Comparison of Diagnostic Efficacy Between AFI, NBI, and AFI Combined with NBI for Colonic Cancers: A Meta-Analysis

Xiuhe Lv, Chunhui Wang, Yan Xie

Department of Gastroenterology, West China Hospital of Sichuan University, Sichuan, China

Address for correspondence:
Dr. Yan Xie,
No. 37 Guo Xue Xiang, Chengdu, Sichuan - 610041, China.
E-mail: xier917@126.com

ABSTRACT

Background/Aims: Advanced endoscopic imaging technologies have been used for the early detection and differentiation of colonic cancers recently. We aim to evaluate the diagnostic efficacy of autofluorescence imaging (AFI), narrow-band imaging (NBI), and AFI combined with NBI for colonic cancers. **Materials and Methods:** We searched Medline/PubMed, Embase, Web of Science, and Cochrane Library databases for relevant articles. A random-effects model was used to assess diagnostic efficacy. Heterogeneity was tested by the I^2 statistic and Chi-square test. Meta-regression was used to analyze the sources of heterogeneity. **Results:** The pooled sensitivities for AFI, NBI, and AFI plus NBI were 0.84 (95% confidence interval (CI) 0.82–0.87), 0.84 (95% CI 0.81–0.86), and 0.93 (95% CI 0.90–0.95), respectively. The pooled specificities were 0.44 (95% CI 0.40–0.48), 0.69 (95% CI 0.65–0.72), and 0.69 (95% CI 0.64–0.74), respectively. The sensitivity estimate was significantly higher for AFI plus NBI than AFI or NBI alone (P = 0.041), and the specificity estimates were significantly higher for NBI and AFI plus NBI than AFI (P = 0.031). The pooled diagnostic odds ratio for AFI, NBI, and AFI plus NBI were 8.71 (95% CI 2.90–26.16), 16.02 (95% CI 7.05–36.39), and 57.55 (95% CI 9.82–337.33), respectively. Furthermore, the summary receiver operating characteristic curve area under the curve for AFI, NBI, and AFI plus NBI were 0.8125 with Q^* =0.7469, 0.8696 with Q^* =0.8001, and 0.9447 with Q^* =0.8835, respectively. The Q^* index for AFI plus NBI was significantly higher than AFI or NBI alone (P = 0.048). **Conclusion:** The combination of AFI and NBI was associated with increased diagnostic value for colonic cancers compared with AFI and NBI alone.

Key Words: Autofluorescence imaging, colonic cancer, colonoscopy, narrow band imaging

Received: 07.03.2016, Accepted: 17.06.2016

How to cite this article: Lv X, Wang C, Xie Y. Comparison of diagnostic efficacy between AFI, NBI, and AFI combined with NBI for colonic cancers: A meta-analysis. Saudi J Gastroenterol 2017;23:82-90.

The aim of screening colonoscopy is to prevent the development of colonic cancer by means of colonoscopic detection and polyp resection. However, some specific lesions may be missed (such as small or flat adenomas) or difficult to detect (such as depressed-type colorectal tumors and nongranular-type laterally spreading tumors) during conventional colonoscopy examinations;[1] Removal of non-neoplastic polyps with standard white light colonoscopy (WLC) occurs occasionally, and such inappropriate polyp resection may lead to unnecessary risks of perforation or bleeding.[2] Advanced endoscopic imaging technologies are needed to assist endoscopists in dealing with these problems.

In recent years, several clinical trials have shown that chromoendoscopy (CE) could increase the detection rate of colonic neoplasia.[3,4] However, this procedure is labor-intensive, time-consuming, and requires special training. Narrow-band imaging (NBI) is a novel imaging technique that uses special narrow-band filters to highlight mucosal and vascular details of the gastrointestinal tract. It has been demonstrated to improve the detection of colonic lesions and to help distinguish adenoma from hyperplastic polyps.[5-8] Autofluorescence imaging (AFI) is another imaging technique that can be employed to polyp detection.

Access this article online

Quick Response Code:

Website: www.saudijgastro.com

DOI: 10.4103/1319-3767.203355

It can be used for differentiation based on the differences of emitted autofluorescent light between neoplastic and non-neoplastic polyps.[9] Several studies have attempted to assess the diagnostic performance of AFI and NBI for colonic neoplasms, but the results of these studies are heterogeneous.[10] On the other hand, the appearance of endoscopic trimodal imaging (ETMI), which integrates AFI, NBI, and high-resolution endoscopy (HRE) into one system, brings about the possibility to combine AFI and NBI conventionally in the future. Therefore, we performed this meta-analysis to assess the diagnostic efficacy of AFI, NBI, and AFI combined with NBI for colonic neoplasms.

MATERIALS AND METHODS

This study did not require any ethical approval and informed consent because only published material was included.

Literature search

A systematic literature search was conducted to identify relevant studies which compared the diagnostic value of AFI, NBI, and AFI combined with NBI in the diagnosis of colonic neoplasms. We searched Medline/PubMed, Embase, Web of science, and Cochrane Library databases for articles that were published in English up to 30th September, 2015. The following search terms were used: "autofluorescence imaging," "AFI," "narrow band imaging," "NBI," "colonic neoplasm," "colon neoplasm," "colonic cancer," and "colon cancer." The references in the available studies and abstracts from important GI meetings, such as Digestive Disease Week and Asian Pacific Digestive Week, were also reviewed systematically. Two investigators independently reviewed each publication for applicable studies. Disagreements were settled by a discussion with a third investigator.

