The Impact of Narrow Band Imaging in Screening Colonoscopy: A Randomized Controlled Trial

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BACKGROUND & AIMS: Narrow band imaging (NBI) is an imaging technique that allows a better definition of capillary pattern and improves the contrast between adenomas and the surrounding mucosa. Conflicting data exist on the ability of NBI to improve detection of colonic neoplasm; the impact of NBI is being tested in several screening scenarios. We evaluated whether the routine use of NBI, compared with white light (WL), during the withdrawal phase of screening colonoscopy improved adenoma detection. METHODS: This randomized controlled study included consecutive 50- to 69-year-old patients with positive immunologic fecal occult blood tests. They were randomly assigned to groups that were examined with WL (n = 108) or NBI (n = 103) during the withdrawal phase of their colonoscopies. The primary end point was the adenoma detection rate. The prevalence of non-polypoid and the total number of adenomas were also evaluated. RESULTS: The number of total and mean per-patient adenomas were 201 (1.95 ± 2.3) and 198 (1.83 ± 2.1) in the NBI and WL groups, respectively (P = .69). The adenoma detection rates were 57.3% for patients examined by NBI and 58.3% for those examined by WL (P = .88). A total of 41 non-polypoid adenomas were identified (26 in the NBI and 15 in the WL groups, P = .16). The flat adenoma detection rates were 21.4% and 9.3% in the NBI and WL groups, respectively (P = .019). CONCLUSIONS: The routine use of NBI in screening colonoscopy did not increase the adenoma detection rate. NBI seems to improve the detection of flat adenomas, although additional studies are necessary.

Because missed lesions are the probable contributors to the development of most interval cancers after a putatively clearing colonoscopy, in the last few years many efforts have been made to maximize the sensitivity of the examination. Besides implementing continuous quality improvement in colonoscopy practice to optimize the technique and to reduce variations among endoscopists in adenoma detection,12,13 new technologies have been developed to enhance the visualization of colonic mucosa14–19 and better highlight flat lesions.20,21 In particular, pancolonic-chromoendoscopy has been shown to increase the adenoma detection in randomized trials and to be useful in differentiating neoplastic from non-neoplastic lesions.22–24 However, this technique is time-consuming because of both the dye spraying and observation, and therefore it is unsuitable for routine application.25

Narrow band imaging (NBI) is a new optical technology that, by means of optical interference filters that spectrally narrow the bandwidths used in conventional white light (WL) videocolonoscopy, improves the definition of the epithelial surface and emphasizes the contrast of mucosal microvessels, which appear as dark brownish structures (virtual chromoscopy).26 Because of the density and shape of microvessels in neoplasia, NBI might potentially improve the identification of adenomas, which usually appear darker than normal mucosa. This is obtained by simply pressing an “on/off” button on the head of the endoscope that switches the optical filter to change from conventional imaging to NBI.

The actual role of NBI in enhancing the detection of colonic neoplastic lesions is still controversial. Conflicting data from published randomized controlled trials27–29 might partially be explained by differences in the adenoma prevalence among the studies as a result of the heterogeneity of study populations. Furthermore, the role of NBI in screening colonoscopy is still under investigation.

In a randomized controlled trial we tested the hypothesis that in a homogeneous population of average-risk CRC subjects with positive fecal occult blood test (FOBT) undergoing colonoscopy screening, the routine use of NBI during instru-

Abbreviations used in this paper: CRC, colorectal cancer; FOBT, fecal occult blood test; HD, high definition; NBI, narrow band imaging; SD, standard deviation; WL, white light.

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1542-3565/09/$36.00
doi:10.1016/j.cgh.2009.06.028
ment withdrawal could improve adenoma detection as compared with standard WL examination.

Materials and Methods

The study was conducted in a community-based hospital. The protocol was approved by the Ethics Committee; written and informed consent was obtained from all the patients enrolled in the study.

