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Magnifying endoscopy in detecting early gastric cancer

A network meta-analysis of prospective studies

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Abstract

Background: Conventional white-light imaging endoscopy (C-WLI) had a significant number of misdiagnosis in early gastric cancer (EGC), and magnifying endoscopy (ME) combined with different optical imaging was more accurate in the diagnosis of EGC. This study aimed to evaluate the accuracy of ME and compare the accuracy of ME with different optical imaging in detecting EGC.

Methods: A comprehensive literature search was conducted to identify all relevant studies. Pair-wise meta-analysis was conducted to evaluate the accuracy of ME, and Bayesian network meta-analysis was performed to combine direct and indirect evidence and estimate the relative effects.

Results: Eight prospective studies were identified with a total of 5948 patients and 3 optical imaging in ME (ME with WLI (M-WLI), ME with narrow-band imaging (M-NBI), and ME with blue laser imaging (M-BLI)). Pair-wise meta-analysis showed a higher accuracy of ME than C-WLI (OR: 2.97, 95% CI: 1.68~5.25). In network meta-analysis, both M-NBI and M-BLI were more accurate than M-WLI (OR: 2.56, 95% CI: 2.13~3.13; OR: 3.13, 95% CI: 1.85~5.71). There was no significant difference between M-NBI and M-BLI.

Conclusion: ME was effective in improving the detecting rate of EGC, especially with NBI or BLI.

Abbreviations: BLI = blue laser imaging, CI = confidence interval, C-WLI = conventional white-light imaging, EGC = early gastric cancer, LCI = linked color imaging, ME = magnifying endoscopy, NBI = narrow-band imaging, NOS = Newcastle-Ottawa Scale, OR = odds ratio.

Keywords: blue laser imaging, magnifying endoscopy, narrow-band imaging, network meta-analysis

1. Introduction

Gastric cancer (GC) is one of the most common cancers worldwide, with an estimated 951,600 new cases and 723,100 deaths per year.[1] Although the death rate has declined during the past years, the rate of early diagnosis was still low. Early gastric cancer (EGC) was considered curative, and after endoscopic resection, the 5-year survival rate was more than 95%.[2] Thus, if GC could be early detected, we would be able to improve the prognosis.[3] Conventional white-light imaging (C-WLI) has been applied in clinical practice for many years, but the accuracy in diagnosing gastric cancer was still low, with a sensitivity of 40% to 60% and a specificity of 67.9% to 94.3%.[4] It was really difficult to detect EGC and conduct accurate biopsies using C-WLI alone. To overcome the limitation, several enhanced endoscopic imaging techniques have occurred, including narrow-band imaging (NBI), blue laser imaging (BLI) and linked color imaging (LCI). Magnifying endoscopy (ME) combined with these optical imaging could help improve EGC detection. Several meta-analyses reported the superiority of magnifying endoscopy with NBI (M-NBI) to C-WLI in detecting EGC.[5–7] However, these studies ignored ME with other optical imaging, such as WLI, and the newly occurred systems of BLI and LCI.[8] Furthermore, no studies compared the accuracy between different optical imaging. Thus, we conducted a pair-wise meta-analysis to evaluate the accuracy of ME, and then a network meta-analysis to compare the accuracy of ME with different optical imaging in detecting EGC.

2. Materials and methods

2.1. Search strategy

The database of PubMed and Web of Science were searched for related studies published up to March 8th, 2020, using the Key

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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words: ("magnifying endoscopy (ME)"' OR "blue laser imaging (BLI)" OR "narrow-band imaging (NBI)" OR "linked color imaging (LCI)") AND "early gastric cancer (EGC)." Studies in languages other than English were excluded. Moreover, the references of all relevant studies, reviews and meta-analyses were reviewed for undetected studies. This study was approved by the ethics committee of The Central Hospital of Enshi Tujia And Miao Autonomous Prefecture.

