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Original Article

The Diagnostic Performance of Linked Color Imaging Compared to White Light Imaging in Endoscopic Diagnosis of *Helicobacter pylori* Infection: A Systematic Review and Meta-Analysis

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Background/Aims: Recognizing *Helicobacter pylori* infection during endoscopy is important because it can lead to the performance of confirmatory testing. Linked color imaging (LCI) is an image enhancement technique that can improve the detection of gastrointestinal lesions. The purpose of this study was to compare LCI to conventional white light imaging (WLI) in the endoscopic diagnosis of *H. pylori* infection.

Methods: We conducted a comprehensive literature search using PubMed, Embase, and the Cochrane Library. All studies evaluating the diagnostic performance of LCI or WLI in the endoscopic diagnosis of *H. pylori* were eligible. Studies on magnifying endoscopy, chromoendoscopy, and artificial intelligence were excluded.

Results: Thirty-four studies were included in this meta-analysis, of which 32 reported the performance of WLI and eight reported the performance of LCI in diagnosing *H. pylori* infection. The pooled sensitivity and specificity of WLI in the diagnosis of *H. pylori* infection were 0.528 (95% confidence interval [CI], 0.517 to 0.540) and 0.821 (95% CI, 0.811 to 0.830), respectively. The pooled sensitivity and specificity of LCI in the diagnosis of *H. pylori* were 0.816 (95% CI, 0.790 to 0.841) and 0.868 (95% CI, 0.850 to 0.884), respectively. The pooled diagnostic odds ratios of WLI and LCI were 15.447 (95% CI, 8.225 to 29.013) and 31.838 (95% CI, 15.576 to 65.078), respectively. The areas under the summary receiver operating characteristic curves of WLI and LCI were 0.870 and 0.911, respectively.

Conclusions: LCI showed higher sensitivity in the endoscopic diagnosis of *H. pylori* infection than standard WLI. **(Gut Liver 2024;18:444-456)**

Key Words: *Helicobacter pylori*; Gastrointestinal endoscopy; Image enhancement; Sensitivity and specificity

INTRODUCTION

Helicobacter pylori causes chronic inflammatory reaction in the gastric mucosa, which leads to atrophy, intestinal metaplasia, and precancerous changes.[1] Since *H. pylori* is a major risk factor for gastric cancer, it must be diagnosed and managed early for the presence or absence of infection.[1,2]

Various confirmatory tests are currently being used to investigate *H. pylori* infectivity, such as urea breath test, serologic test, rapid urease test, histology, culture, and stool antigen test.[3] However, the prediction of *H. pylori* infection from endoscopic findings can play a decisive role in determining whether the confirmatory test should be conducted.[4,5]

Mucosal nodularity, rugal hypertrophy, mucosal edema, turbid gastric juice, diffuse redness, the absence of regular arrangement (RAC) of collecting venules, and hemor-

rhagic spots are typical endoscopic findings in the endoscopic diagnosis of *H. pylori* infection.[4,6] However, since the accuracy of the endoscopic diagnosis of *Helicobacter*-associated gastritis using conventional white light imaging (WLI) is relatively low at 64% to 74%, there is a need for a better imaging technique.[7-12]

Linked color imaging (LCI) is an image-enhanced endoscopy method created by Fujifilm in 2013. This makes it easier to distinguish differences in mucosal color through expansion and reduction of color information.[13-18] LCI enhances color contrast while maintaining the actual color of the target object, thereby making reds appear redder and whites appear whiter. Previous studies have shown that the sensitivity and accuracy of the endoscopic diagnosis of *H. pylori* infection using LCI were higher than those of conventional WLI.[3,11,13-15,19,20]

In this study, we tried to confirm the usefulness of LCI over WLI in the diagnosis of *H. pylori* infection based on previous studies. Therefore, we performed a systematic review and meta-analysis to determine the sensitivity and specificity of LCI as compared with WLI in the endoscopic diagnosis of *H. pylori* infection.

MATERIALS AND METHODS

1. Search strategy

We conducted a systematic literature search in PubMed, Embase, and the Cochrane Library. In this process, we retrieved all human research articles published in English up to October 2022. We also hand-searched the reference lists of identified studies to ensure the relevance of all articles. The search string consisted of a combination of the following search terms: "*Helicobacter pylori*", "*H. pylori*", "linked color*", "LCI", "white light*", "endoscop*", "gastroscop*", "sensitivity", "specificity." The detailed search strategies used for each database are presented in the Supplementary Material. This study was admitted by the Institutional Review Board affiliated with Hallym University School of Medicine (HDT 2022-11-016).

2. Study selection

All studies that evaluated the performances of WLI or LCI in the endoscopic diagnosis of *H. pylori* infection were considered eligible for inclusion. The exclusion criteria were as follows: (1) studies that only assessed magnifying endoscopy; (2) studies that only assessed chromoendoscopy; (3) studies that assessed the performance of artificial intelligence (AI); (4) studies that did not report sensitivity and specificity, or the absolute numbers of true positives, false positives, true negatives, and false negatives; (5) abstract-only publications; (6) non-original articles including review, editorial, opinion, letter, and case reports; and (7) non-English publications.

Two investigators (J.G.L. and I.K.Y.) independently screened and selected the literature. All duplicate articles that had been obtained from multiple databases were removed. And then, irrelevant articles were excluded based on the titles and abstracts. The full texts of the remaining articles were examined for eligibility. Any discrepancies between the two reviewers were resolved through discussion. A third party (S.P.L.) determined eligibility if such discrepancies could not be resolved. The study selection process was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Test Accuracy Studies Statement.[21]

3. Data extraction and outcome measures

We extracted data from the included studies by using a standardized collection sheet. If true negative, true positive, false negative, and false positive values were not presented in the study, they were calculated from total numbers, case numbers, sensitivity, and specificity. The study characteristics such as study design, study year, country, number of patients, prevalence of *H. pylori* infection, study population, method of reference standard testing, and criteria for endoscopic diagnosis were investigated.

The primary endpoint of this study was the pooled diagnostic performances of WLI and LCI in the endoscopic diagnosis of *H. pylori* infection. The pooled sensitivity, specificity, and diagnostic odds ratios of WLI and LCI, respectively, were evaluated.

