

Diagnostic accuracy of narrow-band imaging for the differentiation of neoplastic from non-neoplastic colorectal polyps: a meta-analysis

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Abstract

Aim Narrow-band imaging (NBI) is a novel imaging technology that makes the superficial vasculature of gastrointestinal mucosa visible. However, the real accuracy for the differentiation of neoplastic from non-neoplastic polyps by NBI for the colorectum is still unknown.

Method A meta-analysis was carried out of studies which assessed the precision of NBI in the diagnosis of colorectal neoplastic polyps. Searches included PubMed and Embase and two reviewers independently assessed their quality with a modified version of the QUADAS and STARD tools. The study pooled estimates of sensitivity, specificity, diagnostic odds ratio (DOR) and area under the curve (AUC).

Results There were 11 relevant original papers which fulfilled the inclusion criteria. The pooled sensitivity and specificity were 0.92 (95% CI 0.90–0.93) and 0.83 (95%

CI 0.81–0.86) respectively. The AUC for NBI was 0.95 [SE 0.01; DOR 53.72 (95% CI 35.66–80.92)]. The sensitivity and specificity were 0.92 (95% CI 0.90–0.94) and 0.81 (95% CI 0.78–0.84) with magnification, and 0.91 (95% CI 0.88–0.93) and 0.86 (95% CI 0.82–0.89) without magnification. For the mucosal pattern sensitivity and specificity were 0.90 (95% CI 0.85–0.94) and 0.88 (95% CI 0.82–0.93), and for vascular pattern intensity they were 0.92 (95% CI 0.90–0.94) and 0.88 (95% CI 0.83–0.91).

Conclusion Narrow-band imaging, with or without magnification, has a high diagnostic precision for colorectal neoplastic polyps using either vascular pattern intensity or mucosal pattern assessment as the measure.

Keywords Narrow-band imaging, NBI, colonoscopy, neoplastic lesions, meta-analysis

Introduction

Most colorectal cancers develop from an adenoma and its removal might decrease the incidence [1]. There is evidence that removal of colorectal adenomas may reduce the risk of colorectal cancer by 70–90% over 10 years [2]. If the diagnosis of the neoplastic polyps under colonoscopy is inaccurate, this will lead to additional unnecessary polypectomy in clinical practice, while having potential negative consequences to both the patients and society. For the patients, biopsy or polypectomy measurably increases procedural risk such as bleeding during a colonoscopy, which increases about 10-fold

with polyp resection [3]. From the societal perspective, removal of all lesions increases both the time and cost of colonoscopy. But with conventional video-endoscopy it is difficult to differentiate between neoplastic and non-neoplastic lesions and video-endoscopy still has the drawbacks of poor performance in some cases and of an adenoma miss rate of between 10% and 30% [4,5]. Therefore, narrow-band imaging (NBI) has been developed as a safer examination which can minimize polyp resection and enhance adenoma detection. It uses special narrow-band filters in the endoscopic system, which can increase the contrast between the epithelial surface and subjacent vascular pattern [6]. But the precision of NBI for detecting adenomas varied in previous studies, so we performed this meta-analysis to assess the precision of NBI as a predictor of adenomas and to define its precision with or without magnification.

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Method

Search strategy

Sources in PubMed and Embase were searched to identify published papers until 21 May 2010 for this meta-analysis. The papers were about NBI-based characterization to differentiate neoplastic from non-neoplastic colorectal polyps. The keywords were as follows: narrow-band imaging or NBI, polyps and colonoscopy. Two independent assessors (Z. M. Li and Y. Z. Li) reviewed the relevance of the citations. Further searches for additional relevant papers were done by reviewing the reference lists of all available primary studies, reviews and meta-analyses.