2.2. Study selection and exclusion

Two authors reviewed the studies independently. The inclusion criteria were as follows:

(1) prospective designed study;
(2) compared the accuracy of conventional white-light imaging (WLI) endoscopy, ME-BLI, ME-NBI and ME-LCI in detecting early gastric cancer;
(3) The endoscopic diagnosis was confirmed by pathology.

The exclusion criteria were as follows:

(1) abstracts without full text,
(2) case-control studies and
(3) reviews.

2.3. Data extraction and quality assessment

Two authors extracted the data by a standardized collection form. Disagreements were solved by discussion. The following information was extracted from each study: first author, publication year, study area, study duration, study design, number of included patients, sex, age, lesion number, lesion size, endoscopy equipment, optical imaging type, assessment, and number of total cases and cases with accurate diagnosis. The Newcastle-Ottawa Scale was used to assess the methodological quality of included studies.

2.4. Statistical analysis

Pair-wise meta-analysis was conducted by Review Manager 5.2 to evaluate the accuracy of ME in comparison to C-WLI. Odds ratios (OR) with 95% confidence intervals (CI) were used to report the estimates following the Mantel-Haenszel method. The heterogeneity between studies was estimated by Q test and I^2 statistic. $I^2 > 50\%$ represented substantial heterogeneity, and a random-effects analysis was conducted. Otherwise, a fixed-effects model was used. Furthermore, subgroup analysis on the main confounders and sensitivity analysis by omitting 1 study at a time during repeated analyses were conducted to evaluate the stability of the primary result. Egger test was used to detect publication bias. All tests were sided with a significance level of 0.05.

To incorporate the indirect comparisons among ME, ME-BLI and ME-NBI, we conducted a Bayesian network meta-analysis by using the R packages of "gemtc" and "coda" and following the methods described by Dias et al.[9] Fixed- and random-effect model were evaluated, and the goodness fit of each model was assessed by the Deviance Information Criterion. The posterior densities for the outcome were estimated using the Markov Chain Monto Carlo simulations for each model. The results were based on 1000 simulation iterations and 5000 adaptation iterations.

3. Results

3.1. Study characteristics

The search strategy resulted in 457 records: 118 from PubMed, 296 from Web of Science, and 43 through other sources (Fig. 1). After excluding duplicated and irrelevant records, 8 studies were included in this meta-analysis with a total of 5948 patients and 5731 lesions (Table 1).[6,10–16] Three studies were conducted in multiple centers, while 5 studies were crossover designed. Six studies took the endoscopy of Olympus, while 2 selected Fujifilm. Six studies conducted a real-time assessment, while 2 studies made a diagnosis after the procedure. In quality assessment, the included studies had an average score of 7.78.

3.2. The accuracy of ME in detecting EGC

Yu *et al* study compared C-WLI with M-NBI and M-BLI respectively, and thus it was regarded as 2 separate studies in the pair-wise meta-analysis. Finally, 8 studies were included. ME showed a higher accuracy than C-WLI in detecting EGC (OR: 2.97, 95% CI: 1.68~5.25) (Fig. 2). Sensitivity analysis showed that the result was robust. Egger test detected no significant publication bias ($P = .116$).

Subgroup analysis was conducted on study design, number of lesions, EGC proportion, endoscopy equipment, optical imaging, and assessment (Table 2). No substantial changes of the primary result were found between subgroups, except for the comparison between M-WLI and C-WLI which contributed to the limited number of included studies (n = 1).

3.3. Network meta-analysis of ME with different optical imaging in detecting EGC

Five subgroups were included into the network meta-analysis, namely C-WLI, ME, ME-BLI and ME-NBI. There existed direct comparisons between M-BLI and C-WLI, M-NBI and C-WLI, M-WLI and C-WLI, and M-NBI and M-WLI (Fig. 3). Compared with C-WLI, the diagnostic accuracy was higher in M-WLI (OR: 1.43, 95% CI: 1.12~1.85), M-NBI (OR: 2.56, 95% CI: 2.13~3.13) and M-BLI (OR: 3.13, 95% CI: 1.85~5.71) (Table 3). Among the 3 types of ME, both M-NBI and M-BLI were more accurate than M-WLI (OR: 2.56, 95% CI: 2.13~3.13; OR: 3.13, 95% CI: 1.85~5.71). However, there was no significant difference between M-NBI and M-BLI.