4. Study quality assessment

To assess the quality of the included studies, we used the Quality Assessment of Diagnostic Accuracy Studies-2 tool.[22] It assesses the risk of bias of diagnostic studies in the following four domains: index test, patient selection, flow and timing, and reference standard. Each domain is assessed for the risk of bias with signaling questions, and the first three domains are assessed for concerns regarding applicability.

5. Statistical analysis

True negative, true positive, false negative, and false positive were calculated for all included studies. Meta-DiSc 1.4 software was used to perform a meta-analysis.[23] The DerSimonian-Laird random effects method was used for data integration. The diagnostic performances of LCI and WLI in the endoscopic diagnosis of *H. pylori* infection were determined by estimating the pooled sensitivity, specificity, and diagnostic odds ratios with 95%

confidence intervals (CIs). To compare the sensitivity and specificity of WLI and LCI, we analyzed data from studies in which both imaging modalities were conducted in the same population, and the McNemar test was used for statistical comparison. Forest plot and summary receiver operator characteristic curves were also constructed. We performed a two-sample Z-test to compare the differences in the area under the curve (AUC) of the two tests (WLI and LCI) based on Q* values and their standard errors. Heterogeneity between studies was evaluated using Higgins I^2 statistics. To assess the effects of possible sources of heterogeneity, meta-regression and subgroup analyses were performed while including the following covariates: study year, study location, number of patients, study population, prevalence of *H. pylori* infection, reference standard, and index test.

RESULTS

1. Literature search

In total, 2,063 potentially relevant articles were extracted from databases through a systematic literature search and confirmed by manual searching. First, 730 duplicate articles were removed from the initial extracted articles. Next, 1,258 articles were excluded by titles and abstracts. Subsequently, we reviewed the full text of 75 articles for eligibility. Forty-one articles were excluded because they had irrelevant intervention or outcomes (n=15), were review articles (n=2), were conference abstracts without a full text (n=22), or had insufficient detailed data (n=2). As a result, 34 articles were ultimately included in the meta-analysis.[10,11,13,14,20,24-52] Fig. 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart of this process.

2. Study characteristics

Table 1 lists the characteristics of the 34 studies included in the meta-analysis. Out of these, 32 evaluated the diagnostic performance of WLI and eight evaluated LCI, and six evaluated both WLI and LCI. Of the 32 studies evaluating WLI, 17 studies were conducted in Asia and 15 studies were conducted in non-Asia regions; eight studies investigated endoscopic evaluations in children. All studies evalu-

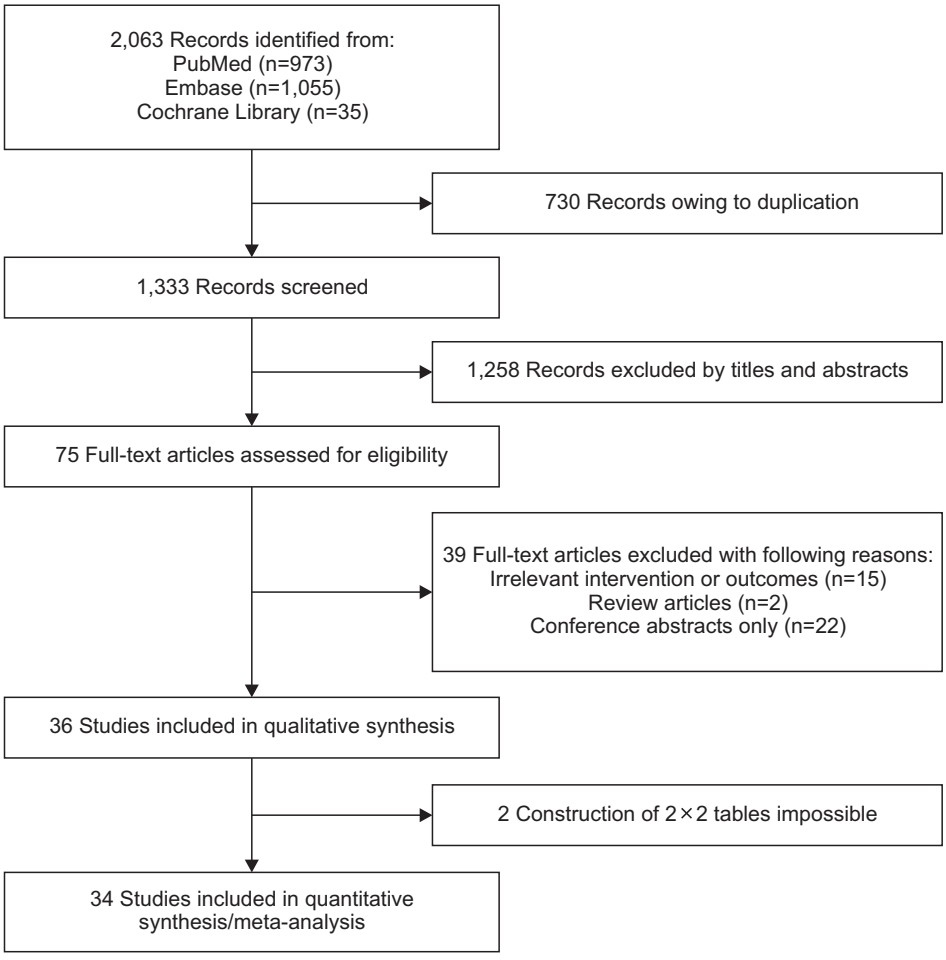

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart.