Inclusion and exclusion criteria

Inclusion criteria include the following: (1) diagnostic clinical trials that used AFI and NBI to differentiate colonic neoplastic lesions from non-neoplastic lesions; (2) diagnostic efficacies of AFI and NBI compared in the references; (3) inclusion of more than 20 lesions; (4) use of histopathologic analysis as the reference standard (gold standard) for the diagnosis of lesions; (5) absolute numbers of true positive (TP), false positive (FP), true negative (TN), and false negative (FN) cases were provided or could be calculated from primary data; and (6) latest reported article was chosen if the same study was repeatedly reported.

Exclusion criteria include the following: (1) patients without colonic lesions but with other gastrointestinal lesions, or diagnosis of colonic neoplasms with other existing disease that could not be differentiated; (2) data or subsets of data without pathological confirmation of lesions, or were reported in duplicate in similar studies, and (3) publication types as reviews, case reports, editorials, comments, and letters.

We did not attempt to contact the authors for unpublished data or to locate unpublished material.

Data extraction

The following data were extracted from each report: first author's name, year of publication, country of origin, number of patients and lesions, age and sex of participants, diagnostic classifications for AFI and NBI, study design, reference standard. The numbers of TP, FP, TN, and FN were also extracted for the construction of 2 × 2 contingency tables. All data were extracted by two investigators independently.

Quality assessment

The quality of diagnostic accuracy studies (QUADAS) tool was used to assess the quality of selected studies. QUADAS is a validated clinometric tool used to assess the overall quality of diagnostic accuracy studies through individual quality component questions.[11] Each of the 14 items in the QUADAS checklist was scored as "Yes," "No," or "Unclear." Each item was scored "Yes" if reported, "No" if not reported, or "Unclear" if sufficient information was not available to make an accurate decision.

Statistical analysis

The possibility of a threshold effect was first tested by calculating the Spearman correlation coefficient for the included studies. We calculated the pooled sensitivity, specificity, and diagnostic odds ratio (DOR) for each modality by using a random effects model to derive estimates and 95% confidence intervals (CIs) if the evidence of a threshold effect was not found. In this case, the summary receiver operating characteristic curves (SROC) and the $*Q$ index were also calculated. The SROC area under the curve (AUC) and integrated DOR value were used to analyze the diagnostic efficacy of each modality if the evidence of a threshold effect was found. The Z test was performed to determine statistical differences between sensitivity, specificity, DOR, and $*Q$ index of different modalities. The I^2 statistic and Chi-square test were used to detect statistically significant heterogeneity. All P values less than 0.05 were considered to indicate heterogeneity between studies. Meta-DiSc (version 1.4, XI Cochrane Colloquium, Barcelona, Spain) and STATA (version 11.0, College Station, TX) software were used for data analyses in this study.

RESULTS

Search results and study description

A total of 948 primary studies were identified for literature screening [Figure 1]. From these studies, 210 were excluded

as duplicates and 723 were excluded after reviewing the titles and abstracts. After a review of the full-texts, the reasons for the final study exclusion were as follows: (1) insufficient data were reported to calculate TP, FP, TN, and FN ($N = 2$);[12,13] (2) different evaluation methods for diagnostic efficacy were used ($N = 2$);[1,14] (3) suspicious data duplications appeared in similar studies ($N = 3$).[15-17] Finally, 8 studies were included in our analysis, comprising a total of 660 patients and 1426 lesions. All of them were prospective studies.[18-25] Table 1 shows the principal characteristics of the studies included in the meta-analysis.

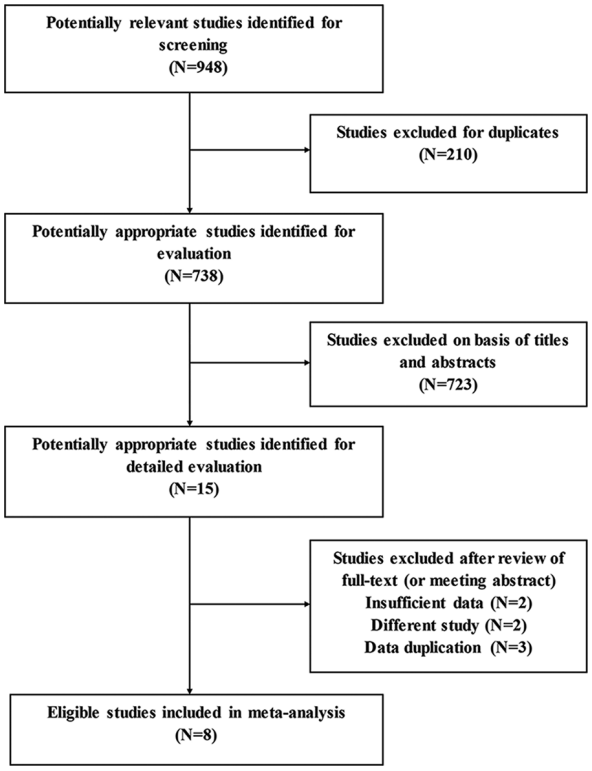

Figure 1: Flow diagram showing the selection process of articles

Quality assessment

Detailed information regarding the quality of eligible studies is shown in Table 2. The items 4, 10, 11, and 13 were scored "unclear" for the studies published by Probst *et al.* and Goelder *et al.* because relevant information could not be extracted from existing data. In addition to these two meeting abstracts, the other selected studies achieved most of the quality items, suggesting a good quality of included studies. Not all samples received verification by using a reference standard of diagnosis for the results published by Van den Broek *et al.*, Kuiper *et al.*, and Sato *et al.*, hence item 5 was scored "no" in these 3 studies. Furthermore, as the reasons for such exclusions were not explained, item 13 was scored "no" in these 2 studies published by Kuiper *et al.* and Sato *et al.*