4. Discussion

GC is the fourth most common cancer and the second most common cause of cancer death worldwide. Although the early detection of GC is necessary to improve patient survival, the identification of small GC is difficult. High-resolution endoscopic system has increased the probability of finding small and depressed lesions in the stomach, which include gastritis and EGC. Thus, the differential diagnoses are clinically important. For the images obtained using WLE, the endoscopic distinctive diagnosis between cancer and non-cancer for each lesion is made based on an assessment of the color and appearance. Therefore, the accurate diagnosis of EGC by C-WLI is difficult, and it also increases the number of unnecessary biopsies.

Magnifying endoscopy could visualize the microstructures and microvessels of the lesions. Endoscopic changes in these structures were useful for the early and differential diagnosis

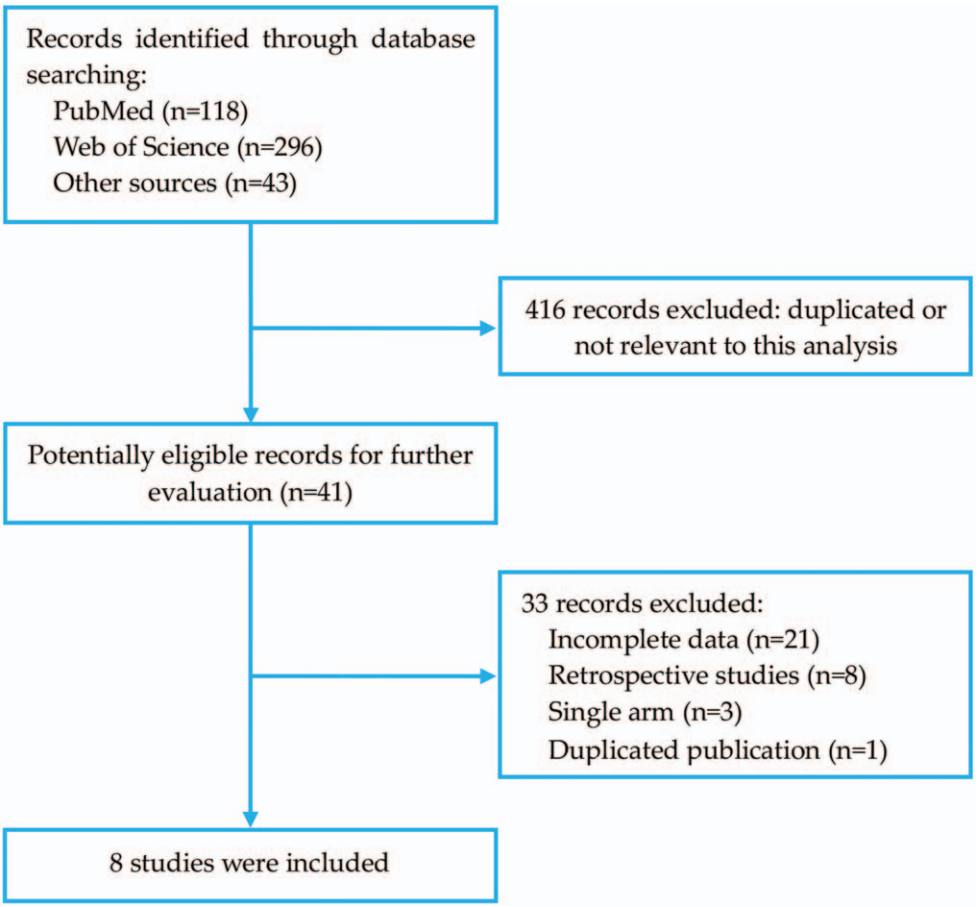

Figure 1. Flow chart of literature search.

of GC.[10] The diagnosis criteria by Yao et al were as following: an irregular microvascular pattern with a demarcation line and/or the presence of an irregular microsurface pattern with a demarcation line.[17] However, as for the low contrast of imaging in M-WLI, it is not easy to accurately visualize and evaluate the magnifying endoscopic findings such as demarcation line and microvascular pattern . A novel technique and an excellent diagnostic capacity for magnifying endoscopy are required for an accurate diagnosis when using M-WLI.