Study Population

All consecutive 50- to 69-year-old asymptomatic subjects at average risk of CRC with positive immunologic FOBT participating in a national mass-screening program and referred to our Gastroenterology Unit for outpatient colonoscopy between November 2007 and April 2008 were considered eligible. Patients taking anticoagulants that precluded removal of polyps during colonoscopy and those undergoing incomplete procedure for inadequate bowel cleansing (as detailed below) or failure to reach the cecum were excluded from randomization. Patients who refused to participate or were unable to provide informed consent to the study were also excluded.

Study Procedure

Procedures were performed with conscious sedation (intravenous midazolam plus meperidine) by a total of 6 board-certified gastroenterologists. Four of them were highly experienced (each one of them with more than 5000 colonoscopies performed and a polyp detection rate in routine procedures greater than 25%), whereas the other 2 had a much more limited practice and were considered as being still in training (less than 300 previous colonoscopies). For all the study procedures, high-resolution wide-angle (170 degrees) adult video-colonoscopes with push button switch from WL to NBI (Olympus HD 180 series; Olympus Corp, Hamburg, Germany) were used. NBI-equipped colonoscopes had been available for 3 months before starting the study, so that each examiner had the opportunity to carry out specific training to become acquainted with the technique by performing at least 20 NBIs in presence of a tutor (F.R.) with a particular expertise in the NBI technology.

The scope was inserted to the cecum by using WL modality (intravenous midazolam plus meperidine) by a total of 6 board-certified gastroenterologists. Four of them were highly experienced (each one of them with more than 5000 colonoscopies performed and a polyp detection rate in routine procedures greater than 25%), whereas the other 2 had a much more limited practice and were considered as being still in training (less than 300 previous colonoscopies). For all the study procedures, high-resolution wide-angle (170 degrees) adult video-colonoscopes with push button switch from WL to NBI (Olympus HD 180 series; Olympus Corp, Hamburg, Germany) were used. NBI-equipped colonoscopes had been available for 3 months before starting the study, so that each examiner had the opportunity to carry out specific training to become acquainted with the technique by performing at least 20 NBIs in presence of a tutor (F.R.) with a particular expertise in the NBI technology.

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derived from our regional screening database, which had shown a 51.4% adenoma detection rate in 2005–2006 in patients with FOBT positivity (www.sanita.regione.lombardia.it/pubblicazioni/scree_carcinoma_colrettale_20052006.pdf; accessed on October 27, 2008).

For statistical analysis, data were entered into a statistical software program (Intercooled Stata; Stata Corp, College Station, TX). Student t test and Fisher exact test were used to compare means and proportions, respectively. For the purposes of the analysis, examiners were dichotomized in 2 groups (experts and trainees), according to their endoscopy expertise, as detailed above. For all tests, a P value of less than .05 was considered statistically significant.

Results

Between November 2007 and April 2008, 222 subjects (male, 54.4%), with a mean age of 60 years (standard deviation [SD], 5.5), were evaluated. Two subjects were considered not eligible for the study as a result of ongoing anticoagulation, and 9 were excluded from randomization as a result of inadequate bowel cleansing. No patients were excluded as a result of failure to reach the cecum. A total of 211 subjects were randomized; 103 were allocated to NBI and 108 to WL examination, respectively. Both study arms were well-balanced as concerns demographics and baseline data, as detailed in Table 1. A total of 399 adenomas were detected in the study population, 205 (51%) of which were classified as advanced adenomas. When considering the morphology, 358 (89%) were classified as polypoid, and the other 41 (11%) were classified as flat or depressed lesions. Overall, 175 of 358 (49%) and 10 of 41 (24%) polypoid and non-polypoid adenomas, respectively, were identified in the insertion phase. High-grade dysplasia was found in 13.1% (47/358) polypoid lesions and in 26.8% (11/41) flat/depressed ones (P = .018). An invasive cancer was diagnosed in 13 (6.2%) patients, 6 in the NBI and 7 in the WL arms.

No perforation or major bleeding occurred in both study arms.