Analysis results

Spearman correlation coefficients for AFI, NBI, and AFI plus NBI were 0.870 ($P = 0.349$), 0.381 ($P = 0.352$), and 0.400 ($P = 0.600$), respectively. These results indicated the lack of a definite threshold effect-induced heterogeneity of different modalities. When a random effects model was used, the pooled sensitivities for AFI, NBI, and AFI plus NBI were 0.84 (95% CI 0.82–0.87), 0.84 (95% CI 0.81–0.86), and 0.93 (95% CI 0.90–0.95), respectively. The pooled specificities were 0.44 (95%

Table 1: Characteristics of the studies selected for the meta-analysis

Study (year)	Country	Patients	Lesions	Sex (M/F)	Mean age	Diagnostic classification for AFI	Diagnostic classification for NBI	Reference standard	Study design	Restrictions
Probst[18] *et al.*(2006)	Germany	19	24	NS	NS	Green-purple- ambiguous	Kudo pit-pattern	NS	Prospective	None
Goelder[19] *et al.*(2007)	Germany	19	51	NS	NS	Green-purple- ambiguous	Kudo pit-pattern	NS	Prospective	None
Vanden Broek[20] *et al.*(2008)	Netherlands	50	98	31/19	50.5	Green-purple- ambiguous	Kudo pit-pattern	Vienna criteria	Prospective	UC
Boparai[21] *et al.*(2009)	Netherlands	7	66	5/2	55.8	Green-purple- ambiguous	Kudo pit-pattern	WHO guidelines	Prospective	HPS
Vanden Broek[22] *et al.*(2009)	Netherlands	100	208	43/57	52	Green-purple- ambiguous	Kudo pit-pattern	Vienna criteria	Prospective	None
Ignjatovic[23] *et al.*(2011)	Britain	48	80	30/18	64.7	Green-purple- ambiguous	Kudo pit-pattern	WHO guidelines	Prospective	SCP
Kuiper[24] *et al.*(2011)	Netherlands	234	256	128/106	59	Green-purple- ambiguous	Kudo pit-pattern	Vienna criteria	Prospective	None
Sato[25] *et al.*(2011)	Japan	183	424	128/55	64.9	Green-purple	Sano pattern	Vienna criteria	Prospective	None

NS, not stated, Green-purple-ambiguous, green was considered non-neoplastic and purple or ambiguous colors were considered neoplastic, Green-purple, green or green with purple spots group were considered non-neoplastic and purple with green spots or purple group were considered neoplastic, Kudo pit-pattern, the classification was proposed by Kudo *et al.*,[32] Sano pattern, the classification was proposed by Sano *et al.*;[33] UC, ulcerative colitis; HPS, hyperplastic polyposis syndrome; SCP, small colonic polyp (≤10 mm); None, the study was conducted without following specific requirements

CI 0.40–0.48), 0.69 (95% CI 0.65–0.72), and 0.69 (95% CI 0.64–0.74), respectively. The sensitivity estimate was significantly higher for AFI plus NBI than AFI or NBI alone ($P = 0.041$), and the specificity estimates were significantly higher for NBI and AFI plus NBI than AFI ($P = 0.031$). The pooled estimates were not different between AFI and NBI for sensitivity, or NBI and AFI plus NBI for specificity. The forest plots for the sensitivity and specificity of AFI, NBI, and AFI plus NBI are shown in Figures 2-4.

The pooled DOR for AFI was 8.71 (95% CI 2.90–26.16), and the Cochran's Q and I^2 were 64.71 ($P = 0.0001$) and 89.2%, respectively. The pooled DOR for NBI was 16.02 (95% CI 7.05–36.39), and the Cochran's Q and I^2 were 37.83 ($P = 0.0001$) and 81.5%, respectively. The DOR for AFI plus NBI was 57.55 (95% CI 9.82–337.33), and the Cochran's Q and I^2 were 18.88 ($P = 0.0003$) and 84.1%, respectively. The DOR estimate for AFI plus NBI was significantly higher than AFI or NBI alone ($P = 0.038$). Furthermore, The AUCs for AFI, NBI, and AFI plus NBI were 0.8125 (Standard error (SE) =0.0597) with Q^* =0.7469 (SE = 0.0531), 0.8696 (SE = 0.0340) with Q^* =0.8001 (SE = 0.0335) and 0.9447 (SE = 0.0357) with Q^* =0.8835 (SE = 0.0464), respectively. The Q^* index for AFI plus NBI was significantly higher than AFI or NBI alone ($P = 0.048$). All these data indicated higher diagnostic accuracy for AFI plus NBI compared to AFI or NBI alone. These results can be seen from Figure 5.