ME-NBI is an advanced endoscopic imaging technology launched recently, in which spectral bandwidth filters in a red-green-blue (R/G/B) sequential illumination system, and could be used to improve the diagnostic accuracy.[17] It has been developed to enhance the visualization of the superficial mucosal structure and vascular architecture. Several meta-analyses reported the superiority of magnifying endoscopy with NBI (M-NBI) to C-WLI in detecting EGC.[5] Moreover, it has also been applied to evaluate the histological type of EGC and measure the horizontal

Table 1

Characteristics of included studies.

Study	Area	Study design	No. of patients	Sex (M/F)	Age (y)	Lesion number	Lesion size (mm)	Endoscopy equipment	Optical imaging	Assessment
Ezoe 2010	Kashiwa, Japan	Crossover	53	NA	NA	57 (30 CA)	≤10	GIF-Q240Z, GIF-H260Z	M-WLI, M-NBI	Real-time
Kato 2010	Tokyo, Japan	Crossover	111	98/13	66.3±9.8	201 (14 CA)	7.0±4.0	GIF-H260Z	C-WLI, M-NBI	Real-time
Ezoe 2011	Multicenter, Japan	Parallel	353	278/75	69 (37~93)	353 (40 CA)	≤10	GIF-Q240Z, GIF-H260Z, GIF-FQ260Z	C-WLI, M-NBI	Real-time
Tao 2014	Beijing, China	Crossover	508	316/192	63 (41~78)	643 (24 CA)	7 (3~20)	GIF-H260Z	C-WLI, M-NBI	Post-procedure
Yu 2015	Multicenter, China	Crossover	3616	1910/1706	56 (40~90)	3675 (257 CA)	NA	GIF-H260Z	C-WLI, M-WLI, M-NBI	Post-procedure
Ang 2015	Multicenter, Asia	Parallel	579	236/343	62±9	579 (10 CA)	NA	Olympus	C-WLI, M-NBI	Real-time
Dohi 2017	Kyoto, Japan	Crossover	132	95/23	70 (41~91)	127 (32 CA)	NA	EG-L590ZW	C-WLI, M-BLI	Real-time
Dohi 2018	Kyoto, Japan	Parallel	596	385/211	73 (66~80)	90 (53 CA)	NA	EG-L590ZW, EG-L600ZW	C-WLI, M-BLI	Real-time

CA = cancer, C-WLI = conventional white-light imaging, M-BLI = magnifying blue laser imaging, M-NBI = magnifying narrow-band imaging, M-WLI = magnifying white-light imaging, NA = not available.