Table 1. Characteristics of the Included Studies

Study	Country	No. of patients	Prevalence of HP infection	Population	Reference standard	Index test
Studies evaluating WLI (n=32)						
Adu-Aryee *et al.* (2016)[24]	Ghana	76	51.3	Adult	RUT	Comprehensive
Bah *et al.* (1995)[25]	Switzerland	86	46.5	Adult	RUT, histology	Comprehensive
Cho *et al.* (2013)[26]	Korea	617	58.2	Adult	RUT, histology	Comprehensive
Cho *et al.* (2021)[27]	Korea	254	64.2	Adult	RUT, molecular test	Comprehensive
Dohi *et al.* (2016)[11]	Japan	60	50.0	Adult	RUT, histology, serology, UBT	Single finding(s)
Emami *et al.* (2007)[28]	Iran	501	65.1	Adult	RUT, histology	Single finding(s)
Fiuza *et al.* (2021)[29]	Brazil	187	25.1	Adult	RUT, histology	Single finding(s)
Garcés-Durán *et al.* (2019)[30]	Spain	140	31.4	Adult	RUT, histology	Single finding(s)
Gonen *et al.* (2009)[31]	Turkey	129	76.0	Adult	RUT, histology, UBT	Single finding(s)
Hidaka *et al.* (2010)[32]	Japan	87	28.7	Children	Histology, serology, UBT	Single finding(s)
Katake *et al.* (2013)[33]	Japan	723	70.5	Adult	Histology, serology	Single finding(s)
Laine *et al.* (1995)[34]	US	52	53.8	Adult	Histology	Single finding(s)
Łazowska-Przeorek *et al.* (2015)[35]	Poland	341	31.4	Children	RUT, histology, stool antigen, UBT	Single finding(s)
Lee *et al.* (2020)[20]	Korea	100	37.0	Adult	RUT, histology	Comprehensive
Luzza *et al.* (2001)[36]	Italy	174	48.3	Children	RUT, histology	Single finding(s)
Machado *et al.* (2008)[37]	Brazil	99	32.3	Children	RUT, histology	Single finding(s)
Matrakool *et al.* (2016)[38]	Thailand	200	66.0	Adult	RUT, histology	Comprehensive
Mazigh Mrad *et al.* (2012)[39]	Tunisia	49	71.4	Children	RUT, histology	Single finding(s)
Niyasom *et al.* (2019)[40]	Thailand	48	25.0	Children	RUT, histology	Single finding(s)
Ono *et al.* (2020)[41]	Japan	127	50.4	Adult	UBT, serology	Single finding(s)
Rafeey *et al.* (2004)[42]	Iran	124	46.0	Children	RUT, histology	Single finding(s)
Redéen *et al.* (2003)[10]	Sweden	488	40.4	Adult	RUT, histology	Comprehensive
Sun *et al.* (2019)[43]	China	253	42.3	Adult	RUT, histology	Comprehensive
Tahara *et al.* (2019)[44]	Japan	163	46.9	Adult	Histology, serology, UBT	Comprehensive
Tomić *et al.* (2009)[45]	Bosnia	195	20.5	Children	Histology	Single finding(s)
Toyoshima *et al.* (2020)[46]	Japan	265	15.8	Adult	RUT, histology	Single finding(s)
Wang *et al.* (2019)[47]	China	103	26.2	Adult	RUT, histology	Comprehensive
Xiu *et al.* (2021)[48]	China	392	34.4	Adult	RUT, histology, UBT	Comprehensive
Yagi *et al.* (2014)[49]	Japan	56	58.9	Adult	Stool antigen	Comprehensive
Yan *et al.* (2010)[50]	Taiwan	112	67.9	Adult	RUT, histology	Comprehensive
Yela *et al.* (1997)[51]	Spain	150	76.7	Adult	RUT, histology, tissue culture	Comprehensive
Zhao *et al.* (2020)[52]	China	583	42.2	Adult	RUT, UBT	Comprehensive
Studies evaluating LCI (n=8)						
Chen *et al.* (2018)[13]	Taiwan	111	27.9	Adult	RUT, histology, UBT	Single finding(s)
Dohi *et al.* (2016)[11]	Japan	60	50.0	Adult	RUT, histology, serology, UBT	Single finding(s)
Jiang *et al.* (2019)[14]	China	358	35.5	Adult	RUT, histology, UBT	Comprehensive
Lee *et al.* (2020)[20]	Korea	100	37.0	Adult	RUT, histology	Comprehensive
Ono *et al.* (2020)[41]	Japan	127	50.4	Adult	UBT, serology	Single finding(s)
Sun *et al.* (2019)[43]	China	253	42.3	Adult	RUT, histology	Comprehensive
Wang *et al.* (2019)[47]	China	103	26.2	Adult	RUT, histology	Comprehensive
Xiu *et al.* (2021)[48]	China	392	34.4	Adult	RUT, histology, UBT	Comprehensive

HP, *Helicobacter pylori*; WLI, white light imaging; LCI, linked color imaging; RUT, rapid urease test; UBT, urea breath test.

ating LCI were conducted in Asia. Almost all studies used tissue-based confirmatory testing as a reference standard for *H. pylori* infection. Rapid urease test and histological assessment were the most common methods for confirmatory testing. Only three studies used noninvasive testing as reference standard, including urea breath test, serological testing, or stool antigen testing. Of the 34 studies, 16 used comprehensive diagnostic criteria for the endoscopic diagnosis of *H. pylori* infection whereas the other 18 used single endoscopic findings.

3. Quality assessment

The Quality Assessment of Diagnostic Accuracy Studies-2 criteria were used to assess the quality of the included studies. Thirteen studies were ranked as having a high or unclear risk of bias in patient selection. All studies were rated as having a low risk of bias in the reference standard and the flow and timing domains. The overall quality assessment is presented in Supplementary Table 1.

4. Diagnostic performance of WLI and LCI in diagnosing *H. pylori* infection

Figs 2 and 3 show pooled estimates of the sensitivity and specificity of WLI and LCI in the endoscopic diagnosis of *H. pylori* infection. The pooled sensitivity values of WLI and LCI for diagnosing *H. pylori* infection were 0.528 (95% CI, 0.517 to 0.540) and 0.816 (95% CI, 0.790 to 0.841), respectively. The pooled specificity values of WLI and LCI were 0.821 (95% CI, 0.811 to 0.830) and 0.868 (95% CI, 0.850 to 0.884), respectively. The pooled diagnostic odds ratios of WLI and LCI were 15.447 (95% CI, 8.225 to 29.013) and 31.838 (95% CI, 15.576 to 65.078), respectively. The summary receiver operator characteristic curves showed that the derived AUC of WLI and LCI for diagnosing *H. pylori* infection were 0.870 and 0.911, respectively, and the difference was statistically significant (p<0.001) (Fig. 4).