Heterogeneity exploration

Significant heterogeneities were found in the sensitivity, specificity, and DOR estimate of different modalities, which can be seen from Figures 2-5. Thus, sensitivity analysis was performed first according to the inclusion criteria of different studies [Table 3]. We included 6 studies after exclusion of 2 studies as abstracts, and 7 studies after the exclusion of

Table 2: Quality assessment of the studies selected for the meta-analysis

	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13	Item 14	Score
Probst *et al.*(2006)	Y	Y	Y	U	Y	Y	Y	Y	Y	U	U	Y	U	Y	10
Goelder *et al.*(2007)	Y	Y	Y	U	Y	Y	Y	Y	Y	U	U	Y	U	Y	10
Vanden Broek *et al.*(2008)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Boparai *et al.*(2009)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Vanden Broek *et al.*(2009)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	13
Ignjatovic *et al.*(2011)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	14
Kuiper *et al.*(2011)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y	12
Sato *et al.*(2011)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	N	Y	12

Y, Yes; N, no; U, unclear, 1. Was the spectrum of patients representative of the patients who will receive the test in practice? 2. Were selection criteria clearly described? 3. Is the reference standard likely to correctly classify the target condition? 4. Is the time period between reference standard and index test short enough to be reasonably sure that target condition did not change between two tests? 5. Did the whole sample or a random selection of the sample receive verification using a reference standard? 6. Did patients receive the same reference standard regardless of the index test result? 7. Was the reference standard independent of the index test (i.e., the index test did not form part of the reference standard)? 8. Was the execution of the index test described in sufficient detail to permit replication of the test? 9. Was the execution of the reference standard described in sufficient detail to permit its replication? 10. Were the index test results interpreted without knowledge of the results of the reference standard? 11. Was the reference standard results interpreted without knowledge of the results of the index test? 12. Were the same clinical data available when test results were interpreted as would be available when the test is used in practice? 13. Were uninterpretable/intermediate test results reported? 14. Were withdrawals from the study explained?

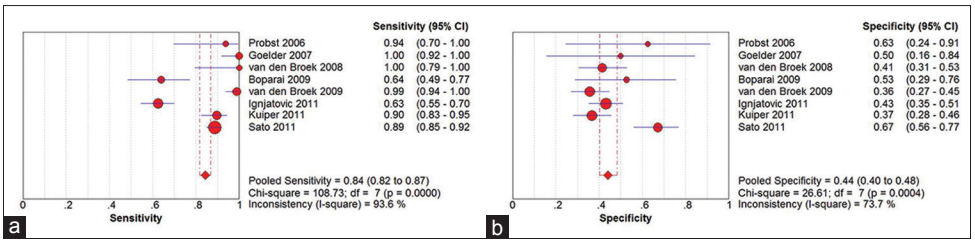

Figure 2: Analysis of the diagnostic efficacy results of AFI. (a) Pooled sensitivity of AFI for diagnosing colonic cancers. (b) Pooled specificity of AFI for diagnosing colonic cancers

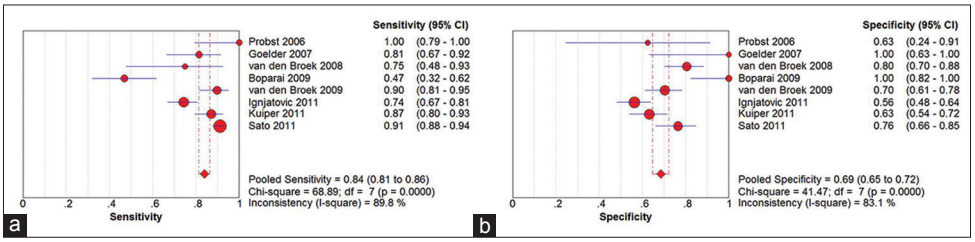

Figure 3: Analysis of the diagnostic efficacy results of NBI. (a) Pooled sensitivity of NBI for diagnosing colonic cancers. (b) Pooled specificity of NBI for diagnosing colonic cancers

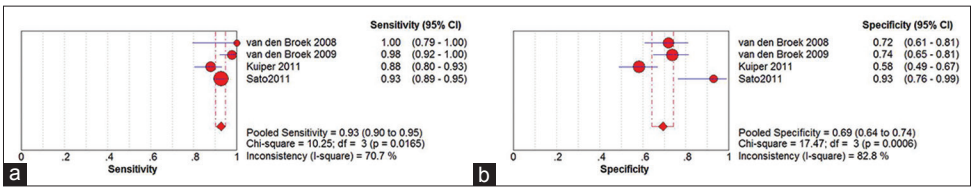

Figure 4: Analysis of the diagnostic efficacy results of AFI plus NBI. (a) Pooled sensitivity of AFI plus NBI for diagnosing colonic cancers. (b) Pooled specificity of AFI plus NBI for diagnosing colonic cancers