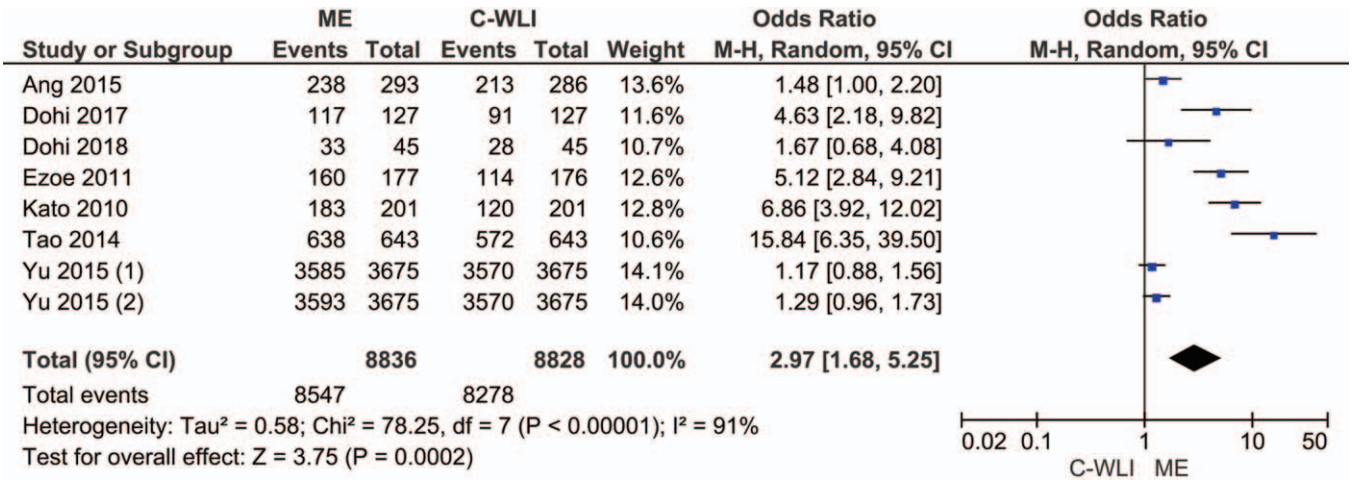

Figure 2. Forest plot of magnifying endoscopy in detecting early gastric cancer. C-WLI = conventional white-light imaging, ME = magnifying endoscopy.

extent of the stomach tumor before endoscopic submucosal dissection (ESD).[18,19]

Recently, Fujifilm developed an endoscope system with a semiconductor laser as a light source.[20] The system includes 2 types of lasers with wavelengths of 410 and 450 nm. The 450 nm laser irradiates phosphor to produce illumination light similar to that obtained with a xenon lamp. The combination of strong 410 nm laser light, weak 450 nm laser light, and fluorescent light

Table 2

Subgroup analysis of magnifying endoscopy in detecting early gastric cancer.

Subgroup	No. of studies	OR (95% CI)	I^2
Study design			
Parallel	3	2.34 (1.00~5.48)	83%
Crossover	5	3.50 (1.53~7.99)	94%
No. of lesions			
>500	4	2.05 (1.10~3.82)	90%
<500	4	4.39 (2.61~7.39)	57%
EGC proportion			
>10%	3	3.64 (1.93~6.87)	55%
<10%	5	2.71 (1.34~5.48)	93%
Endoscopy equipment			
Olympus	5	4.21 (2.03~8.75)	87%
Fujifilm	2	1.23 (1.00~1.51)	0%
Optical imaging			
NBI	4	3.79 (1.64~8.77)	93%
BLI	2	2.86 (1.05~7.78)	66%
WLI	1	1.17 (0.88~1.56)	–
Assessment			
Real time	5	3.33 (1.66~6.68)	85%
Post-procedure	3	2.46 (1.00~6.02)	94%

BLI = blue laser imaging, CI = confidence interval, NBI = narrow-band imaging, OR = odds ratio, WLI = white-light imaging.

