Advances in colonoscopic imaging and the approach to dysplasia in IBD

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CHAPTER 1

Quality of colonoscopy and advances in detection of colorectal lesions: a current overview

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ABSTRACT

Colonoscopy is the gold standard for the detection of colorectal cancer and its precursors. Nevertheless multiple studies have demonstrated a significant miss-rate for polyps and, more importantly, demonstrated the occurrence of interval cancers in the years after colonoscopy. This imperfect protection against colorectal cancer can be explained by multiple factors related to both the endoscopist and the equipment. To ensure the quality of colonoscopy, several quality indicators have been described. These include bowel preparation, cecal intubation rate, withdrawal time, adenoma detection rate and complication rate. Measurement of these quality indicators, followed by awareness, benchmarking and additional training will hopefully optimize daily practice. If these basic quality parameters are well taken care of, advanced colonoscopic techniques will aim at further increasing the detection and differentiation of colonic lesions. In this review, the authors discuss the literature on quality indicators for colonoscopy and give a comprehensive overview of the advanced colonoscopic techniques currently available.
INTRODUCTION

Although colonoscopy is considered the gold standard for adenoma detection, a previous systematic review published in 2006 showed that 22% (95% CI: 19–26%) of all adenomas were missed.1 These missed adenomas were mainly diminutive (26%) and small (13%), but also large adenomas (2%) were missed. More importantly, in recent years, multiple studies have demonstrated that colonoscopy does not perfectly protect against colorectal cancer (CRC). The incidence of post colonoscopy cancers varies in the literature from 2.9 to 9.6%, with post-colonoscopy cancer being defined as a cancer occurring within the years prior to the subsequent surveillance colonoscopy as recommended.2–4 A consistent finding in all studies is that these interval cancers are predominantly located in the proximal colon. A recent study explored the etiology of post-colonoscopy cancers and demonstrated that 58% of these cancers could be explained by missed lesions and 20% by inadequate colonoscopy (e.g., incomplete or poor bowel preparation).5 Thus, current colonoscopy practice is not optimal and there is a clear need for improved detection of colorectal lesions during this procedure.

The causes for suboptimal polyp detection can be subcategorized into factors related to the skills of the endoscopist (low cecal intubation rate [CIR], insufficient inspection and withdrawal time, etc.), to the patient (e.g., inadequate bowel preparation, difficult anatomy), or to limitations of current colonoscopic equipment. Besides these factors, the serrated neoplasia pathway could also account for a percentage of interval carcinomas. It is generally accepted that CRC develops along the adenoma-carcinoma sequence, in which colonic mucosa gradually changes from normal to low-grade dysplasia, high-grade dysplasia and finally cancer.6 However, more recently, an additional pathway for the development of CRC was discovered, the ‘serrated neoplasia pathway.’7 Within this pathway, serrated polyps, once thought to be innocent, are shown to be precursor lesions for CRC as well. The group of serrated polyps comprises hyperplastic polyps, sessile serrated adenomas/ polyps and traditional serrated adenomas. If all adenomas plus all serrated polyps could be perfectly detected and removed during colonoscopy, CRC should almost be prevented completely.

Based on a number of clinical studies that have been published in the last decade, several quality indicators have been established.8,9 These quality indicators can...
be used to evaluate the performance of colonoscopy and set a threshold for high-quality colonoscopy. Measurement and benchmarking of these quality indicators in daily practice forms the basis for continuous improvement in colonoscopic quality. Next to the predefined quality indicators, several quality improving interventions also aim at improving adenoma detection. The basics are simple interventions, for example, dynamic position changes during the procedure and the use of antispasmodic agents. Additionally, more complex interventions consist of the use of advanced imaging techniques.

This review focuses on optimal detection of colorectal lesions in average risk populations.

Previously, studies only focused on the detection of conventional adenomas and not sessile serrated lesions; therefore, less data are available on those lesions. Patients with high-risk syndromes such as adenomatous polyposis syndrome, serrated polyposis syndrome, Lynch syndrome and longstanding inflammatory bowel disease might require specific strategies to prevent CRC. These will not be discussed in this review.