Eligibility criteria

To compare with conventional colonoscopy on histology prediction for colorectal polyps, the inclusion criteria were defined as original studies where (i) NBI was used to characterize colorectal polyps into neoplastic and non-neoplastic categories; (ii) histopathology was used as the reference standard; (iii) data on sensitivity and specificity could be extracted. The exclusion criteria were as follows: (i) data could not be extracted or reconstructed for 2×2 tables; (ii) depressed lesions were included in the data analysis; (iii) studies were especially about hyperplastic polyposis syndrome (HPS), hereditary nonpolyposis colorectal cancer (HNPCC), familial adenomatous polyposis (FAP), familial polyposis and non-polyposis syndrome; (iv) studies were reviews, case reports, editorials, commentaries or data reported as abstracts only. Study selection was done by both review authors (Z. M. Li and Y. Z. Li). Disagreements on study inclusion or exclusion were resolved through discussion or consensus with a third reviewer (L. C. Wu).

Data extraction and quality assessment

The following information was extracted from the studies: the first author, date of publication, study design (prospective or retrospective), place and period of the study, patient characteristics (number, age, sex), number of polyps assessed, polyp characteristics (anatomical site, pathology, morphology), use of magnification and/or high-definition-based measures of NBI to identify the dysplasia degree of the polyps [pit pattern or mucosal pattern (PP or MP), vascular pattern intensity (VPI), meshwork capillaries (MC), combination of the VPI and PP or MP] [7–10], information about the equipment, and number of endoscopists/observers. The polyps which were classified as hyperplastic, inflammatory, lym-

phoid follicles and normal mucosa were regarded as non-neoplastic polyps. Adenoma (tubulovillous adenoma, tubular adenoma and villous adenoma), adenocarcinoma and squamous cell carcinoma were regarded as neoplastic polyps (according to World Health Organization guidelines [11]). If NBI with and without magnification were both used in the study, the data were separately extracted for different subgroups. If there was more than one measure of NBI for characterizing colorectal polyps, the data were separately extracted according to the measure.

Furthermore, the quality of the studies was assessed using the guidelines published by the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) and the Standards of Reporting of Diagnostic Accuracy (STARD) [10,12]. Two assessors (Z. M. Li and Y. Z. Li) assessed the quality of the papers independently. Discrepancy during the assessment was resolved through consensus with a third reviewer (L. C. Wu).

Statistical analysis

This meta-analysis took sensitivity and specificity as the outcome measurements for assessing the diagnostic accuracy of NBI. To calculate the pooled diagnostic accuracy, the absolute numbers of true positives, true negatives, false positives and false negatives for each study were extracted to provide sensitivity and specificity with 95% confidence intervals [13,14]. The summary receiver operating characteristic (SROC) was calculated to present the optimization of the sensitivity and specificity. Both diagnostic odds ratio (DOR) and area under the ROC curve (AUC) were calculated to analyse the diagnostic precision of NBI [15]. A higher DOR suggests that the diagnostic precision of NBI is greater [16], whereas for AUC most clinical tests have a value between 0.5 and 1.0, with a better diagnostic precision correlating with an AUC closer to 1.0 [17].

The Q and I^2 statistic were calculated to assess the impact of heterogeneity on the results. This statistic which describes the percentage of the variability in effect estimates that it is due to heterogeneity rather than sampling error (chance). A value of $I^2 > 50\%$ may be considered substantial heterogeneity [18].

To investigate the possible sources of heterogeneity, data analysis was performed to assess the diagnostic accuracy in different groups. The subgroups analysed were the diagnostic precision for the use of NBI with or without magnification; and the differently based measures of the NBI to assess the polyps' dysplasia degree. All the statistical analyses were performed by using METADISC1.40 (Hospital Ramon Cajal and Universidad Complutense de Madrid, Spain).