To directly compare the sensitivity and specificity of WLI and LCI, we used paired data from six studies that both WLI and LCI were conducted on the same patients.[11,20,41,43,48,53] The pooled sensitivity of LCI was significantly higher than that of WLI (0.818 [95% CI, 0.790 to 0.845] vs 0.651 [95% CI, 0.618 to 0.685], p<0.001). The pooled specificity was also significantly higher for LCI compared to WLI (0.848 [95% CI, 0.828 to 0.867] vs 0.785 [95% CI, 0.762 to 0.807], p<0.001) (Fig. 5).

5. Meta-regression and subgroup analyses

Table 2 lists the results of the univariate meta-regression analysis for determining potential factors of heterogeneity. In studies evaluating WLI, the location of the study was analyzed as a probable source of heterogeneity. The study year was divided into before and after/during 2002, which is the year that high-definition endoscopy began to be used, which did not result in significant heterogeneity. For index tests, endoscopic diagnosis was divided into diagnoses based on single findings or on comprehensive criteria, and this did not result in significant heterogeneity. In stud-

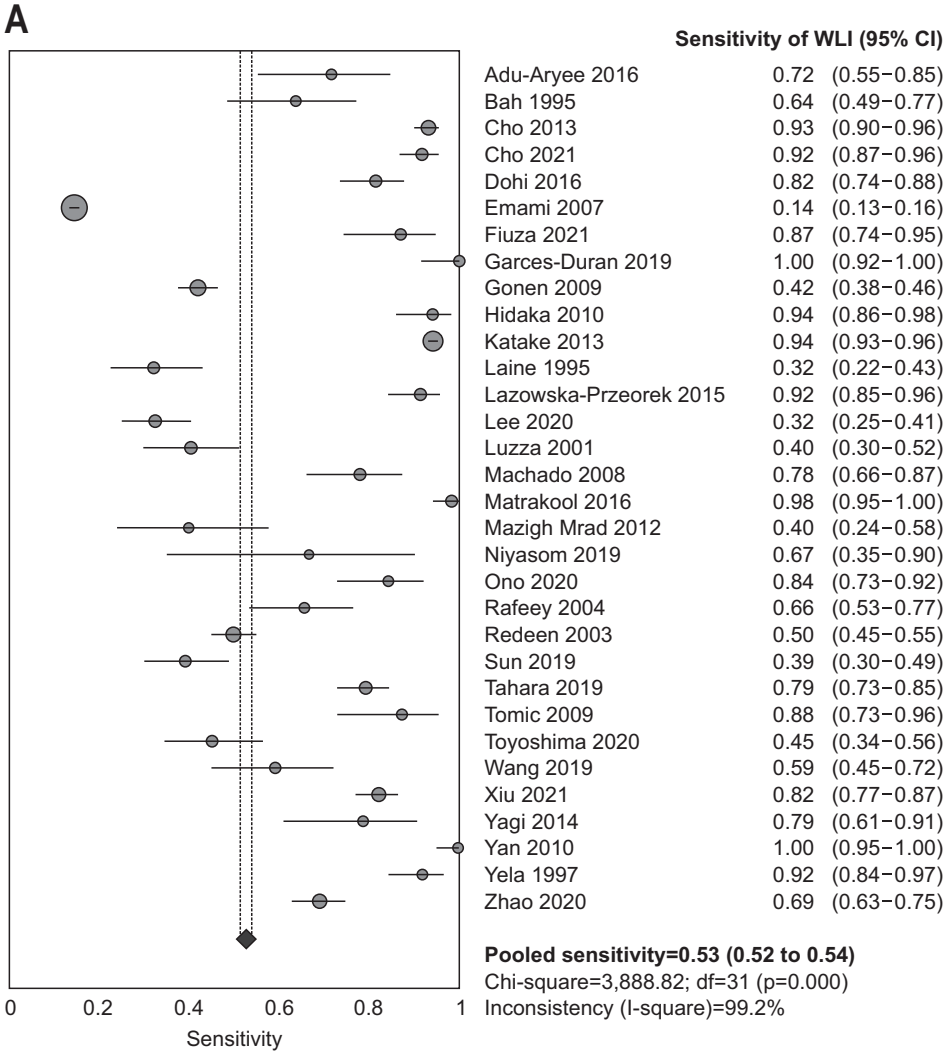

Fig. 2. Pooled estimates of sensitivity and specificity of WLI in endoscopic diagnosis of *Helicobacter pylori* infection. WLI, white light imaging; CI, confidence interval.