Per-Patient Analysis

Sixty-three and 59 subjects in the WL and NBI arms, respectively, had at least 1 adenoma. Corresponding figures for advanced adenomas were 45 and 49 subjects, respectively. No statistically significant differences were observed between the 2 arms in regard to either the percentage of patients with ≥1 adenomas (57.3% in the NBI and 58.3% in the WL arms; P = .88) or ≥1 advanced adenomas (47.6% and 41.7%, respectively; P = .39). On the other hand, 10 subjects in the WL arm and 22 in the NBI arm had 1 or more flat or depressed adenomas. The proportion of patients with at least 1 flat adenoma was significantly higher in the NBI group as compared with the WL group (21.4% vs 9.3%, P = .019) (Figure 1). No significant differences were observed between experts and trainees in regard to the detection rates of total and flat adenomas in both the NBI and WL arms, as detailed in Table 2.

Per-Polyp Analysis

A total of 198 and 201 adenomas were found in WL and NBI groups, respectively. The mean (SD) number of adenomas per patient was 1.83 (SD, 2.1) in the WL arm and 1.95 (SD, 2.3) in the NBI arm (P = .69). Furthermore, no significant differences were observed between the 2 groups in regard to the number of advanced (WL, 0.99 [1.3] vs NBI, 0.95 [1.2]; P = .82), diminutive (WL, 0.81 [1.1] vs NBI, 0.76 [1.0]; P = .73), and flat/depressed adenomas (WL, 0.14 [0.5] vs NBI, 0.25 [0.7]; P = .16) (Table 3).

Discussion

This randomized controlled trial carried out in a homogeneous population of FOBT-positive subjects undergoing screening colonoscopy failed to demonstrate the hypothesis that the routine use of NBI during instrument withdrawal might improve the adenoma detection. We did not find any substantial difference between the 2 arms as regards either the adenoma detection rate or the total number of adenomas. This finding does not validate the results from a recent Japanese randomized controlled trial by Inoue et al,27 in which the use of NBI resulted in a higher total number of adenomas detected, including significantly more diminutive adenomas. Conversely, our data substantially confirm those reported in 2 randomized studies from Germany28 and the United States,29 in which no statistically significant differences in adenoma detection have been reported with the use of NBI.

The high rates of adenomas in this screening population (58.3% in the WL and 57.3% in the NBI group), only comparable

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Table 1. Demographics and Baseline Data of the Procedures in Both Arms

<table>
<thead>
<tr>
<th></th>
<th>HD-WL</th>
<th>HD-NBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>108</td>
<td>103</td>
</tr>
<tr>
<td>Male sex, no. (%)</td>
<td>61 (56.5)</td>
<td>56 (54.3)</td>
</tr>
<tr>
<td>Age, y(a)</td>
<td>61.1 (5.8)</td>
<td>59.6 (5.3)</td>
</tr>
<tr>
<td>Time to cecum, min(b)</td>
<td>6.8 (3.8)</td>
<td>6.0 (3.4)</td>
</tr>
<tr>
<td>Time for withdrawal, min(b)</td>
<td>11.5 (3.7)</td>
<td>11.5 (3.7)</td>
</tr>
<tr>
<td>Quality of bowel cleansing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent, no. (%)</td>
<td>53 (49.1)</td>
<td>48 (46.6)</td>
</tr>
<tr>
<td>Good, no. (%)</td>
<td>48 (44.5)</td>
<td>46 (44.7)</td>
</tr>
<tr>
<td>Sufficient, no. (%)</td>
<td>7 (6.4)</td>
<td>9 (8.7)</td>
</tr>
<tr>
<td>Endoscopists’ expertise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experts, no. (%)</td>
<td>68 (63)</td>
<td>68 (66)</td>
</tr>
<tr>
<td>Trainees, no. (%)</td>
<td>40 (37)</td>
<td>35 (34)</td>
</tr>
</tbody>
</table>

\(a\)Expressed as mean value (SD).