Results

Literature search and study selection

After scanning the papers by title and abstract, 37 papers in all remained to be screened for the full text. By reading the full text carefully, we excluded nine papers which were without enough data on sensitivity and specificity for the dysplasia characterization of polyps with NBI; three papers which were only concerned with neoplasm; four papers about FAP or HNPCC and the detection rate of the adenoma; one case report; four papers with different classification of the lesions or a special method which may affect the facticity of the result; one paper containing suspicious data; and two papers that included a personal history of adenomas/cancer or a positive family history of colorectal cancer. There was discrepancy about the dysplasia degree of sessile serrated adenoma (SSA), and the two papers which included SSA were not included at first. In the end, 11 eligible studies were included for the meta-analysis (Table 1). The procedure of the study selection is shown in Fig. 1.

Characteristics of the included studies

Table 1 shows the characteristics of the 11 included studies. The total number of patients was 822; they had 1351 polyps assessed with NBI and compared with histopathology. The histopathology of the polyps included adenoma (tubulovillous adenoma, tubular adenoma, villous adenoma), adenocarcinoma, squamous cell carcinoma, hyperplastic, inflammatory, lymphoid follicles and normal mucosa. The polyps were classified as 0-Is, 0-Ip, 0-Iia, 0-Iib, 0-Iic, 0-Iia Iic, 0-IIa Is, 1, 3 on morphology according to the Paris classification [11]. All but one of the studies was prospective. The included studies were assessed to a high quality accord-

ing to the QUADAS and STARD. The QUADAS score was ≥ 11 for all of the included studies. The STARD score was ≥ 18 for all but one (STARD score 16) of the included studies [19].

Among the 11 studies, six studies used NBI with high magnification [7,19–23], and four studies used low magnification or did not use magnification [24–27]. One study discussed the use of NBI with magnification and without magnification [28], where data extraction was performed separately as different subgroups according to the use of magnification or not. In six studies the dysplasia degree was assessed based on VPI [19,20,22,23,27,28], in three studies it was based on PP or MP [19,22,26], in three further studies it was based on MC [7,21,24], and in three studies a combination of VPI with PP or MP was used [22,23,25]. Some of the studies discussed more than one measure of NBI to assess the dysplasia degree and included different groups of data for each measure [19,22,23]. The data extraction for these studies was performed separately according to the different measures. Different sets of data were extracted according to different interpreters and levels of experience and the studies' images were assessed by different interpreters with different levels of experience [19,21,25–27]. Table 2 shows the extracted data of the 11 studies.

Results of the accuracy analyses

Figure 2 shows the summary of overall sensitivity and specificity of NBI for diagnosing neoplasia. The results show a high diagnostic accuracy with the pooled sensitivity, specificity and DOR being 0.92 (95% CI 0.90–0.93), 0.83 (95% CI 0.81–0.86) and 53.72 (95% CI 35.66–80.92) respectively. Heterogeneity was not observed among the studies for sensitivity (Cochran Q test = 37.33, df = 27, I^2 = 27.7%), but was present for specificity (Q test = 70.41, df = 27, I^2 = 61.7%) and

Table 1 Characteristics of the included studies.

First author	Study style	No. of patients	M/F	Average age (year)	No. of polyps	Reference standard	QUADAS / STARD	Reference no.
Henry (2010)	Retrospective	52	33/19	59.5	126	Histology	13/20	24
Tischendorf (2010)	Prospective	128	–	–	209	Histology	12/19	20
Tischendorf (2009)	Prospective	131	92/39	64.7	200	Histology	14/22	28
Chang (2009)	Prospective	104	64/40	55.8 $\pm$ 12.3	163	Histology	13/19	21
Rastogi (2009)	Prospective	40	40/0	62 $\pm$ 9.5	65	Histology	12/18	25
Sano (2008)	Prospective	92	76/16	63.6	150	Histology	14/19	7
East (2008)	Prospective	62	24/38	46	116	Histology	14/22	22
Sikka (2008)	Prospective	63	25/38	60.3	80	Histology	12/22	26
Tischendorf (2007)	Prospective	52	–	–	100	Histology	13/19	23
East (2007)	Prospective	20	–	–	32	Histology	11/16	19
Su (2006)	Prospective	78	42/36	51.3	110	Histology	13/21	27