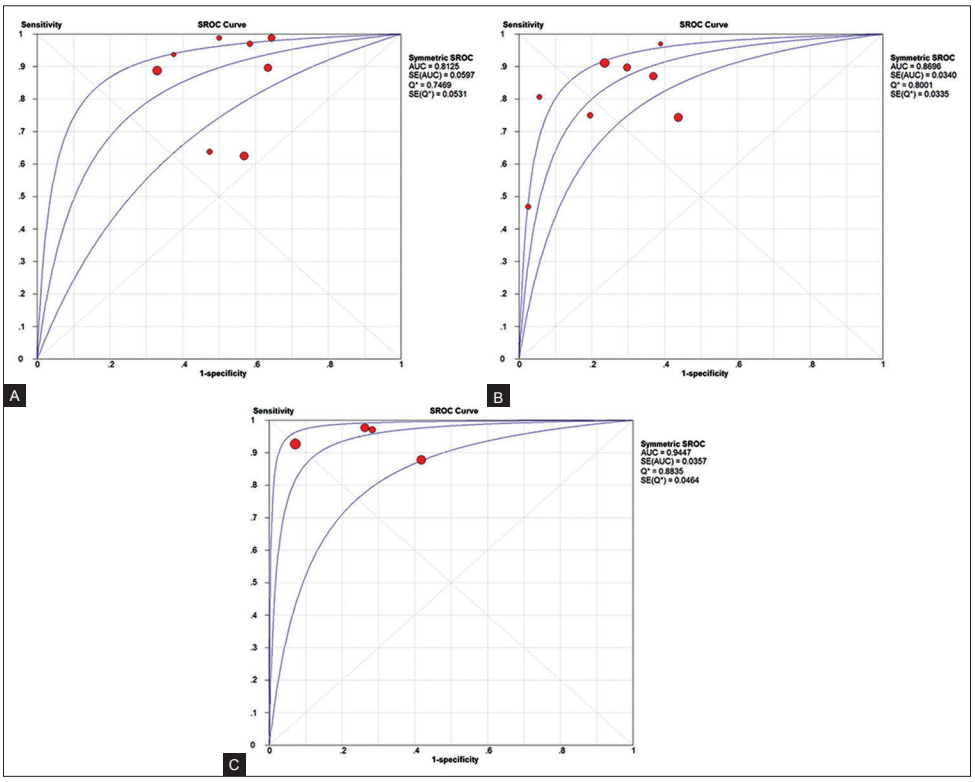

Figure 5: Symmetric receiver operating characteristic (SROC) curve and area under the curve (AUC) of different modalities. (a) SROC curve and AUC of AFI. (b) SROC curve and AUC of NBI. (c) SROC curve and AUC of AFI plus NBI

1 study from Japan. The results showed that the diagnostic efficacy of AFI or NBI for colonic cancers was similar to the originally pooled measures, which implies that the stability of the study results was good. However, heterogeneity was still significant among the studies. Therefore, a meta-regression analysis was conducted subsequently to explore the possible sources of heterogeneity. Specific variables assessed were as follows: number of patients (<50 or ≥50), number of lesions (<200 or ≥200), restriction setting (present or absent), diagnostic classification for AFI (green-purple-ambiguous or green-purple), and diagnostic classification for NBI (Kudo pit pattern or Sano pattern). Detailed information is presented

Table 3: Sensitivity analysis of selected studies for assessing the stability of diagnostic accuracy of AFI and NBI

Study characteristics	No. of studies	Imaging	Pooled estimates*		Inconsistency		AUC
			Sensitivity	Specificity	I^2 for sensitivity	I^2 for specificity	
Study with full-text	6	AFI	0.83 (0.80-0.86)	0.44 (0.40-0.48)	94.6%	80.3%	0.7759
		NBI	0.84 (0.81-0.87)	0.68 (0.64-0.72)	91.3%	83.0%	0.8623
Study from Europe	7	AFI	0.81 (0.78-0.85)	0.40 (0.36-0.45)	94.0%	0.0%	0.7925
		NBI	0.79 (0.75-0.83)	0.67 (0.63-0.71)	86.6%	84.4%	0.8515

*The 95% confidence interval is given in parentheses

in Tables 4 and 5. It can be seen from the tables that the diagnostic classification and restriction setting was found to affect the heterogeneity for AFI and NBI. Subsequently, we performed the subgroup analysis with two groups for each modality based on the corresponding variables. Subgroup analysis for AFI indicated that the heterogeneity remained high in sensitivity and DOR estimate of 7 studies using the "green-purple-ambiguous" pattern, however, the heterogeneity decreased greatly in specificity. On the other hand, subgroup analysis for NBI indicated that the heterogeneity decreased greatly in all pooled estimates of 5 studies without restrictions, however, heterogeneity increased in all pooled estimates of studies with restrictions. All these results indicate that meta-regression analysis only solved the problem of heterogeneity partially.

Table 4: Meta-regression analysis for possible sources of heterogeneity for AFI

Variances	Coefficient	Standard error	*P* value
Inverse variance weights 1			
Cte	1.331	1.5801	0.4882
S	0.770	0.3999	0.1941
Classification (AFI)	2.161	0.7808	0.1095
Patient	0.473	1.9205	0.8283
Lesion	−2.231	2.2134	0.4195
Restriction	−1.602	1.3776	0.3648
Inverse variance weights 2			
Cte	1.135	1.3646	0.4666
S	0.833	0.3056	0.0722
Classification (AFI)	2.263	0.6618	0.0418
Lesion	−1.750	1.0422	0.1917
Restriction	−1.447	1.2256	0.3228
Inverse variance weights 3			
Cte	−0.436	0.3050	0.2264
S	1.039	0.2511	0.0144
Classification (AFI)	2.594	0.5997	0.0124
Lesion	−0.789	0.6513	0.2922
Inverse variance weights 4			
Cte	0.427	0.7439	0.5909
S	0.679	0.3000	0.0730
Lesion	0.331	0.8946	0.7264
Inverse variance weights 5			
Cte	−0.295	0.2820	0.3436
S	0.797	0.1522	0.0034
Classification (AFI)	1.993	0.3371	0.0020

DISCUSSION

The AFI and NBI video endoscope systems have been considered to play an important role in the future detection of colonic cancers because both systems have been shown to improve the mucosal visualization compared to WLC. Our meta-analysis focused on evaluating the diagnostic ability of AFI and NBI for colonic cancers and revealed that both AFI and NBI had relatively high sensitivities but low specificities in the differentiation of colonic lesions. Furthermore, the combination of AFI and NBI was associated with increased diagnostic value for colonic cancers compared with AFI and NBI alone.