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Figure 1. Prevalence of adenomas, according to the study arm.
to those reported in a recent study in which all the procedures were performed by a single highly experienced endoscopist by using high-definition (HD) colonoscopies,29 are the highest ever reported in colonoscopy studies. It might be argued that the high rates of adenomas in the study are mainly related to a referral bias of patients, selected on the basis of positive FOBT and not referred to colonoscopy as primary screening tool. However, recent data from a French regional FOBT-based colorectal cancer screening program reported a prevalence rate of overall adenomas of 33.1%, which is much lower than that observed in our study.33 Because we could not demonstrate any objective benefit of NBI in adenoma detection, it might be hypothesized that the high prevalence rates of adenomas found in our study might be the result of HD imaging provided by the last generation videendoscopes we used in the trial. However, in a recent randomized controlled trial by Pellisé et al20 aimed at comparing the performance of HD wide-angle colonoscopy versus a standard one for the detection of neoplasia in a large cohort of patients undergoing examination for various indications, the use of HD endoscopy did not result in a higher detection of adenomas than standard endoscopy. In summary, if we look at our results and those from the above mentioned Western studies evaluating the impact of either NBI or HD endoscopy on the diagnosis of colorectal neoplasia,20,28,29 we can conclude that so far, colonoscopy performance is probably more influenced by the quality of the examination and the adoption of continuous quality improvement programs in the daily practice13 than by technology progress. However, it is worth noting that, regardless of the results obtained, technology improvement and studies evaluating its impact on clinical practice are useful to increase cultural growth of the endoscopists and to sensitize them toward the detection of subtle mucosal changes, also when performing traditional WL colonoscopy. Moreover, the high adenoma detection rate might partially depend on the very high proportion (>90%) of patients with excellent–good bowel cleansing, which is a factor potentially affecting diagnostic sensitivity of colonoscopy for adenomas, independent of technological improvements applied.

With regard to non-polypoid (flat and depressed) neoplasms, our study provided interesting findings. First, the study showed that non-polypoid neoplasms of the colon are relatively common in Western asymptomatic, average-risk positive FOBT subjects undergoing screening colonoscopy. One in 7 subjects was found to have at least 1 non-polypoid lesion, which represented 11% of the total adenomas. The prevalence rate of non-polypoid neoplasms described in our study is almost 3-fold greater than that reported by Soetikno et al11 in a cohort of 616 asymptomatic patients undergoing screening examinations. Nevertheless, in this study, flat and depressed adenomas represented 11% of the total adenomas, consistent with our results. The higher prevalence of non-polypoid lesions found compared with that reported above11 might likely be explained by the higher prevalence rate of total adenomas in our screening population, selected for colonoscopy according to FOBT result, and not invited to the procedure as a primary screening option.

In contrast with Rex and Helbig,29 our study seems to support a potential role of NBI in improving the detection of flat and depressed lesions. The technique was able to identify a statistically significant higher proportion of patients with at least 1 non-polypoid adenoma (21.4% in the NBI arm vs 9.3% in the WL arm), with a positive trend also on the total number of flat adenomas diagnosed. The study was not set up and powered to test a potential benefit of NBI in detecting non-polypoid adenomas, which are much less common than the polypoid ones. These findings could suggest the opportunity for new larger studies focused and powered on flat lesions as primary end point. The potential benefit of NBI in detecting flat and depressed adenomas might have important clinical implications, especially in a screening scenario. Our data, in line with the literature,9–11 confirmed that these lesions harbor a higher incidence of advanced histopathology, thus having a more ag-

Table 2. Prevalences of Adenomas and Flat Lesions, According to Endoscopist’s Expertise, in Each Study Arm

<table>
<thead>
<tr>
<th></th>
<th>HD-WL</th>
<th></th>
<th>P value</th>
<th>HD-NBI</th>
<th></th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients evaluated</td>
<td>68</td>
<td>40</td>
<td>.87</td>
<td>68</td>
<td>35</td>
<td>.76</td>
</tr>
<tr>
<td>No. patients with ≥ 1 adenomas (%)</td>
<td>38 (55.8)</td>
<td>23 (57.5)</td>
<td>.87</td>
<td>41 (60.2)</td>
<td>20 (57.1)</td>
<td>.76</td>
</tr>
<tr>
<td>No. patients with 1 flat adenoma (%)</td>
<td>7 (10.2)</td>
<td>3 (7.5)</td>
<td>.62</td>
<td>15 (22.1)</td>
<td>7 (20)</td>
<td>.81</td>
</tr>
</tbody>
</table>

Figure 2. Flat adenoma under WL (A) and NBI (B).
gressive biologic behavior than the protruding adenomas. Non-polypoid neoplasms are surely a contributor to the imperfect cancer sensitivity of colonoscopy, and the enhancement of their detection is crucial to improve the effectiveness of colonoscopy screening programs (Figure 2).