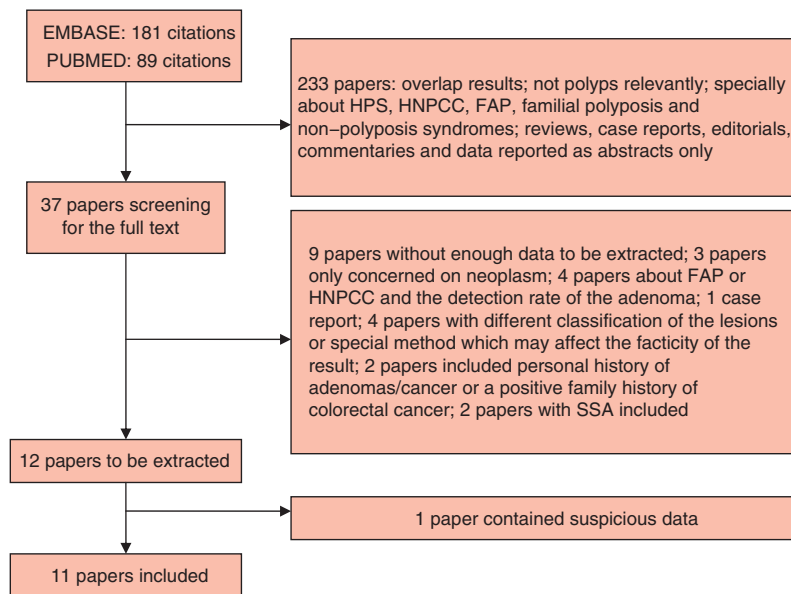


Figure 1 The procedure of study selection.

DOR (Cochran Q test = 63.57, $df = 27$, $I^2 = 57.5\%$). The forest plots of these results are presented in Fig. 2 and the corresponding ROC plot with SROC is displayed in Fig. 3. The AUC under the SROC was 0.95 (SE = 0.01), with $Q^* = 0.89$, which also indicated a high level of accuracy.

Table 3 shows the pooled sensitivity, specificity, DOR and AUC for the two subgroups of NBI with or without magnification. The sensitivity, specificity, DOR and AUC of NBI endoscopies with magnification were 0.92 (95% CI 0.90–0.94, $I^2 = 38.8\%$), 0.81 (95% CI 0.78–0.84, $I^2 = 76.4\%$), 50.35 (95% CI 25.79–98.27, $I^2 = 69.3\%$) and 0.95 (SE = 0.02) respectively. For the NBI endoscopies without magnification, the sensitivity, specificity, DOR and AUC were 0.91 (95% CI 0.88–0.93, $I^2 = 10.3\%$), 0.86 (95% CI 0.82–0.89, $I^2 = 0.0\%$), 55.74 (95% CI 34.13–91.03, $I^2 = 38.3\%$) and 0.94 (SE = 0.02). The results indicated a similar diagnostic precision for NBI endoscopies with and without magnification.

The pooled accuracy for different measures of NBI to identify dysplasia was also calculated. Sensitivity and specificity of the NBI diagnosis of dysplasia based on MP [Se = 0.90 (95% CI 0.85–0.94), Sp = 0.88 (95% CI 0.82–0.93)] were similar to those based on VPI [Se = 0.92 (95% CI 0.90–0.94); Sp = 0.88 (95% CI 0.83–0.91)]. When compared with each method alone, a combination of VPI- and MP-based measures to indicate neoplasia had similar sensitivity (0.90, 95% CI 0.86–0.92) and small decreased specificity (0.83, 95% CI 0.79–0.87). However, by using the MC measures, the sensitivity (0.94, 95% CI 0.91–0.96) was improved compared with each method alone or combined, at the cost of a small decrease in specificity (0.75, 95% CI 0.69–0.80).

