ENDOSCOPY CORNER

Clinical Evaluation of Endoscopic Trimodal Imaging for the Detection and Differentiation of Colonic Polyps

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Background & Aims: **Endoscopic trimodal imaging (ETMI) incorporates high-resolution endoscopy (HRE) and autofluorescence imaging (AFI) for adenoma detection, and narrow-band imaging (NBI) for differentiation of adenomas from nonneoplastic polyps. The aim of this study was to compare AFI with HRE for adenoma detection and to assess the diagnostic accuracy of NBI for differentiation of polyps. This was a randomized trial of tandem colonoscopies. The study was performed at the Academic Medical Center in Amsterdam.** ***Methods:*** **One hundred patients underwent colonoscopy with ETMI. Each colonic segment was examined twice for polyps, once with HRE and once with AFI, in random order per patient. All detected polyps were assessed with NBI for pit pattern and with AFI for color, and subsequently removed. Histopathology served as the gold standard for diagnosis. The main outcome measures of this study were adenoma miss-rates of AFI and HRE, and diagnostic accuracy of NBI and AFI for differentiating adenomas from nonneoplastic polyps.** ***Results:*** **Among 50 patients examined with AFI first, 32 adenomas were detected initially. Subsequent inspection with HRE identified 8 additional adenomas. Among 50 patients examined with HRE first, 35 adenomas were detected initially. Successive AFI yielded 14 additional adenomas. The adenoma miss-rates of AFI and HRE therefore were 20% and 29%, respectively ($P = .351$). The sensitivity, specificity, and overall accuracy of NBI for differentiation were 90%, 70%, and 79%, respectively; corresponding figures for AFI were 99%, 35%, and 63%, respectively.** ***Conclusions:*** **The overall adenoma miss-rate was 25%; AFI did not significantly reduce the adenoma miss-rate compared with HRE. Both NBI and AFI had a disappointing diagnostic accuracy for polyp differentiation, although AFI had a high sensitivity.**

Colorectal cancer (CRC) is one of the most common cancers in Western countries.[1,2] Genetic alterations in the mucosa lead to the formation of adenomas, which take a varying time span to progress into CRC.[3] This time span provides an opportunity for detection and removal of adenomas by colonoscopy, thereby preventing their progression into CRC.[4] Periodic removal of all adenomas is estimated to reduce the CRC incidence by 76% to 90%.[5] Recent reports showed that patients under close colonoscopic surveillance still develop CRC.[6] This may be explained by either rapid progression of adenomas, or by the fact that colonoscopy is not infallible for the detection of adenomas.[7,8] A systematic review of back-to-back colonoscopies showed that 15% to 32% of adenomas were overlooked.[9] Furthermore, flat and depressed adenomas were long thought to be rare in Western countries until colonoscopies were performed in conjunction with Japanese endoscopists and advanced techniques, showing that 7% to 40% of adenomas in the Western world were of the flat and depressed type as well.[10–14]

Advanced endoscopic techniques may improve the yield of adenomas and optimize the potential for CRC prevention. In addition, endoscopic differentiation of neoplastic and nonneoplastic polyps would improve the efficacy of colonoscopy further because adenomas should be removed and nonneoplastic lesions may be left in situ. Only chromoendoscopy (CE) has been shown to improve both the detection of adenomas, as well as the differentiation of polyps.[15–20] However, CE is labor-intensive, time-consuming, and operator-dependent. Furthermore, it is impossible to switch back and forth between the conventional and CE image. As a result, the implementation of CE in Western countries has fallen short.

Narrow-band imaging (NBI) is a new endoscopic technique, using spectral characteristics of the endoscopic light to enhance mucosal patterns and capillaries without dyes.[21,22] Concerning the detection of adenomas, NBI has failed to show an increased yield compared with high-resolution endoscopy (HRE) in 2 randomized studies.[23,24] For the differentiation of neoplastic from nonneoplastic lesions, however, NBI has an accuracy comparable with CE.[25–31]

Autofluorescence imaging (AFI) is another novel technique that might improve the detection of adenomas.[32] During AFI, blue light is used for illumination of the mucosa, which leads to fluorescent light emission of colonic tissue.[33] Differences in

Abbreviations used in this paper: AFI, autofluorescence imaging; CE, chromoendoscopy; CI, confidence interval; CRC, colorectal cancer; ETMI, endoscopic trimodal imaging; HRE, high-resolution endoscopy; NBI, narrow-band imaging; SSA, sessile serrated adenoma.

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fluorescence spectra between adenomas and normal mucosa are translated into a real-time pseudo color image. The use of AFI has shown an improved yield of neoplasia in patients under surveillance for Barrett's esophagus or ulcerative colitis.[34–37]

Endoscopic trimodal imaging (ETMI) integrates AFI, NBI, and HRE into one system.[36,37] For the purpose of this system, AFI functions as a red-flag detection technique, whereas NBI serves for differentiation. The aims of this randomized trial of tandem colonoscopies with ETMI were as follows: (1) to compare AFI with HRE for adenoma detection, and (2) to determine the diagnostic accuracy of NBI for polyp differentiation.