QUALITY PARAMETERS

*Cecal intubation rate*

Several studies demonstrated that colonoscopy does not protect as well for right-sided CRC as it does for left-sided CRC.² One of the possible explanations for this difference is that the proximal colon is not always completely visualized. A colonoscopy is considered as complete when the cecum is completely visualized and intubated behind the ileocecal valve. In a publication by Baxter and colleagues, a significant number of right-sided cancers occurred in patients who underwent an incomplete colonoscopy.⁴ This has led to the introduction of CIR as an important quality indicator. To demonstrate cecal intubation, photographs of the cecal landmarks (ileocecal valve, appendiceal orifice and ileal mucosa) should be documented (Table 1).
Table 1 Quality indicators

<table>
<thead>
<tr>
<th>Quality indicator</th>
<th>Outcome measure</th>
<th>Standard</th>
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<tbody>
<tr>
<td>Adenoma detection</td>
<td>ADR: number of patients with at least 1 adenoma/total number of patients</td>
<td>ADR ≥ 25% in men and ≥ 15% in women during screening colonoscopies or, average ADR ≥ 20% during screening colonoscopy 8,17</td>
</tr>
<tr>
<td>Bowel preparation</td>
<td>Quality of bowel preparation, preferably assessed using a validated bowel preparation scale</td>
<td>≥ 90% described as “excellent” or “adequate” 8,9</td>
</tr>
<tr>
<td>Cecal intubation</td>
<td>CIR with photo-documentation of the cecal landmarks</td>
<td>≥ 90% unadjusted CIR (intention to scope) in unselected colonoscopies and ≥ 95% in screening colonoscopies 8,9</td>
</tr>
<tr>
<td>Withdrawal time</td>
<td>Total time for inspection from cecal pole to anus (in minutes)</td>
<td>Withdrawal time ≥ 6 minutes for normal colonoscopies 8,9,13,40</td>
</tr>
<tr>
<td>Discomfort</td>
<td>Assessment of discomfort by a validated scale (e.g., the Gloucester Comfort Scale)</td>
<td>Not established</td>
</tr>
<tr>
<td>Complications</td>
<td>Percentage of colonoscopies with a complication (up to 30 days after the procedure)</td>
<td>≤ 0.3% 9,29</td>
</tr>
<tr>
<td></td>
<td>Incidence of perforation during colonoscopy</td>
<td>Perforation rate ≤ 1:1000 for colonoscopies (diagnostic or therapeutic) or ≤ 1:500 for colonoscopies with polypectomy</td>
</tr>
<tr>
<td></td>
<td>Incidence of postpolypectomy bleeding</td>
<td>≤ 1:100 colonoscopies with polypectomy</td>
</tr>
</tbody>
</table>

The current threshold for CIR is 90% in unselected colonoscopies. 8 When corrected for circumstances in which intubation is impossible, for instance, in patients with strictures and stenosing tumors or poor bowel preparation, a 95% threshold is generally used. 9

There are multiple factors that might make complete colonoscopy difficult, such as a dolichocolon, unacceptable patient discomfort, insufficient bowel preparation, female sex and previous abdominal surgery. 10,11 Before starting a colonoscopy, endoscopists should always consider potential complicating factors by checking the medical history and previous endoscopy reports of the patient. Use of a pediatric colonoscope can be considered if previous colonoscopies were documented as difficult and incomplete. Furthermore, magnetic endoscopic imaging (MEI) could facilitate cecal intubation. MEI is developed by Olympus and provides real-time 3D views of the colonoscope shaft configuration and its location within the abdomen. A recent meta-analysis showed that the use of MEI improved CIR in both experienced and nonexperienced endoscopists. 12 In eight randomized controlled trials, the overall odds ratio for CIR...
with MEI was 1.92 (95% CI 1.13–3.27) when compared to standard colonoscopy. Cecal intubation times were not significantly different between both groups.

Withdrawal time
After reaching the cecum, the endoscope is slowly pulled back while the endoscopist closely inspects the colonic mucosa. Optimal inspection requires time, patience and optimal technique, looking behind folds and flushing away debris.