Discussion

Narrow-band imaging is a novel imaging technology that makes the superficial vasculature of gastrointestinal mucosa visible [29]. This feature is potentially advantageous to provide useful information about the process of tumourigenesis [30]. In this meta-analysis, a high level of diagnostic precision was achieved for NBI-based characterization of the dysplasia degree of colorectal polyps. The overall sensitivity of NBI for diagnosing neoplastic polyps was 0.92 (95% CI 0.90–0.93) with an overall specificity of 0.83 (95% CI 0.81–0.86). Similarly, the pooled accuracy for NBI assessing dysplasia degree of the polyps based on VPI was not much higher than with NBI based on MP. For the MC measures, the sensitivity was improved compared with VPI or MP alone, but at the cost of a small decrease in specificity. The overall DOR for each subgroup (range 40.19–86.02) indicated a high diagnostic precision with a high AUC range from 0.88 to 0.99. Although there was significant heterogeneity among the studies, the present results suggest that NBI is a promising method to differentiate neoplastic from non-neoplastic colorectal polyps, which may help avoid additional unnecessary polypectomy and increase the detection rate of colorectal cancer. Compared with white-light colonoscopy, studies by Chang *et al.* [21], Sikka *et al.* [26], Tischendorf *et al.* [23] and Su *et al.* [27] confirmed its diagnostic performance was significantly higher.

Subgroup analysis did not find a difference in diagnostic performance between NBI endoscopies with and without magnification. To get a much clearer image, magnification was used in most of the studies.

Table 2 Technical features.

Use of magnification	Measure of NBI*	First writer	Interpreter of the images	No. neoplastic	No. non-neoplastic
With MAG	VPI	Tischendorf (2010)	Two persons	160	49
		Tischendorf (2009)	Two persons	63	37
		East (2008)	Three persons	50	66
		Tischendorf (2007)	Two persons	63	37
		East (2007)	European trained	21	11
	Kudo pit pattern		Japanese trained	21	11
		East (2008)	Three persons	50	66
		East (2007)	European trained	21	11
	Kudo pit pattern + VPI		Japanese trained	21	11
		East (2008)	Three persons	50	66
		Tischendorf (2007)	Two persons	63	37
	MC	Chang (2009)	Trainee	82	81
			Experienced	82	81
		Sano (2009)	One person	111	39
Without MAG	MC	Henry (2010)	One person	67	59
	VPI	Tischendorf (2009)	Two persons	58	42
		Su (2006)	Reader 1	70	40
			Reader 2	70	40
	VPI + MP	Rastogi (2009)	One experienced	38	27
			One after 2 months	38	27
			Two less experienced	38	27
			Two after 2 months	38	27
			Three experienced	38	27
			Three after 2 months	38	27
			Four less experienced	38	27
			Four after 2 months	38	27
	PP	Sikka (2008)	Reader 1	49	31
			Reader 2	49	31