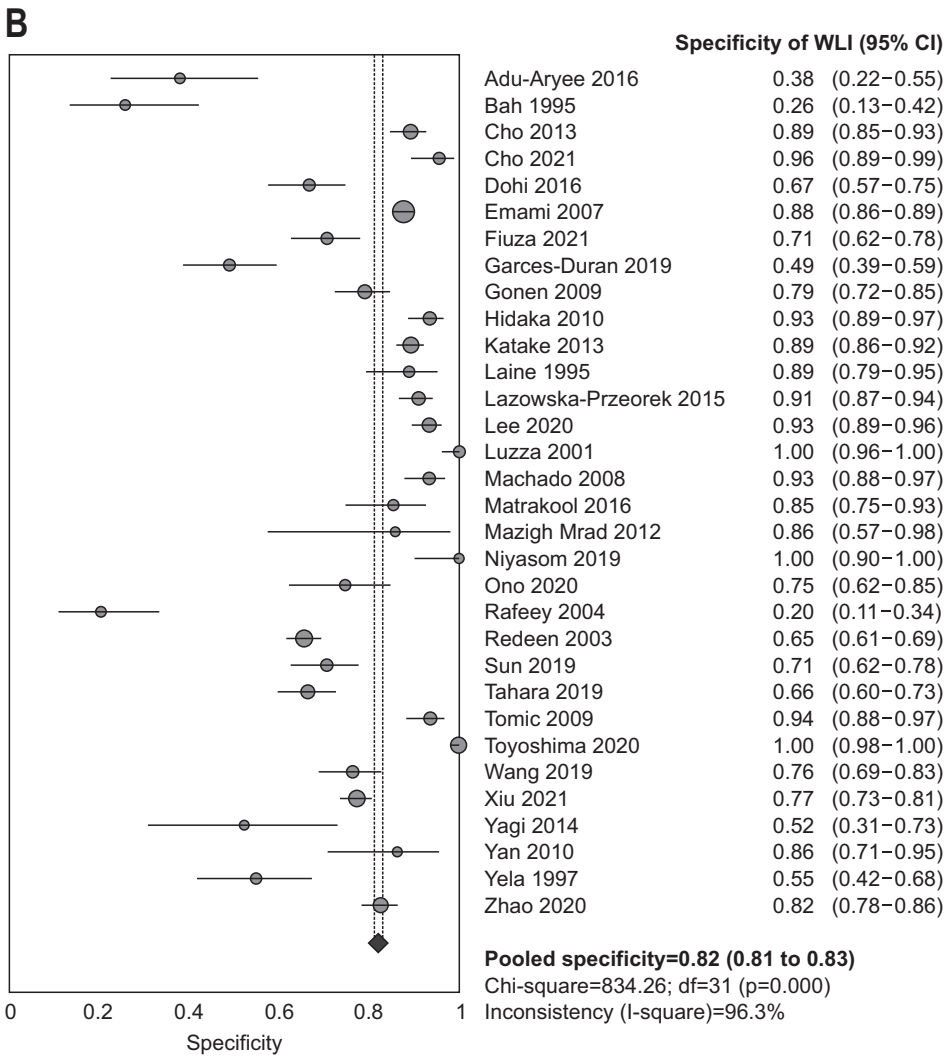

Fig. 2. Continued.

ies evaluating LCI, all studies were conducted in Asia and in 2016 or later. We could not identify any factors that were a possible source of heterogeneity.

Table 3 presents the results of the subgroup analysis. Comparing the diagnostic performance of WLI according to study location, the pooled sensitivity values were 0.828 (95% CI, 0.814 to 0.841) in 17 Asian studies and 0.311 (95% CI, 0.297 to 0.325) in 15 non-Asian studies. Meanwhile, the pooled specificity values were 0.845 (95% CI, 0.833 to 0.857) and 0.795 (95% CI, 0.781 to 0.809) in Asian and non-Asian studies, respectively.

DISCUSSION

Our meta-analysis showed that LCI was more sensitive than WLI in the endoscopic diagnosis of *H. pylori* infection, with a pooled sensitivity of 0.816 compared to 0.528 for WLI. Redness of the fundus gland mucosa, mucosal edema, mucosal nodularity, mucus lake turbidity, rugal hypertrophy, loss of RAC of collecting venules, and hemorrhagic spots are all markers for diagnosing *H. pylori* gastritis.[6] Since LCI enhances color contrast, it facilitates the identification of these typical endoscopic findings.[14,15,54] Moreover, under LCI, *H. pylori*-infected mucosa appeared deep red (crimson) in color, while *H. pylori*-negative mucosa (past infection or uninfected patients) could clearly be observed as apricot in color, which could be detected better because of distinctive color differences.[11,13,41] Dohi *et al.*[11] showed that LCI improved the endoscopic diagnosis of active *H. pylori* infections, with 10% to 15% improvements in accuracy, sensitivity, and specificity over WLI. In a multicenter prospective study reported by Ono *et al.*[41] comparing the accuracy of LCI and WLI for the endoscopic diagnosis of *H. pylori* gastritis, LCI was found to be significantly more accurate than WLI in patients with past infections. Our meta-analysis also demonstrated that the LCI patterns are more sensitive than the WLI patterns

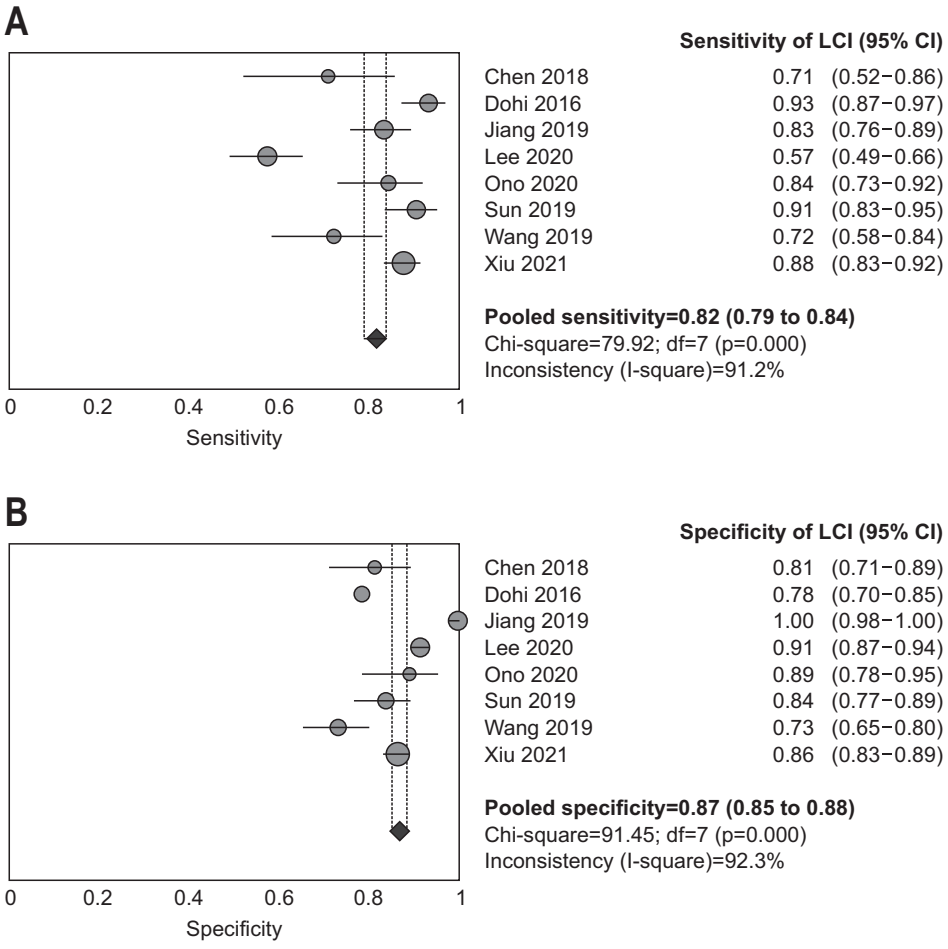

Fig. 3. Pooled estimates of the sensitivity and specificity of LCI in endoscopic diagnosis of *Helicobacter pylori* infection. LCI, linked color imaging; CI, confidence interval.