Some methodologic issues of our study need to be discussed. First, all subjects were referred to colonoscopy for positive FOBT finding on a screening program, thus creating a highly homogeneous population, secondarily randomized in the 2 groups. The inclusion in the study of patients referred to colonoscopy for heterogeneous indications might create unbalanced prevalence of adenomas or cancer risk between the subgroups obtained by blind randomization. Second, 6 endoscopists with different expertise participated in the study. This gave us the chance to evaluate whether NBI might reduce the variation in adenoma detection among differently experienced examiners. We dichotomized the examiners in 2 groups (experts and trainees), but no significant differences between them in regard to both the total and flat adenoma detection rates within the NBI and WL arms were observed. As a consequence, the hypothesis that less experienced endoscopists could primarily benefit from this technique cannot be supported by the results of the present study. Conversely, NBI was able to improve flat adenoma detection rate for both experts and trainees, independent of the endoscopists’ expertise.

Potential study limitations concern the study design. First, it might be argued that a tandem colonoscopy study could be preferred to simple randomization to compare diagnostic performances of NBI and WL, as recently published. The study considered a second “back to back” colonoscopy with standard WL as the reference standard to evaluate the adenoma detection rates for NBI and WL, concluding that NBI did not improve either the adenoma detection or miss rates. However, our study was designed to reproduce a “realistic screening colonoscopy scenario” and to evaluate whether the use of NBI during instrument withdrawal might be really clinically useful for the patients, allowing for a diagnosis of more adenomas. Second, we did not randomize the insertion phase of the exam, in which actually some adenomas were detected, despite no attempt in the systematic evaluation of colonic mucosa being made. Thus, it might be argued that the NBI procedure was contaminated by WL polyp visualization during insertion. However, as regards polypoid lesions, all adenomas detected during insertion by WL were then identified by NBI. Therefore, it is unlikely that the use of WL in the insertion phase might have substantially improved the adenoma detection in the NBI arm. With regard to non-polypoid adenomas, most of them (76%) were identified, as expected as a result of their characteristics, in the withdrawal phase of the procedure. This makes it unlikely that the additional benefit of NBI in this subset might be attributed to the adenoma detection during the insertion phase.

In conclusion, in our study the routine use of NBI did not increase the adenoma detection rate in colonoscopy screening. In this setting, the prevalence of non-polypoid adenomas is relevant, representing 11% of total adenomas diagnosed. Interestingly, NBI might increase flat-depressed adenoma detection rate, although further evaluations are needed. The hypothesis that NBI might reduce the variations of diagnostic performances between expert and trainee endoscopists is not supported by the present data.

### References


### Table 3. Adenoma Findings

<table>
<thead>
<tr>
<th></th>
<th>HD-WL (n = 108)</th>
<th>HD-NBI (n = 103)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total adenomas</td>
<td>198</td>
<td>201</td>
<td>.69</td>
</tr>
<tr>
<td>Advanced adenomas</td>
<td>197</td>
<td>98</td>
<td>.82</td>
</tr>
<tr>
<td>Diminutive (&lt;5 mm) adenomas</td>
<td>88</td>
<td>78</td>
<td>.73</td>
</tr>
<tr>
<td>Non-polypoid adenomas</td>
<td>15</td>
<td>26</td>
<td>.16</td>
</tr>
</tbody>
</table>

*Expressed as mean value (SD).


29. Rex DK, Helbig CC. High yields of small and flat adenomas with high-definition colonoscopes using either white light or narrow band imaging. Gastroenterology 2007;133:42–47.


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Acknowledgments
Clinical Trials.gov identifier: NCT 00251914.

Conflicts of interest
The authors disclose no conflicts.