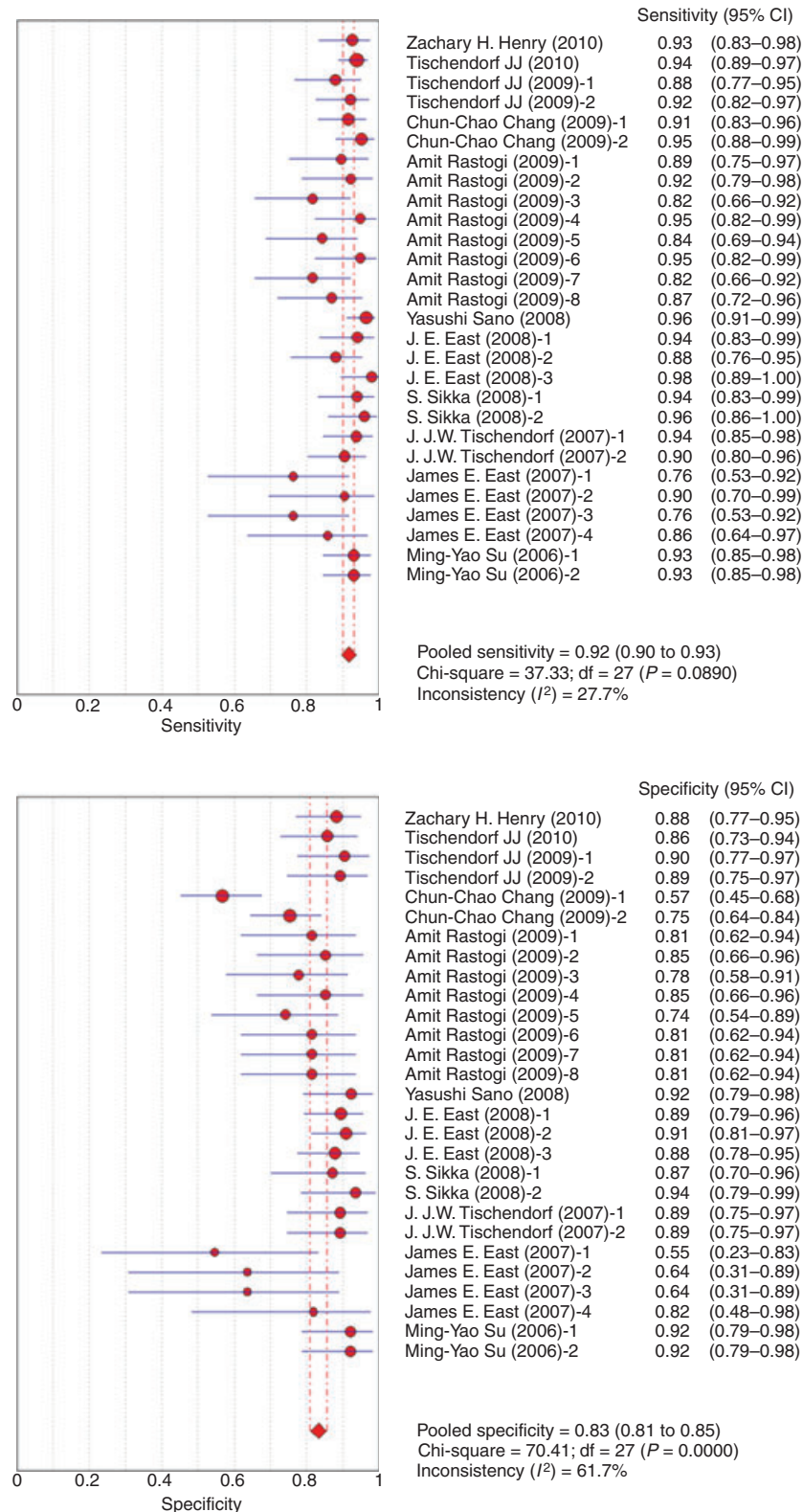
*Measure of NBI: VPI, vascular pattern intensity [16]; PP, pit pattern; MP, mucosal pattern [13,14]; MC, meshwork capillaries [15]. MAG, magnifying.

Usually magnification ranged from 100- to 150-fold; low magnifying by 10- to 15-fold was not considered magnification. More polyps were detected by the magnifying NBI compared with without magnification, which may affect the result but to what extent is unclear. This is consistent with a previous study in which meta-regression indicated no significant difference between NBI with or without magnification [15].

Another subgroup analysis was about the assessment measures of NBI to define the dysplasia degree of colorectal polyps. The present study shows similar accuracy between the VPI- and MP-based measures, with not much change when the two measures were combined. In the study of East *et al.*, [19] the results indicated that the PP measure was not always identical for the same diminutive polyp viewed with NBI. Compared with the chromoendoscopic PP in their study, VPI, which showed a simple colour change of the neoplasia and required less magnification than PP

or ‘meshed capillary vessels’, was more accurately diagnosed [19]. It indicated that NBI can achieve better sensitivity with the MC measure, but obvious heterogeneity was detected between studies. Further analysis could not be carried out due to insufficient data. The change with the MC-based measure may suggest a new approach to improve the diagnostic accuracy of NBI [24]. More studies concerning NBI with MC-based measures should be performed in the future.