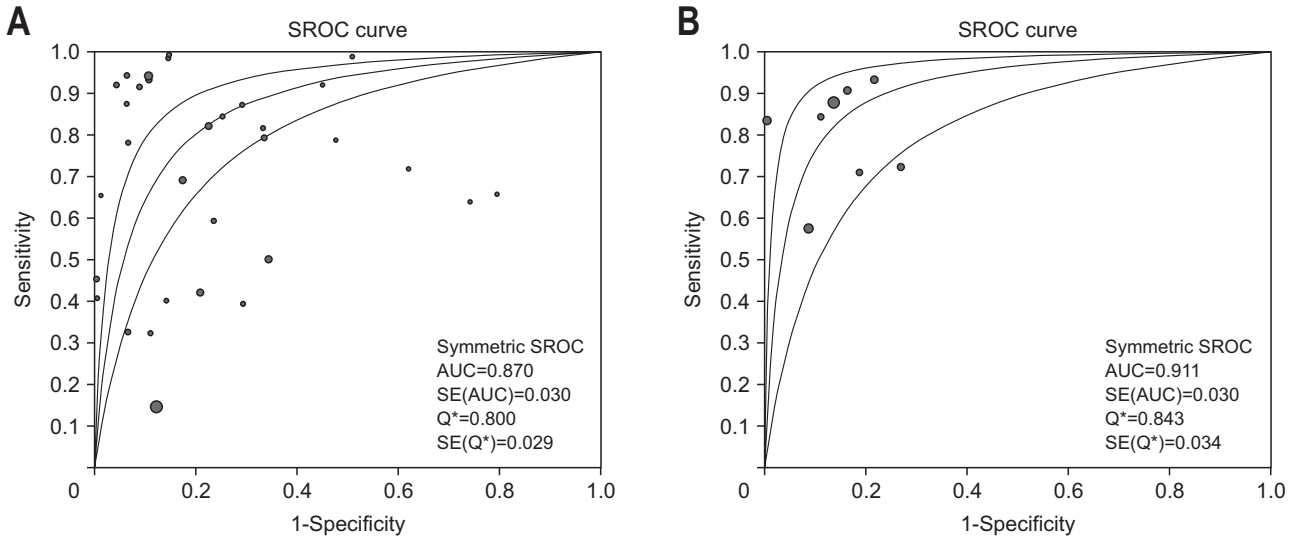

Fig. 4. SROC curves of (A) white light imaging and (B) linked color imaging in diagnosing *Helicobacter pylori* infection. SROC, summary receiver operating characteristic; AUC, area under the curve; SE, standard error.

in diagnosing *H. pylori* infection, suggesting that LCI can compensate for the low sensitivity of WLI.

When typical endoscopic findings such as mucosal nodularity or mucosal swelling appear, the accuracy of endoscopic diagnosis of *H. pylori* infection is very high, even under WLI.[8] However, in the absence of these typical

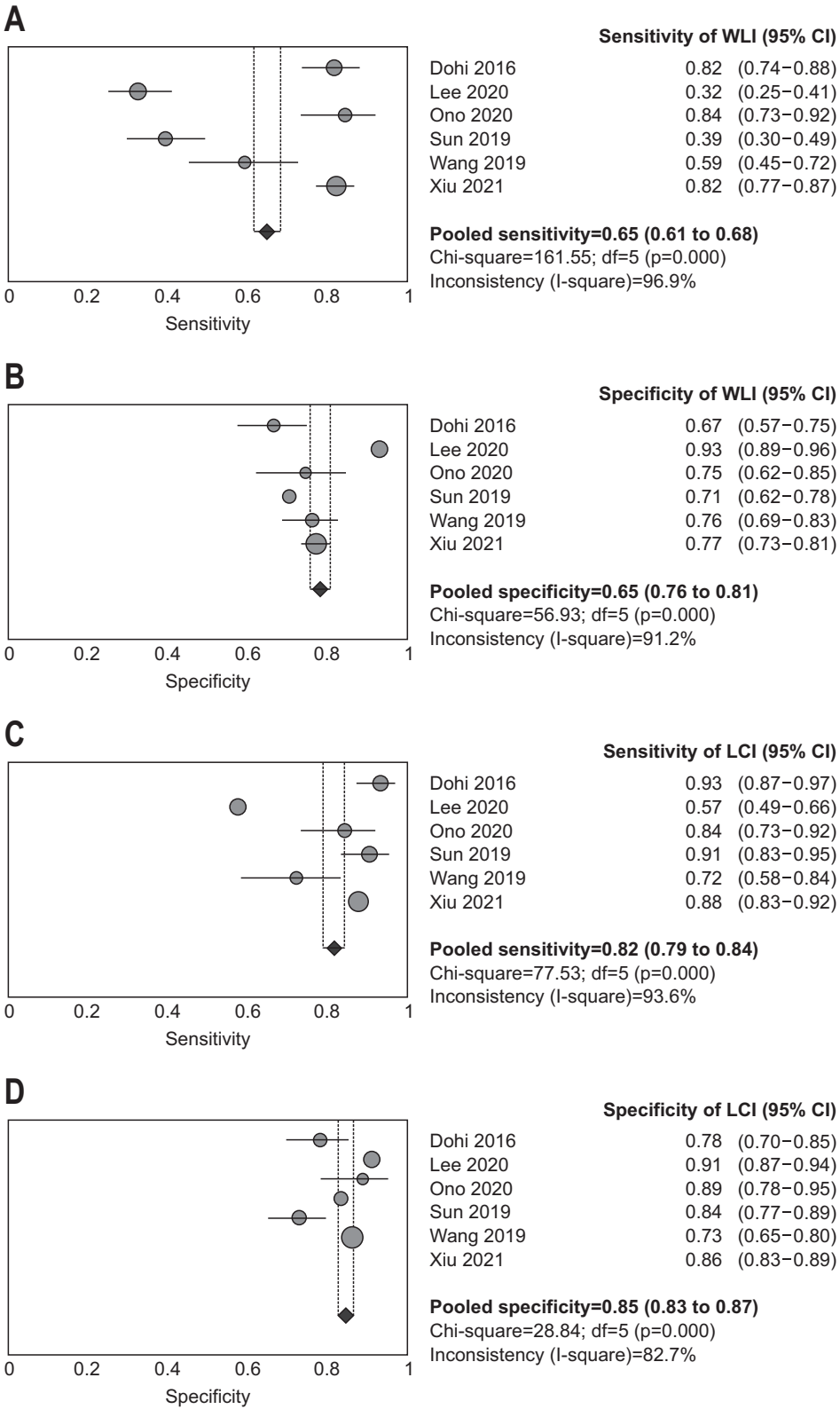

Fig. 5. Pooled estimates of the sensitivity and specificity of WLI and LCI from paired data of six studies in which both imaging modalities were performed on the same patients. (A) Pooled sensitivity of WLI. (B) Pooled specificity of WLI. (C) Pooled sensitivity of LCI. (D) Pooled specificity of LCI. WLI, white light imaging; LCI, linked color imaging; CI, confidence interval.