To evaluate the effort taken to inspect the colonic mucosa, withdrawal time can be measured. Withdrawal time is defined as the time taken from the cecal pole to the anus. In the study by Barclay and colleagues, withdrawal time of at least 6 minutes was associated with a higher adenoma detection rate (ADR) than a shorter withdrawal time. Based on this study, the minimal withdrawal time in an intact colon without specific findings is set at 6 minutes as a quality indicator. Two years later the same research group published a study showing a further improvement in ADR with withdrawal time over 8 minutes in an intact colon. However, a systematic review by Corley et al. in 2011 suggested that total withdrawal time alone is not an effective goal for quality improvement. Withdrawal time is likely a surrogate measure for the time taken to carefully inspect the colorectal mucosa for adenomas and not a useful metric solely by itself. We agree that time is certainly not the only factor contributing to an appropriate inspection by the endoscopist. Appropriate withdrawal technique and changing positions of the patient during withdrawal also contribute importantly to the ADR. As these practices are more difficult to quantify and are not assessed as a quality parameter, we suggest a minimum withdrawal time of 6 minutes as this quality parameter can be measured more easily.

Adenoma detection rate & polyp detection rate
The ADR reflects the performance of endoscopists in detecting precursor lesions for cancer, in this case adenomas. ADR is defined as the number of patients with at least one adenoma divided by the total number of patients who underwent a colonoscopy. In a Polish landmark paper, Kaminski and colleagues demonstrated in the setting of primary colonoscopy screening that patients who were scoped by an endoscopist with an ADR <20% have a greater chance of having post-colonoscopy cancer within the time of screening colonoscopy and
the scheduled time of surveillance colonoscopy than patients scoped by an endoscopist with an ADR >20%. Therefore, an ADR of 20% was set as a minimum threshold for screening colonoscopies. A recent study by Corley and colleagues confirmed these findings and also demonstrated an inverse correlation between ADR and death caused by CRC.

In a screening program in which patients who have a colonoscopy are selected by a positive fecal occult blood test (FOBT), one would expect a much higher ADR as a positive FOBT selects individuals with a higher chance of having adenomas from an average risk population. Accordingly, the mean ADR per endoscopist in the UK screening program with guaiac FOBT was 46.5%. Less data are available on the threshold ADR in symptomatic or surveillance populations. In these patients, ADRs described in the literature vary from 17 to 49%.

Although the ADR is accepted as one of the most important quality measures for colonoscopy, measuring the ADR can be time consuming and tedious as it requires reviewing both endoscopy and pathology reports. It has been advocated that the polyp detection rate (PDR) or the polypectomy rate (PR) could be a surrogate marker that is easier to assess. In our opinion, one should be cautious with the use of PR/PDR as a surrogate marker for the ADR as also irrelevant polyps are then considered part of the quality measurement. So far, only ADR has been associated with the risk of interval cancers and more data are needed to further explore the value of PDR and PR.

As ADR only measures the presence of at least one adenoma per patient, another potential drawback is that it introduces the risk that endoscopists could become less attentive to adenomas in the rest of the colon after they already detected one adenoma in a patient. Therefore, the UK NHS Bowel Cancer Screening workgroup has introduced the concept of MAP, the mean number of adenomas per procedure, and MAP+, the mean number of adenomas per procedure in which at least one adenoma was detected. MAP+ provides extra information in situations in which ADR is high (e.g., in FOBT screening). More data are needed to prove the added value of these parameters.

For a long time, adenomas have been regarded as the sole precursors of CRC and therefore only adenomas and not serrated polyps were reported and
used to establish quality parameters. Nowadays we know that serrated polyps are also potential precursors of CRC. Therefore, these polyps should also be detected, removed and reported. Serrated polyps are more difficult to detect during colonoscopy because of their flat morphology and ambiguous color. Proximally located serrated polyps are especially likely to be missed as bowel preparation in the proximal colon is more often insufficient. So far, only a few studies have reported on proximal serrated polyp detection. In these studies, it has been argued to introduce proximal serrated PDR as a quality measure and demonstrated detection rates varying from 6 to 22%. More evidence is needed before a threshold in proximal serrated PDR or serrated PDR can be established.

Bowel preparation

Although being one of the most burdensome parts of colonoscopy for our patients, bowel preparation is of utmost importance to facilitate efficient intubation and optimize the detection of lesions. Bowel preparation is considered sufficient if the view is not impaired by residual feces or fluids and at least 90% of the mucosal surface can be visualized. PEG in combination with bisacodyl appears to be the most optimal and tolerable for bowel preparation. The quality as well as the tolerability of bowel preparation can be enhanced by splitdose regimens, in which half the volume (1L) is consumed on the night before and the other half in the morning on the day of colonoscopy.