Although the merit of these two systems have been recognized in a number of studies, there have been mixed results in the use of AFI and NBI for the detection and characterization of polyps in the colon. Matsuda *et al.* demonstrated that AFI improved the detection of colonic polyps, with lower miss-rate compared with WLC.[26] The large study conducted by Sato *et al.* reported that AFI could distinguish adenoma from hyperplastic polyps with an accuracy of 84.9%, whereas HRE exhibited an accuracy of 75.9%.[25] On the contrary, Kuiper *et al.* demonstrated that AFI did not significantly reduce the adenoma miss-rate compared with the standard WLC,[24] and the results from Ignjatovic *et al.* indicated that AFI was not useful in the differentiation of small polyps (≤10 mm).[23] On the other hand, Rastogi *et al.* and Inoue *et al.* have proved the usefulness of NBI for detecting colon polyps,[5,27] and a meta-analysis also revealed that NBI has a high diagnostic precision for colorectal neoplastic polyps with or without magnification.[28] However, from another aspect, a review indicated that high-definition (HD) NBI did not increase the detection of colon polyps, adenomas, or flat adenomas nor did it decrease the miss-rate of colon polyps or adenomas in

Table 5: Meta-regression analysis for possible sources of heterogeneity for NBI

Variances	Coefficient	Standard error	*P* value
Inverse variance weights 1			
Cte	4.371	1.1088	0.06
S	−0.368	0.2692	0.31
Classification (NBI)	0.757	0.4137	0.21
Patient	0.768	0.7359	0.41
Lesion	−1.960	1.3884	0.29
Restriction	−2.740	1.1184	0.13
Inverse variance weights 2			
Cte	4.444	1.1067	0.03
S	−0.472	0.2501	0.16
Classification (NBI)	0.737	0.4133	0.17
Lesion	−1.125	1.1345	0.39
Restriction	−2.661	1.1158	0.10
Inverse variance weights 3			
Cte	3.425	0.4103	0.0011
S	−0.508	0.2475	0.11
Classification (NBI)	0.672	0.4080	0.18
Restriction	−1.621	0.3827	0.01
Inverse variance weights 4			
Cte	2.615	0.4228	0.0016
S	−0.135	0.2767	0.65
Classification (NBI)	1.051	0.9120	0.30
Inverse variance weights 5			
Cte	3.676	0.4117	0.0003
S	−0.495	0.2617	0.12
Restriction	−1.826	0.4675	0.01

patients undergoing screening colonoscopy when compared with HD-WLC.[29] Some studies have also pointed out that NBI did not have better sensitivity, specificity, or accuracy for colonic polyp characterization compared with WLC.[22,23] We first reported that AFI and NBI had similar sensitivities of 84% and specificities of 44% and 69%, respectively, in the differentiation of colonic lesions when the diagnostic indices were pooled with a random effects model. In general, a high sensitivity is considered more important than a high specificity in differentiating lesions because it is imperative to not leave any adenomas *in situ*.[22,24] However, in the current study, sensitivities of NBI and AFI should be deemed clinically unacceptable because approximately 16% of all detected adenomas would be left *in situ*.

In our study, the AFI had a similar sensitivity but a lower specificity compared with NBI, and the diagnostic efficacy of AFI was also lower than NBI. These results seem to be inconsistent with the study from Suzuki *et al.*, which concluded that AFI might be more effective for the characterization of colorectal adenomas than NBI.[1] The main reason for this difference may be that a unique research method was used by Suzuki *et al.*, which compared the visualization quality between the two modalities. The inclusion of patients may also play a role in this situation. Although the AFI system demonstrates significantly better visualization of colorectal adenomas compared to the NBI system, the results may be different when the diagnostic performance is compared, including colonic lesions such as inflammatory bowel disease or familial adenomatous polyposis.

AFI uses tissue function to yield real-time pseudocolor images and has a potential to serve as a "red flag" technique for the detection of neoplastic lesions. Several studies in recent years have proved that AFI could improve the detection of relevant lesions but might give false positive findings concerning Barrett's esophagus or gastric neoplasia;[30,31] the results from our study proved the similarity for colonic cancers. On the other hand, NBI can enhance the contrast of the superficial mucosal and vascular patterns. This is helpful to confirm the suspicious surface structures, which may provide a possibility of reducing the false positive rate caused by AFI. This assumption has been certified by the same studies which also tried to explore the role of NBI for esophageal and gastric lesions.[30,31] Therefore, we aimed to find out the diagnostic efficacy of AFI combined with NBI for colonic cancers in our study as well. Four studies were selected for our analysis, for which AFI was used for the detection of lesions and NBI was used for differentiation of lesions subsequently. It can be observed from Figure 4 that AFI plus NBI had a higher sensitivity estimate compared to AFI or NBI alone, and the specificity estimate was also higher than AFI alone. Such findings indicate that an additive effect may exist, and a lower false positive rate of AFI can be achieved after detailed inspection with NBI. Furthermore, the higher DOR estimate and AUC for AFI plus NBI compared with AFI or NBI alone in this study also arouses our interest toward the utility of this combination for routine inspection. ETMI has brought convenience to the conventional use of AFI and NBI by allowing switching from one imaging mode to another with a button in the control head of an endoscope. Moreover, combining AFI and NBI data has been proved to provide greater accuracy, with equal results between experienced and nonexperienced endoscopists.[15]