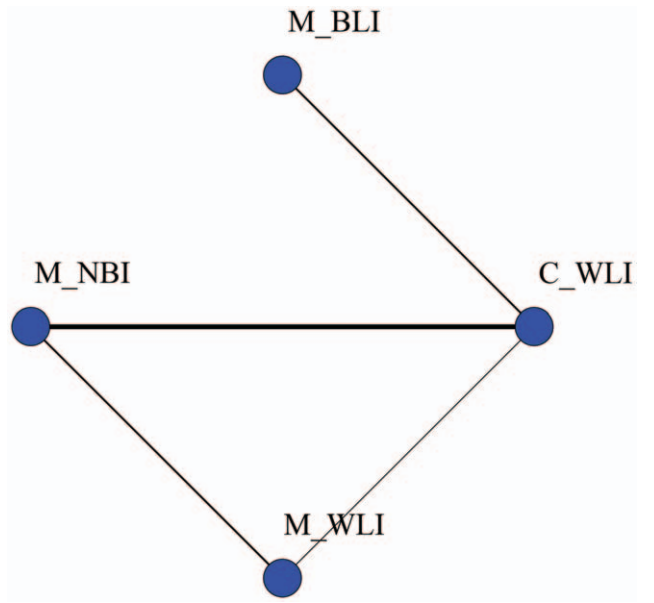

Figure 3. Network meta-analysis map. C-WLI = conventional white-light imaging, M-BLI = magnifying blue laser imaging, M-NBI = magnifying narrow-band imaging, M-WLI = magnifying white-light imaging.

Table 3

Network meta-analysis of magnifying endoscopy with different optical imaging in detecting early gastric cancer.

	Odds ratio (95% confidence interval)			
Optical imaging	**C-WLI**	**M-WLI**	**M-NBI**	**M-BLI**
C-WLI	–	1.43 (1.12~1.85)	2.56 (2.13~3.13)	3.13 (1.85~5.71)
M-WLI	0.70 (0.54~0.89)	–	1.79 (1.37~2.38)	2.22 (1.20~4.17)
M-NBI	0.39 (0.32~0.47)	0.56 (0.42~0.73)	–	1.22 (0.69~2.22)
M-BLI	0.32 (0.18~0.54)	0.45 (0.24~0.83)	0.82 (0.45~1.45)	–

CA = cancer, C-WLI = conventional white-light imaging, M-BLI = magnifying blue laser imaging, M-NBI = magnifying narrow-band imaging, M-WLI = magnifying white-light imaging, NA = not available.

enables blue laser imaging (BLI) via narrow-band light observation. M-BLI is useful for evaluating mucosal surface changes. M-BLI has the potential to diagnose EGC as efficiently as M-NBI because it uses narrow-band laser light combined with illumination light.[8] However, no studies have compared the accuracy between M-NBI and M-BLI in detecting EGC.

This meta-analysis has several strengths. First, to our knowledge, this is the first meta-analysis to evaluate the accuracy of ME with different optical imaging in detecting EGC. Previous studies mainly focused on the comparison between ME and C-WLI to emphasize on the clinical significance of endoscopic magnification. However, no studies have compared the accuracy between M-NBI and M-BLI in detecting EGC. As M-NBI was base on the platform of Olympus endoscopic system and M-BLI on the platform of Fujifilm, it was difficult to make a direct comparison of M-NBI and M-BLI on the same patient. Our network meta-analysis solved this problem. To our knowledge, this is also the first network meta-analysis to compare the efficacy of ME with different optical imaging in detecting EGC. Our findings could help the endoscopic physicians to make a better choice in the EGC screening. There were also a few limitations in this meta-analysis. First, the number of included studies was relatively small. Second, not all included studies had a large sample size. Third, not all potential confounders were adjusted in every study, like the operator‘s experience and the equipment generation. Nevertheless, these limitations could not prevent us from investigating an effective endoscopic pattern to improve the detecting rate of EGC. We thought that its clinical significance was far greater than its limitations. We expected large-scale prospective designed studies in the future to overcome the shortcomings in this study.

In conclusion, ME was effective in improving the detecting rate of EGC, and there was no significant difference between M-NBI and M-BLI.

Author contributions

Conceptualization: Hao Le, Dengfa Peng, Yong Tan, Changsong Cai, Huqing Li, Qiu Zhao.
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Supervision: Yong Tan, Lan Zhang.
Visualization: Lianjun Wang, Ming Yang.
Writing – original draft: Hao Le, Yong Tan, Huqing Li.
Writing – review & editing: Huqing Li.