Previously, bowel preparation was only adequate in approximately 75% of patients. Fortunately, more recent studies have shown better results, and in the British NHS screening program 94% of all colonoscopies had an excellent or adequate bowel preparation. The informed consent procedure for colonoscopy is an ideal moment to emphasize the importance of a clean colon and carefully explain the schedule for laxatives. Several patient characteristics are predictors of poor bowel preparation, such as decreased bowel motility in immobilized, hospitalized or elderly patients, and previous suboptimal bowel preparation. Identifying these risk factors is important to give high-risk patients personal advice to improve the quality of their bowel preparation. This could include a longer duration of
fiber-restricted diet, extra laxatives or drinking more clear fluids. However, the ingestion of a high volume of PEG solution is challenging and often described by the patient as being a greater burden than the colonoscopy procedure itself.\textsuperscript{31}

To be able to assess the quality of a colonoscopy, the appropriateness of the bowel cleansing should be assessed using a validated bowel preparation scale. The most common scales used are the Ottowa Bowel Preparation Scale and the Boston Bowel Preparation Scale (BBPS).\textsuperscript{32,33} The Ottowa Bowel Preparation Scale was developed and validated to evaluate systematically the colon segments, with a scoring list ranging from 0 to 14, and includes the amount of irrigating and suctioning required for adequate visualization of each segment of the colon (left colon, transverse colon and right colon). The validated BBPS is a 4-point scoring system applied to each of the three broad regions of the colon: the right colon (including the cecum and the ascending colon), the transverse colon (including the hepatic and splenic flexures) and the left colon (including the descending colon, sigmoid colon and rectum), and should be used after optimal cleaning, reflecting the maximum achievable by inspection. More recently, a new bowel preparation assessment scale that combined pre- and post-cleaning was developed: the Chicago Bowel Preparation Scale.\textsuperscript{34} This is a more extended and laborious scale that seems ideal for scientific studies on bowel cleansing but less practical for daily use.

Of all bowel preparation scales, the BBPS seems the most easy and representative scale for daily practice. This scoring system scores the visibility of the colonic mucosa, which is eventually the final assessment.

**Sedation & discomfort**

To reduce the burden of colonoscopy, most colonoscopies are performed with some form of sedation. Worldwide, the two most commonly used methods of sedation are conscious sedation using benzodiazepines and/or opiates and deep sedation using propofol. The choice depends on both the preference of the patient and the preference of the endoscopist.

Conscious sedation allows the patient to report their discomfort, which could indicate severe stretch of the colon (e.g., by loop formation) or perforation of the colonic wall. This allows the endoscopist to anticipate this, potentially resulting
in safer practice. Recently, a study showed a higher perforation rate in patients undergoing therapeutic colonoscopy under propofol compared to conscious sedation (odds ratio 8.7 vs 2.6 per 10,000; p = 0.0016); for diagnostic colonoscopies there was no significant difference.\textsuperscript{35}

A common reaction to midazolam is a slight respiratory depression. It is therefore important to monitor the heart rate, blood pressure and oxygen levels as well as capnography when required. After the procedure, the patient should be monitored in the recovery ward before being discharged.

Deep sedation with propofol carries a higher risk of respiratory depression than conscious sedation and should be administered in an ensured situation, for example, by an anesthesiologist or an anesthesiology nurse.\textsuperscript{36} This results in higher costs and a more complex logistic process.\textsuperscript{37} Another disadvantage of propofol is the difficulty of changing a patient’s position, which is considered very helpful for appropriate colonoscopy technique, and much easier to achieve with a conscious and more cooperative patient. In our opinion, deep sedation should be reserved for specific indications such as very difficult colonoscopies, severe discomfort or anxiety.

Because colonoscopy is considered a burdensome procedure, it is important to measure the patient’s comfort during colonoscopies.\textsuperscript{9} To assess the deepest level of sedation, the validated Leeds scale is used.\textsuperscript{38} The Gloucester Comfort score (ranging from no discomfort to severe discomfort) is a validated tool to quantify the discomfort of the patient. This is preferably assessed by nurses and not by the endoscopist himself/ herself to enable a more objective assessment.\textsuperscript{39} Systematically measuring and benchmarking the patients’ comfort with the Gloucester Comfort Scale related to the sedation levels with the Leeds scale could help identify factors that would make the procedure more comfortable for the patient.
Complications