As the dysplasia degree of sessile serrated polyps (SSPs) or SSAs is still disputed at present, studies [31–35] that included SSPs or SSAs were not included in this meta-analysis at first. But emerging evidence suggests that SSPs or SSAs have malignant potential [36]. So if studies [33,34] in which SSPs or SSAs are treated as ‘adenoma’ are included in this meta-analysis, the overall sensitivity and specificity of NBI for neoplasia are 0.92 (95% CI 0.91–0.93) and 0.84 (95% CI 0.82–0.86).

**Figure 2** Sensitivity and specificity of NBI for characterization of neoplasia.

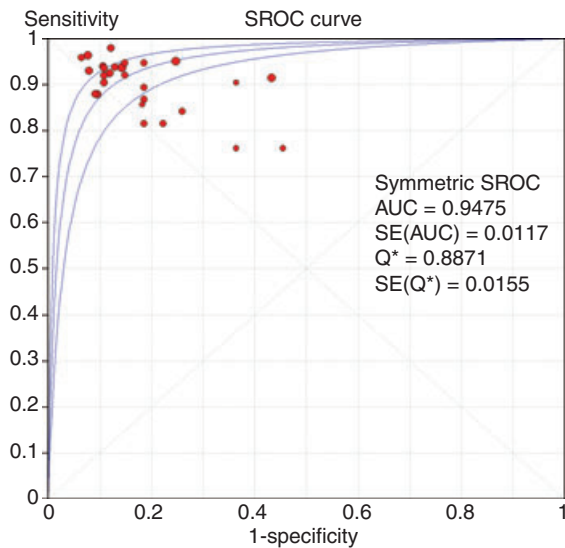


Figure 3 SROC curve of the diagnostic precision of NBI for characterization of neoplasia.

The effect of a learning curve was not formally evaluated because of insufficient data, but according to Rastogi *et al.* a learning curve of NBI exists [21,25,35]. In the study of Rastogi *et al.*, [25] no significant difference in κ values was observed for experienced *vs* less experienced endoscopists for either the surface patterns ($\kappa = 0.52$ *vs* 0.61) or the prediction of polyp type ($\kappa = 0.62$ *vs* 0.66). The study of Chang *et al.* [21] showed that the κ values of interobserver agreement for experienced endoscopists using conventional white-light colonoscopy was 0.77 and for magnifying NBI was 0.80. All these studies showed that NBI produced images of

sufficient contrast to enable both experienced and inexperienced readers to predict dysplasia degrees with similar capacity [26]. Thus, compared with white light, a shorter learning curve in predicting adenoma can be achieved when using NBI [26]. But the precise learning curve and the effects of training on NBI still need further evaluation.

Stratified analyses were not done in this analysis. All colorectal polyps were just categorized as ‘any polyp’, i.e. a report of any polyp found, regardless of size. The analysis did not analyse the influence of the diameter of the polyps on the overall accuracy. Therefore, future large multicentre randomized studies should address whether the polyps diameter has an impact on the accuracy of NBI [37,38].

Significant heterogeneity was observed in this meta-analysis. This could be due to many aspects such as the random variation between studies, the variation of study characteristics, and the variation in the diagnostic threshold required for a positive test result and so on. The different systems of NBI may also cause heterogeneity as a previous study had indicated [15]. In this review, only two studies used the NBI system of Excera II, while the other studies used the NBI system of Lucera [20,24]. Whether different NBI systems and their technical characteristics affect the diagnostic accuracy was not further investigated in this meta-analysis.