References

[1] Torre LA, Siegel RL, Ward EM, et al. Global cancer incidence and mortality rates and trends - an update. Cancer Epidemiol Biomarkers Prev 2016;25:16–27.
[2] Crew KD, Neugut AI. Epidemiology of gastric cancer. World J Gastroenterol 2006;12:354–62.
[3] Soetikno R, Kaltenbach T, Yeh R, et al. Endoscopic mucosal resection for early cancers of the upper gastrointestinal tract. J Clin Oncol 2005;23:4490–8.
[4] Zhou F, Wu L, Huang M, et al. The accuracy of magnifying narrow band imaging (ME-NBI) in distinguishing between cancerous and noncancerous gastric lesions: a meta-analysis. Medicine (Baltimore) 2018;97: e9780.
[5] Zhang Q, Wang F, Chen ZY, et al. Comparison of the diagnostic efficacy of white light endoscopy and magnifying endoscopy with narrow band imaging for early gastric cancer: a meta-analysis. Gastric Cancer 2016;19:543–52.
[6] Kato M, Kaise M, Yonezawa J, et al. Magnifying endoscopy with narrow-band imaging achieves superior accuracy in the differential diagnosis of superficial gastric lesions identified with white-light endoscopy: a prospective study. Gastrointest Endosc 2010;72:523–9.
[7] Zhao Z, Yin Z, Wang S, et al. Meta-analysis: the diagnostic efficacy of chromoendoscopy for early gastric cancer and premalignant gastric lesions. J Gastroenterol Hepatol 2016;31:1539–45.
[8] Miyaki R, Yoshida S, Tanaka S, et al. A computer system to be used with laser-based endoscopy for quantitative diagnosis of early gastric cancer. J Clin Gastroenterol 2015;49:108–15.
[9] Dias S, Sutton AJ, Ades AE, et al. Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. Med Decis Making 2013;33:607–17.
[10] Ezoe Y, Muto M, Horimatsu T, et al. Magnifying narrow-band imaging versus magnifying white-light imaging for the differential diagnosis of gastric small depressive lesions: a prospective study. Gastrointest Endosc 2010;71:477–84.
[11] Ezoe Y, Muto M, Uedo N, et al. Magnifying narrowband imaging is more accurate than conventional white-light imaging in diagnosis of gastric mucosal cancer. Gastroenterology 2011;141:2017–25.
[12] Tao G, Xing-Hua L, Ai-Ming Y, et al. Enhanced magnifying endoscopy for differential diagnosis of superficial gastric lesions identified with white-light endoscopy. Gastric Cancer 2014;17:122–9.
[13] Ang TL, Pittayanon R, Lau JY, et al. A multicenter randomized comparison between high-definition white light endoscopy and narrow band imaging for detection of gastric lesions. Eur J Gastroenterol Hepatol 2015;27:1473–8.
[14] Yu H, Yang AM, Lu XH, et al. Magnifying narrow-band imaging endoscopy is superior in diagnosis of early gastric cancer. World J Gastroenterol 2015;21:9156–62.
[15] Dohi O, Yagi N, Majima A, et al. Diagnostic ability of magnifying endoscopy with blue laser imaging for early gastric cancer: a prospective study. Gastric Cancer 2017;20:297–303.
[16] Dohi O, Yagi N, Naito Y, et al. Blue laser imaging-bright improves real-time detection rate of early gastric cancer: a randomized controlled study. Gastrointest Endosc 2019;89:47–57.
[17] Yao K, Oishi T, Matsui T, et al. Novel magnified endoscopic findings of microvascular architecture in intramucosal gastric cancer. Gastrointest Endosc 2002;56:279–84.
[18] Nakayoshi T, Tajiri H, Matsuda K, et al. Magnifying endoscopy combined with narrow band imaging system for early gastric cancer: correlation of vascular pattern with histopathology (including video). Endoscopy 2004;36:1080–4.
[19] Yao K, Nagahama T, Matsui T, et al. Detection and characterization of early gastric cancer for curative endoscopic submucosal dissection. Dig Endosc 2013;25(Suppl 1):44–54.
[20] Osawa H, Yamamoto H. Present and future status of flexible spectral imaging color enhancement and blue laser imaging technology. Dig Endosc 2014;26(Suppl 1):105–15.