findings, considerable knowledge and experience may be needed to accurately determine the presence or absence of infection. Our subgroup analysis also identified that the sensitivity of diagnosis was higher in Asian countries than in non-Asian countries. These suggest that high incidence of *H. pylori* infection and rich experience in endoscopic diagnosis may play an important role in endoscopic diagnosis of *H. pylori* infection. However, when analyzing the

Table 2. Univariate Meta-Regression Analysis for Identifying Potential Factors of Heterogeneity

Variable	Coefficient	p-value
Studies evaluating WLI (n=32)		
Study year (after or during 2002 vs before 2002)	−1.039	0.359
Study location (Asia vs non-Asia)	1.449	0.043
No. of patients (≥145 vs <145)	1.155	0.111
Study population (adult vs children)	−1.088	0.217
Prevalence of HP infection (≥46.7% vs <46.7%)	0.197	0.791
Reference standard (single testing vs multiple testing)	0.955	0.388
Endoscopic diagnosis (based on single finding(s) vs comprehensive diagnosis)	0.711	0.355
Studies evaluating LCI (n=8)		
No. of patients (≥119 vs <119)	1.585	0.088
Prevalence of HP infection (≥36.25% vs <36.25%)	0.295	0.797
Endoscopic diagnosis (based on single finding(s) vs comprehensive diagnosis)	−0.086	0.944

WLI, white light imaging; HP, *Helicobacter pylori*; LCI, linked color imaging.

Table 3. Subgroup Analysis for the Diagnostic Performance of WLI and LCI

Variable	No. of studies	Sensitivity (95% CI)	Specificity (95% CI)	Diagnostic OR (95% CI)
Studies evaluating WLI (n=32)				
Study year				
After or during 2002	28	0.527 (0.515–0.538)	0.823 (0.814–0.833)	17.569 (8.922–34.596)
Before 2002	4	0.568 (0.510–0.624)	0.753 (0.696–0.804)	5.929 (1.024–34.342)
Study location				
Asia	17	0.828 (0.814–0.841)	0.845 (0.833–0.857)	29.355 (13.734–62.744)
Non-Asia	15	0.311 (0.297–0.325)	0.795 (0.781–0.809)	6.724 (3.263–13.858)
No. of patients				
≥145	16	0.515 (0.503–0.528)	0.834 (0.824–0.844)	27.207 (10.439–70.910)
<145	16	0.578 (0.553–0.603)	0.772 (0.750–0.793)	7.957 (3.794–16.686)
Study population				
Adult	24	0.514 (0.503–0.526)	0.810 (0.799–0.820)	12.069 (6.105–23.859)
Children	8	0.729 (0.687–0.768)	0.892 (0.869–0.911)	35.657 (5.708–222.75)
Prevalence of HP infection				
≥46.7%	16	0.491 (0.478–0.504)	0.840 (0.827–0.853)	17.748 (6.198–50.825)
<46.7%	16	0.646 (0.624–0.669)	0.803 (0.789–0.816)	13.598 (6.102–30.301)
Reference standard				
Single testing	4	0.597 (0.520–0.661)	0.819 (0.769–0.862)	6.884 (1.264–37.475)
Multiple testing	28	0.527 (0.515–0.538)	0.821 (0.811–0.830)	17.432 (8.821–34.449)
Endoscopic diagnosis				
Based on single finding(s)	17	0.435 (0.422–0.449)	0.867 (0.856–0.878)	21.703 (7.255–64.924)
Comprehensive diagnosis	15	0.732 (0.714–0.750)	0.757 (0.741–0.773)	10.812 (5.019–23.295)
Studies evaluating LCI (n=8)				
No. of patients				
≥119	4	0.870 (0.839–0.897)	0.893 (0.871–0.912)	67.727 (29.385–156.10)
<119	4	0.731 (0.681–0.776)	0.828 (0.795–0.857)	14.976 (6.904–32.487)
Prevalence				
≥36.25%	4	0.793 (0.752–0.830)	0.864 (0.833–0.891)	33.296 (15.983–69.363)
<36.25%	4	0.838 (0.802–0.870)	0.870 (0.847–0.890)	34.508 (7.975–149.31)
Endoscopic diagnosis				
Based on single finding(s)	3	0.874 (0.823–0.916)	0.817 (0.765–0.862)	28.734 (10.766–76.692)
Comprehensive diagnosis	5	0.799 (0.767–0.828)	0.878 (0.859–0.895)	35.563 (12.868–98.284)

WLI, white light imaging; LCI, linked color imaging; OR, odds ratio; CI, confidence interval; HP, *Helicobacter pylori*.

results of six Asian studies that assessed the performance of both WLI and LCI in endoscopic diagnosis of *H. pylori* infection in the same population, LCI was superior to WLI in both sensitivity and specificity (sensitivity, 0.818 vs 0.651; specificity, 0.848 vs 0.785). In mass screening for gastric cancer and precursor *H. pylori* gastritis, screening endoscopy with high sensitivity and specificity for endoscopic diagnosis of *H. pylori* infection might have a signifi-

cant impact on reducing gastric cancer-related morbidity and mortality. Image-enhanced endoscopy with LCI is expected to play an important role in screening for *H. pylori* gastritis.