Colonoscopy is an invasive procedure and although the risks of colonoscopy are low, severe complications can occur. A complication is defined as an unintended and undesired outcome during or following the actions of a care provider that has an adverse effect on the health of the patient resulting in an adjustment of the treatment or irreparable damage. Severe complications in an average risk population occur in approximately two in every thousand colonoscopies, and the risk increases when a polypectomy is performed during the procedure. Bleeding is the most frequent complication caused by a colonoscopy, and follows in most cases after polypectomy. Bleeding occurring during the procedure should only be recorded as an adverse event if it results in a change in the normal policy following a colonoscopy. Most bleedings that occur during a polypectomy are immediately treated and therefore these are not considered to be a complication. Post-colonoscopy and postpolypectomy bleedings that occur after discharge from the endoscopy suite should be considered as a complication and should occur in less than 1:100 polypectomies.

A colonic perforation is a perforation of the bowel wall, which can occur due to mechanical forces during insertion of the colonoscope, overinsufflation of the colon (blow-out) or as a result of an endoscopic intervention such as biopsy or polypectomy. Over the past decades, a wide variation in perforation rates has been reported. A threshold of 1:1000 procedures in diagnostic colonoscopies and less than 1:500 after polypectomy is commonly used as an upper limit to be acceptable. If a perforation occurring during the colonoscopic procedure is immediately treated by clips, and this does not result in a change of post-colonoscopy protocol, this should not be considered as a complication.

Post-polypectomy syndrome is a situation which refers to symptoms of abdominal pain, fever and peritoneal inflammation after polypectomy, in the absence of a perforation (no free air on plain abdominal x-ray). This complication occurs in approximately 0.1–0.5% of polypectomies. Lastly, cardiorespiratory events occur in 0.1–0.2% of colonoscopies.

It should be mandatory for each endoscopist to keep a registry of all complications following colonoscopy. For each colonoscopy, complications can occur during the preparation phase, the procedure itself or in the weeks following colonoscopy. To
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ensure a complete registration of complications, complete follow-up until 4 weeks after the procedure is advised.40

Colonoscopy reporting
The quality of a colonoscopy can only be measured if the colonoscopy report includes all the key quality parameters used to measure the quality indicators. However, reporting of colonoscopy quality is often incomplete.47–49 To assist endoscopists in monitoring quality indicators in their practice, in 2007 the Quality Assurance Task Group of the National Colorectal Cancer Roundtable in the USA developed CO-RADS (Colonoscopy Reporting and Data System).50 CO-RADS consists of a list of recommended items for each colonoscopy report, including all colonoscopic findings as well as all suggested quality indicators. However, after introduction of CO-RADS the quality of reporting still varies widely among centers.49,51,52 To complete a high-quality colonoscopy, it is of utmost importance to document all quality indicators of the colonoscopy in a standardized manner. Recently, a novel reporting system (EndoALPHA) was introduced, which enables automatic assessment of the quality indicators in daily colonoscopic practice.53 Feedback and benchmarking of these parameters and subsequent awareness and training can facilitate continuous quality improvement for colonoscopy procedures.

QUALITY IMPROVING INTERVENTIONS: THE BASICS

Patient position
Dynamic position changes during withdrawal could potentially improve adenoma detection. This means that the hepatic flexure, in the right upper quadrant of the abdomen, is best examined with the patient in the left lateral position; the transverse colon, which lies relatively anteriorly in the abdomen with the patient the supine position; and the splenic flexure and the descending colon with the patient in the right lateral position. These positions coincide with intuition taking into account the gravity and the fact that air naturally rises to the highest position. Position changes would then result in better distension with less insufflation of air, shifting of fluids and residues, and opening tight angles at flexures.
The study by East and colleagues in 2011 showed that dynamic patient position changes led to an absolute increase of 11% in the proportion of patients with ≥1 adenoma detected in the colon between the hepatic flexure and the sigmoid descending colon junction.\textsuperscript{16} These results were confirmed by a recent Turkish study.\textsuperscript{54} However, no significant improvement in ADR was seen in a recent randomized study from Canada comparing dynamic changes in colonoscopy with a left lateral side upon withdrawal.\textsuperscript{55}

Dynamic position changes are easy and cheap to apply, especially when the patient is not deeply sedated. Therefore, although there is not yet enough evidence to support the additional value of position changes, we do recommend this for clinical practice to improve cecal intubation.

