negative predictive value.
[a] McNemar's Test was used to test significance of difference.

Table 3
Specificity (%) of different screening by the HP eradication status.

Test	HP Eradication (N = 11)	No HP eradication (N = 100)	*p*[a]
LCI	63.64 (30.79−89.07)	84.06 (73.26−91.76)	0.2042
Magnifying endoscopy	54.55 (23.38−83.25)	86.96 (76.68−93.86)	0.0202
LCI and magnifying endoscopy	45.45 (16.75−76.62)	81.16 (69.94−89.57)	0.0182

[a] The *p* value was derived from Fisher's exact test.

vague LCI enhancement to have *H. pylori* infection. In this case the sensitivity may be underestimated. But we rather overestimate the patients who have *H. pylori* infection than loos anyone who potentially has *H. pylori* infection.

In this situation, an endoscopist can quickly distinguish patients who have *H. pylori* infections from those who do not. Based on these benefits, we could save money, and patients could avoid unnecessary procedures such as biopsies, which would decrease complications including gastric hemorrhages related to biopsies.

In our study, some patients presented with false positive results from LCI; these patients had been infected with *H. pylori* and had undergone successful eradication before. It might attribute to congested mucosa[15] and not totally meet Kazuyoshi Yagi reports.[16] This is also the potential limitation of our study because no available data showed the change of collecting venules after *H. pylori* eradication under LCI. However, LCI still could help us to identify patients who had *H. pylori* infections after eradication, even the specificity is only 63.64%, and take better care of them, especially if they also have intestinal metaplasia, which is seen as the "point of no return" of precancerous lesions. For these patients, we should arrange regular endoscopy examinations.

In conclusion, we found that LCI could be used as a reliable tool for the diagnosis of *H. pylori* infections and this method only requires the switch of a button. However, there still have limitations in our study such as small study numbers and without compare to high resolution white light endoscopy.

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