There are several limitations of our study. But, the main limitation is the heterogenity among the studies that have evaluated in our meta-analysis. We explored the source of heterogeneity by sensitivity analysis and meta-regression analysis, however, this could only solve the problem partially. The diagnostic classification used by Sato *et al.* providing a more unique measurement to the differentiation of neoplastic and non-neoplastic lesions with AFI,[25] brought about heterogeneity with other studies.[32,33] On the other hand, NBI had lower sensitivities for the differentiation of ulcerative colitis, sessile serrated adenomas, and small

colonic polyps (≤10 mm) in the restricted studies,[20,21,23] which was found to affect the heterogeneity for NBI. More related studies are needed to further explore the definite reasons for these specific situations. Another limiting of our study is that the interobserver agreements. High interobserver agreement between all colonoscopists is required if optical diagnosis is to become acceptable in routine clinical practice. However, only two included studies discussed the interobserver agreements of AFI and NBI and provided the kappa values.[23,25] Further studies are needed not only to evaluate the interobserver agreement of each modality but also to evaluate the differences between expert and nonexpert endoscopists.

CONCLUSION

In conclusion, both AFI and NBI have relatively high sensitivities but low specificities in the differentiation of colonic lesions; the diagnostic accuracy requires further improvements for both the modalities. The combination of AFI and NBI, which is generally realized by the use of ETMI, is associated with increased diagnostic value for colonic cancers compared with AFI and NBI alone. More prospective trials should be performed to explore the differences of application values between ETMI and other endoscopic techniques.

Financial support and sponsorship
The National Science Foundation of China, No. 81200333.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Suzuki H, Saito Y, Matsuda T, Nakajima T, Kikuchi T. Prospective Case Study on Characterization of Colorectal Adenomas Comparing AFI with NBI. Diagn Ther Endosc 2011;2011:963618.
2. Gómez V, Wallace MB. Advances in diagnostic and therapeutic colonoscopy. Curr Opin Gastroenterol 2014;30:63-8.
3. Ratiu N, Gelbmann C, Rath HR, Herfarth H, Kullmann F, Schölmerich J, *et al*. Chromoendoscopy with indigo carmine in flexible sigmoidoscopy screening: Does it improve the detection of adenomas in the distal colon and rectum? J Gastrointestin Liver Dis 2007;16:153-6.
4. Park SY, Lee SK, Kim BC, Han J, Kim JH, Cheon JH, *et al*. Efficacy of chromoendoscopy with indigocarmine for the detection of ascending colon and cecum lesions. Scand J Gastroenterol 2008;43:878-85.
5. Inoue T, Murano M, Murano N, Kuramoto T, Kawakami K, Abe Y, *et al*. Comparative study of conventional colonoscopy and pan-colonic narrow-band imaging system in the detection of neoplastic colonic polyps: A randomized, controlled trial. J Gastroenterol 2008;43:45-50.
6. Adler A, Aschenbeck J, Yenerim T, Mayr M, Aminalai A, Drossel R, *et al*. Narrow-band versus white-light high definition television endoscopic imaging for screening colonoscopy: A prospective randomized trial. Gastroenterology 2009;136:410-6.
7. Paggi S, Radaelli F, Amato A, Meucci G, Mandelli G, Imperiali G, *et al*. The impact of narrow band imaging in screening colonoscopy: A randomized controlled trial. Clin Gastroenterol Hepatol 2009;7:1049-54.
8. East JE, Ignjatovic A, Suzuki N, Guenther T, Bassett P, Tekkis PP, *et al*. A randomized, controlled trial of narrow-band imaging vs high-definition white light for adenoma detection in patients at high risk of adenomas. Colorectal Dis 2012;14:e771-8.
9. McCallum AL, Jenkins JT, Gillen D, Molloy RG. Evaluation of autofluorescence colonoscopy for the detection and diagnosis of colonic polyps. Gastrointest Endosc 2008;68:283-90.
10. Yeung TM, Mortensen NJ. Advances in endoscopic visualization of colorectal polyps. Colorectal Dis 2011;13:352-9.
11. Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J. The development of QUADAS: A tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol 2003;3:25.
12. East JE, Suzuki N, Palmer N, Thapar C, Swain D, Saunders BP. Autofluorescence Imaging (AFI) and Narrow Band Imaging (NBI) with Magnification in Colonoscopy: An Early Experience. Gastrointest Endosc 2006;63:AB230-AB230.
13. Rotondano G, Bianco MA, Sansone S, Prisco A, Meucci C, Garofano ML, *et al*. Trimodal endoscopic imaging for the detection and differentiation of colorectal adenomas: A prospective single-centre clinical evaluation. Int J of Colorectal Dis 2012;27:331-6.
14. Matsumoto T, Esaki M, Fujisawa R, Nakamura S, Yao T, Iida M. Chromoendoscopy, narrow-band imaging colonoscopy, and autofluorescence colonoscopy for detection of diminutive colorectal neoplasia in familial adenomatous polyposis. Dis Colon Rectum 2009;52:1160-5.
15. van den Broek FJ, van Soest EJ, Naber AH, van Oijen AH, Mallant-Hent RCh, Böhmer CJ, *et al*. Combining autofluorescence imaging and narrow-band imaging for the differentiation of adenomas from non-neoplastic colonic polyps among experienced and non-experienced endoscopists. Am J Gastroenterol 2009;104:1498-507.
16. Kuiper T, Van Den Broek FJ, Naber AH, Van Soest E, Scholten P, Curvers WL, *et al*. Endoscopic Tri-modal Imaging (ETMI) for the detection and classification of early colorectal neoplasia: A multi-centre randomized controlled trial. Gastrointest Endosc 2010;71:AB142.
17. Rotondano G, Bianco MA, Sansone S, Prisco A, Meucci C, Garofano ML, *et al*. Clinical evaluation of endoscopic trimodal imaging for the detection and differentiation of colorectal adenomas. Digestive and Liver Disease 2010;42:S79.
18. Probst A, Bittinger M, Jechart G, Scheubel R, Messmann H. Usefulness of Autofluorescence Endoscopy (AF) and Narrow Band Imaging (NBI) in the Differentiation of Colonic Polyps. Gastrointest Endosc 2006;63:AB207-AB207.
19. Goelder SK, Arnholdt H, Messmann H, Probst A. Comparison of autofluorescence endoscopy (AF) and narrow band imaging (NBI) with indigocarmine chromoendoscopy (IC) in the differentiation of colonic polyps. Gastrointest Endosc 2007;65:AB274-AB274.
20. van den Broek FJ, Fockens P, van Eeden S, Reitsma JB, Hardwick JC, Stokkers PC, *et al*. Endoscopic tri-modal imaging for surveillance in ulcerative colitis: Randomised comparison of high-resolution endoscopy and autofluorescence imaging for neoplasia detection; and evaluation of narrow-band imaging for classification of lesions. Gut 2008;57:1083-9.
21. Boparai KS, van den Broek FJC, van Eeden S, Fockens P, Dekker E. Hyperplastic polyposis syndrome: A pilot study for the differentiation of polyps by using high-resolution endoscopy, autofluorescence imaging, and narrow-band imaging. Gastrointest Endosc 2009;70:947-955.
22. van den Broek FJ, Fockens P, Van Eeden S, Kara MA, Hardwick JC,