Image-enhanced endoscopy presents images through filtering of illuminating light and/or computing captured electrical images. Narrow-band imaging (NBI; Olympus, Tokyo, Japan) is the most widely used and studied method for the detection of gastrointestinal lesions. Several retrospective studies have shown that NBI is useful in diagnosing *H. pylori* infection. Alaboudy *et al.*[55] retrospectively assessed *H. pylori*-infected gastric mucosa, and they classified mucosal patterns into five categories. The classification was found to be well-correlated with histopathological grades of *H. pylori* gastritis. Tongtawee *et al.*[56] assessed the NBI-based classification system developed by Alaboudy *et al.*[55] and found that types 3, 4, and 5 all had both sensitivity and specificity over 90% for predicting *H. pylori* positivity. However, a prospective multicenter study for the real-time use of NBI in the diagnosis of gastric lesions including *H. pylori* gastritis found that the diagnostic accuracy on *H. pylori* gastritis of WLI and NBI was similar.[57] Data are scarce on the diagnostic accuracy of i-scan, another digital image enhancement technique (Pentax Medical, Tokyo, Japan), in diagnosing *H. pylori* infection. One pilot study has investigated the diagnostic accuracy of i-scan, which showed better diagnostic accuracy of i-scan over conventional WLI in diagnosing *H. pylori* infection.[58]

The utility of LCI compared to other image-enhanced techniques is that it can be easily applied in screening endoscopy. NBI is useful in the characterization of known localized lesions, but it may not be appropriate for screening endoscopy, because the light intensity is insufficient to inspect the stomach from a distant view. By contrast, images produced by LCI are brighter and the color contrast is clearer than WLI.[59] LCI can observe the entire gastric mucosa with bright images, so it is considered to be a useful tool for diagnosing diffuse gastric lesions such as *H. pylori*-associated gastritis. Therefore, LCI could be a good screening tool for the real-time diagnosis of *H. pylori* infection. The routine use of LCI in screening endoscopy would provide valuable information on *H. pylori* infection status that cannot be obtained using conventional WLI alone.

Magnifying NBI may also be helpful for the endoscopic diagnosis of *H. pylori* infection. Yagi *et al.*[60] reported that magnifying NBI can detect the RAC of collecting venules in *H. pylori*-negative normal stomachs. Abnormal mucosal patterns without RAC which were classified as Z-1 to Z-3 were considered as characteristics of *H. pylori*-infected stomach in magnifying NBI.[61] However, magnifying NBI may not be widely used in clinical practice because it takes more time for inspection and has a long learning curve.[31]

AI will be the trend of future diagnostic technology. However, since our meta-analysis aimed to compare the performance of WLI and LCI, our study intentionally excluded AI-related studies from the analysis. There have already been several systematic reviews and meta-analyses related to AI for endoscopic diagnosis of *H. pylori* infection recently. In a meta-analysis published in 2020, the performance of AI was superior to endoscopists in the prediction of *H. pylori* infection (AUC, 0.90 vs 0.82; p<0.001).[62] In another meta-analysis published in the same year, pooled sensitivity, specificity, and AUC of AI for the diagnosis of *H. pylori* infection were 0.87 (95% CI, 0.72 to 0.94), 0.86 (95% CI, 0.77 to 0.92), and 0.92 (95% CI, 0.90 to 0.94).[63] A new meta-analysis was published in 2022, and the pooled accuracy was 79.6% (95% CI, 66.7 to 90.0) with a significant heterogeneity (I^2=97.9%; 95% CI, 97.2 to 98.6).[64] AI-related studies for the diagnosis of *H. pylori* infection are expected to continue in the future, and good results are expected.

The limitations of this study are as follows. First, significant heterogeneity was found in the pooled estimates of each diagnostic testing. Heterogeneity is a common issue reported in systematic reviews of studies on diagnostic test accuracy.[65] Although we identified possible sources of heterogeneity through meta-regression analysis, this heterogeneity was not resolved in the subgroup analysis. The criteria for the endoscopic diagnosis of *H. pylori* infection in the included studies were all different, which may have contributed substantially to the heterogeneity of the pooled estimates. Second, publication bias was not assessed. Because there are no reliable methods for assessing publication bias in diagnostic test accuracy studies,[66] this issue is considered insurmountable. Third, in the quality assessment of the included studies, more than one-third of studies (13 of 34 studies) rated a high or unclear risk of bias in the patient selection domain. This was because these studies were retrospective and did not specify whether or not to enroll patients consecutively. Fourth, since various endoscopic characteristics must be comprehensively judged for endoscopic diagnosis, inter-observer bias exists in these studies. Although there have been many individual studies, the endoscopic features of current *H. pylori* infection using LCI are not yet well standardized. Recently, to compensate for these limitations, a computer-aided diagnostic system for diagnosing *H. pylori* infection status using LCI has been developed, and it has shown good results.[62-64,67-69] AI technology with IEE is likely to become a useful image diagnostic tool in the future. In order to better utilize the AI-based LCI, we should focus on the color variations of gastric mucosa and create sophisticated diagnostic algorithms

in machine-learning system. Finally, all studies evaluating LCI were conducted in Asia. In the future, non-Asian studies on LCI need to be conducted for better meta-analysis.

In summary, this is the first meta-analysis study to evaluate the overall diagnostic ability of conventional WLI and LCI in the endoscopic diagnosis of *H. pylori* infection. This study revealed that LCI could be useful as a diagnostic tool for *H. pylori* infection. LCI can provide additional diagnostic ability to conventional endoscopy for *H. pylori* gastritis, and it could be an effective and convenient tool for detecting and monitoring *H. pylori* infection in clinical practice. We believe that prospective large-scale studies, especially in non-Asian countries, are needed to validate the effectiveness of LCI in diagnosing *H. pylori* gastritis. Further using a combination of image-enhanced endoscopy technology with AI could improve the diagnostic accuracy in the future.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTIONS

Study concept and design: S.P.L. Data acquisition: J.G.L., I.K.Y. Data analysis and interpretation: S.P.L., J.G.L., I.K.Y. Drafting of the manuscript: S.P.L., J.G.L., I.K.Y. Critical revision of the manuscript for important intellectual content: A.O.Y. Statistical analysis: J.G.L. Obtained funding: S.P.L. Administrative, technical, or material support; study supervision: S.P.L. Approval of final manuscript: all authors.

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SUPPLEMENTARY MATERIALS

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