The meta-analysis has some limitations. First, all the studies were performed in adults who were candidates for colonoscopy; therefore, uncertainty remains regarding its application in children. Further studies are necessary to expound its potential for this group of patients. Second,

Table 3 Pooled sensitivity, specificity and diagnostic odds ratio of NBI in the diagnosis of cancer/dysplasia.

Pooled analysis	No. of polyps detected/total	No. of studies	Sensitivity (95% CI)	HG (I^2) %	Specificity (95% CI)	HG (I^2) %	DOR (95% CI)	HG (I^2) %	AUC (SE)
Overall analysis	1351	11	0.92 (0.90–0.93)	27.7	0.83 (0.81–0.86)	61.7	53.72 (35.66–80.92)	57.5	0.95 (0.01)
With MAG	870	7	0.92 (0.90–0.94)	38.8	0.81 (0.78–0.84)	76.4	50.35 (25.79–98.27)	69.3	0.95 (0.02)
Without MAG	481	5	0.91 (0.88–0.93)	10.3	0.86 (0.82–0.89)	0.0	55.74 (34.13–91.03)	38.3	0.94 (0.02)
QUAD $\geq$ 11	1351	11	0.92 (0.90–0.93)	27.7	0.83 (0.81–0.86)	61.7	53.72 (35.66–80.92)	57.5	0.95 (0.01)
STARD $\geq$ 18	1319	10	0.92 (0.91–0.94)	14.2	0.84 (0.82–0.86)	61.8	66.43 (45.43–97.14)	45.8	0.95 (0.01)
VPI	667	6	0.92 (0.90–0.94)	0.0	0.88 (0.83–0.91)	42.5	66.81 (31.86–140.09)	59.4	0.97 (0.01)
PP/MP	228	3	0.90 (0.85–0.94)	45.0	0.88 (0.82–0.93)	36.9	50.69 (14.08–182.53)	67.8	0.94 (0.04)
VPI + PP/MP	281	3	0.90 (0.86–0.92)	36.2	0.83 (0.79–0.87)	0.0	40.19 (22.92–70.49)	32.7	0.88 (0.03)
MC	439	3	0.94 (0.91–0.96)	0.0	0.75 (0.69–0.80)	88.9	64.24 (17.98–229.44)	79.2	0.99 (0.01)

HG, study heterogeneity (I^2); MAG, magnifying.

analysis by polyp size was not performed, and future studies should definitely report this parameter so that whether the polyp size affects its diagnostic performance can be evaluated. Third, the hierarchical structure of the data was not taken into account in the meta-analysis due to the drawback of SROC analysis, such as patient-level and cluster-level covariates of interest (clinical information for patients, experiences and training of endoscopists, and institutional characteristics of hospitals).

In conclusion, NBI, with or without magnification, has a high diagnostic precision for colorectal neoplastic polyps, using either VPI- or MP-based assessment measures of the polyps. NBI is a promising method for differentiating neoplastic from non-neoplastic colorectal polyps, which may help avoid additional and unnecessary polypectomy and increase the detection rate of colorectal cancer.

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Editor's choice

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The field of endoscopy has evolved in recent years to become almost self-contained in terms of diagnosis, treatment and even microscopic assessment of colorectal polyps. Technical development of endoscopic equipment, making endoscopic mucosal and sub-mucosal dissection possible, has been phenomenal. But all new toys need to be assessed in light of their clinical, and ultimately health-economical, value. In this meta-analysis Wu *et al.* studied the accuracy of NBI to differentiate neoplastic from non-neoplastic disease. Some 11 studies that analysed 1351 polyps were included and it was found that NBI, with or

without magnification, had a sensitivity of 0.92, a specificity of 0.83 and an area under the curve of 0.95. We have entered the era of colorectal screening and we will be picking up a significant number of non-neoplastic polyps. The present findings may help endoscopists to select polyps for excision and histological examination. This would reduce cost and, more importantly, polypectomy associated morbidity.

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