Patients and Methods

Patients

Patients scheduled for colonoscopy in the Academic Medical Center in Amsterdam were screened for participation. Inclusion criteria were a personal history of adenomas or CRC, or a positive family history for CRC (one first-degree family member fulfilling one of the revised Bethesda criteria).[38] Exclusion criteria were age younger than 18 years, polyposis syndromes, inflammatory bowel disease, severe coagulopathy, and insufficient bowel preparation. Eligible patients were invited for this study for which informed consent was necessary. This study was approved by the medical ethical committee of our institution.

Endoscopic Equipment

Colonoscopies were performed with the ETMI system (Olympus Inc, Tokyo, Japan). The light source (XCLV-260HP; Olympus Inc) provides sequential red-green-blue illumination and contains 2 rotating filters: one for HRE and one for NBI. The band pass ranges of green and blue light in the NBI filter have been narrowed to 530 to 550 nm and 390 to 445 nm, respectively. In addition, the intensity of blue light is increased. Because blue light penetrates the mucosa superficially and is absorbed by hemoglobin, this setting allows for enhancement of mucosal and capillary details.

A high-resolution colonoscope (XCF-H240FZL; Olympus Inc; magnification, 100×) was used, containing 2 charge-coupled devices: 1 for HRE/NBI and 1 for AFI. For AFI, blue light (390–470 nm) is used for excitation and green light (540–560 nm) is used for reflection. A barrier filter allows passage of light to the charge-coupled devices with wavelengths between 500 and 630 nm only, consisting of autofluorescence emission and green reflectance, which are integrated into a real-time pseudo color AFI image. During AFI, normal mucosa appears green and adenomas are purple (Figure 1).

A high-resolution monitor was used for all procedures and the endoscopists could switch easily between the 3 imaging modes by pressing a button on the endoscope.

Colonoscopy and Randomization

Patients were prepared with 4 L of polyethylene glycol solution (Kleanprep; Norgine GmbH, Marburg, Germany) and underwent colonoscopy under conscious sedation with midazolam and/or fentanyl. The colonoscope was advanced to the cecum using HRE, and cecal intubation was confirmed by identification of the appendiceal orifice and ileocecal valve. Upon reaching the cecum, the level of bowel preparation was determined as good (100% mucosa visibility), moderate (90%–100% mucosa visibility), or poor (<90% mucosa visibility) after extensive cleansing and aspiration of liquid stools. Patients with persisting poor bowel preparation were excluded.

After introduction, each colonic segment (ascending, transverse, descending, rectosigmoid) was inspected twice during withdrawal: once with AFI and once with HRE by the same endoscopist. Randomization determined which technique was used first for the detection of polyps. Allocation was performed by opening opaque sealed envelopes (containing a note with "AFI" or "HRE") by a research fellow after reaching the cecum and confirmation of sufficient bowel preparation.

All procedures were performed by 3 colonoscopists (>2500 standard and >30 ETMI colonoscopies) who were instructed to perform meticulous inspection and equal examination times for both detection techniques. In a random set of 15 patients, examination times for both techniques were recorded by using 2 stopwatches that were started at the cecum and stopped during cleansing, taking biopsy specimens, and, finally, at extubation. The entire procedural time (including time of introduction, cleansing, and polypectomies) was recorded for all patients.

The size (estimated by an 8-mm biopsy forceps) and location (colon segment and distance to anus) of detected lesions were recorded, as well as lesion type according to the Paris classification.[39] Furthermore, each lesion was scored for color (green, ambiguous, purple) on AFI (Figure 2), as well as for Kudo et al[40] pit pattern on NBI using optical magnification, and subsequently was removed for histopathologic evaluation. Lesions detected during the first inspection were removed immediately; therefore, the second inspection could only add lesions that were missed by the first inspection.

Histopathology

Resection specimens were evaluated routinely by a general pathologist; afterwards, all polyps were re-examined by an expert gastrointestinal pathologist who was only aware of the

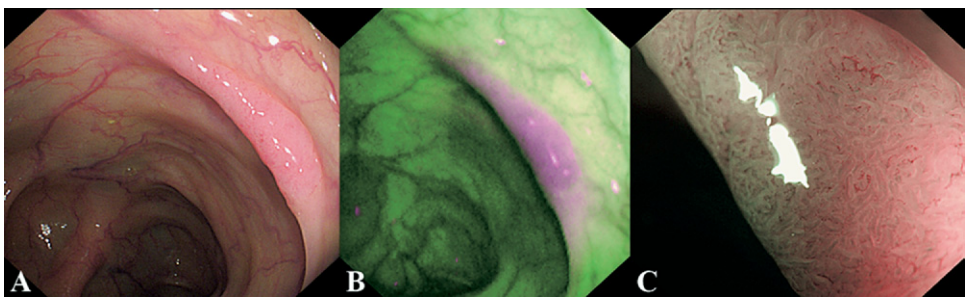

Figure 1. (*A*) High-resolution white-light endoscopy, (*B*) AFI, and (*C*) NBI. On AFI, adenomas become purple and normal colonic mucosa appears green; on NBI a Kudo pitpattern type IIIL is seen.