Reitsma JB, *et al*. Clinical evaluation of endoscopic trimodal imaging for the detection and differentiation of colonic polyps. Clin Gastroenterol Hepatol 2009;7:288-95.
23. Ignjatovic A, East JE, Guenther T, Hoare J, Morris J, Ragunath K, *et al*. What is the most reliable imaging modality for small colonic polyp characterization? Study of white-light, autofluorescence, and narrow-band imaging. Endoscopy 2011;43:94-9.
24. Kuiper T, Van Den Broek FJC, Naber AH, van Soest EJ, Scholten P, Mallant-Hent RCh, *et al*. Endoscopic trimodal imaging detects colonic neoplasia as well as standard video endoscopy. Gastroenterology 2011;140:1887-1894.
25. Sato R, Fujiya M, Watari J, Ueno N, Moriichi K, Kashima S, *et al*. The diagnostic accuracy of high-resolution endoscopy, autofluorescence imaging and narrow-band imaging for differentially diagnosing colon adenoma. Endoscopy 2011;43:862-8.
26. Matsuda T, Saito Y, Fu KI, Uraoka T, Kobayashi N, Nakajima T, *et al*. Does autofluorescence imaging videoendoscopy system improve the colonoscopic polyp detection rate?--A pilot study. Am J Gastroenterol 2008;103:1926-32.
27. Rastogi A, Early DS, Gupta N, Bansal A, Singh V, Ansstas M, *et al*. Randomized, controlled trial of standard-definition white-light, high-definition white-light, and narrow-band imaging colonoscopy for the detection of colon polyps and prediction of polyp histology. Gastrointest Endosc 2011;74:593-602.
28. Wu L, Li Y, Li Z, Cao Y, Gao F. Diagnostic accuracy of narrow-band imaging for the differentiation of neoplastic from non-neoplastic colorectal polyps: A meta-analysis. Colorectal Dis 2013;15:3-11.
29. Pasha SF, Leighton JA, Das A, Harrison ME, Gurudu SR, Ramirez FC, *et al*. Comparison of the yield and miss rate of narrow band imaging and white light endoscopy in patients undergoing screening or surveillance colonoscopy: A meta-analysis. Am J Gastroenterol 2012;107:363-70.
30. Curvers WL, Singh R, Song LM, Wolfsen HC, Ragunath K, Wang K, *et al*. Endoscopic tri-modal imaging for detection of early neoplasia in Barrett's oesophagus: A multi-centre feasibility study using high-resolution endoscopy, autofluorescence imaging and narrow band imaging incorporated in one endoscopy system. Gut 2008;57:167-72.
31. Kato M, Kaise M, Yonezawa J, Goda K, Toyoizumi H, Yoshimura N, *et al*. Trimodal imaging endoscopy may improve diagnostic accuracy of early gastric neoplasia: A feasibility study. Gastrointest Endosc 2009;70:899-906.
32. Kudo S, Rubio CA, Teixeira CR, Kashida H, Kogure E. Pit pattern in colorectal neoplasia: Endoscopic magnifying view. Endoscopy 2001;33:367-73.
33. Sano Y, Ikematsu H, Fu KI, Emura F, Katagiri A, Horimatsu T, *et al*. Meshed capillary vessels by use of narrow-band imaging for differential diagnosis of small colorectal polyps. Gastrointest Endosc 2009;69:278-83.