**Antispasmodics**

Recently, a set of technical quality interventions that could potentially improve adenoma detection during colonoscopy was implemented within a group of FOBT positives in the UK bowel cancer screening program.\textsuperscript{19} The routine use of an intravenous antispasmodic (hyoscine N-butylbromide) was associated with 30% higher adenoma detection. Existing literature on the role of antispasmodic use during colonoscopy in adenoma detection is, however, conflicting.\textsuperscript{56} Therefore, it is not clear whether the administration of an antispasmodic is directly responsible for the increase in adenoma detection or whether antispasmodic use is a more usual practice of better performing colonoscopists. Larger randomized studies are needed to evaluate the effect of these technical quality interventions.

**Rectal retroflexion**

To prevent missing adenomas or carcinomas near the anal verge, rectal retroversion is generally advised.\textsuperscript{18} However, its use in the same set of technical quality interventions in the UK bowel cancer screening program did not result in an association between rectal retroflexion and ADR.

**Cecal retroflexion**

Retroflexion in the proximal colon can also be applied with the aim to reduce the polyp miss rates. Because luminal diameter is wider in the right and the transverse colon, this procedure is often possible in experienced hands. However, only a few studies evaluated the possible benefit of proximal colon retroflexion. Rex and
colleagues performed a study where the proximal colon was first inspected in forward view with removal of all identified polyps from the cecum to the hepatic flexure. After that the colonoscope was reinserted into the cecum and retroflexed, and examination was performed to the hepatic flexure in retroflexion. They found no decrease in adenoma miss rates with a second colonic inspection in retroflexion. We do not recommend this technique in routine colonoscopy practice because of the lack of clear benefit and the possible increased risk of perforation.58,57

QUALITY IMPROVING INTERVENTIONS: ADVANCED IMAGING

Besides clear basic quality issues, there are also other potential explanations for missing colorectal lesions during colonoscopy. Some lesions are flat and/or have subtle features and are therefore difficult to detect with regular white light endoscopy. They might also be located outside of the endoscopic view, for example, in a sharp flexure or hidden behind a haustral fold.

Over the past 10 years, endoscopic imaging techniques have been greatly improved. Equipment for regular white light endoscopy has developed into a high-definition quality enabling a more detailed view. Moreover, advanced imaging techniques have been introduced to obtain enhanced mucosal contrast. For better exposure of the colonic mucosa, new tools have been developed that can either straighten colonic folds by means of plastic caps fixed at the tip of the endoscope or by enlarging the endoscopic view over 180 degrees by special lenses. Currently, these new techniques are being tested in daily practice. However, a major bias in these types of studies is that blinding of the endoscopist for the technique is impossible (Table 2).

High-definition colonoscopy

High-definition (HD) colonoscopy makes use of an HD colonoscope and an HD monitor providing more images per second. Moreover, these images have a higher resolution than standard definition colonoscopy. Although HD colonoscopy provides more detailed images of the colon, studies show conflicting results for adenoma detection. In 2011, a meta-analysis was published comparing HD and standard definition colonoscopy.59 The
meta-analysis combined outcomes of five studies including 4422 patients and showed an increased yield in ADR of 3.5% (95% CI 0.9–6.1%). A more recent randomized study by Longcroft-Wheaton and colleagues did not show differences between HD and standard video colonoscopy in the detection of high-risk adenomas.60 However, although the increase in adenoma detection appears to be minor, there is no additional burden to its use as nowadays all newly developed colonoscopic equipment is equipped with HD scopes and monitors.

Table 2 Advanced imaging techniques

<table>
<thead>
<tr>
<th>Technique</th>
<th>Evidence</th>
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</thead>
<tbody>
<tr>
<td>High-definition endoscopy (HD)</td>
<td>No irrefutable evidence that HD detects more adenomas than conventional white light endoscopy</td>
</tr>
<tr>
<td>Chromoendoscopy (CE)</td>
<td>CE improves adenoma detection compared to conventional white light endoscopy</td>
</tr>
<tr>
<td>Narrow Band Imaging (NBI)</td>
<td>Conflicting results that NBI improves adenoma detection compared to white light endoscopy, but probably not</td>
</tr>
<tr>
<td>i-SCAN</td>
<td>Not enough data to make any statements</td>
</tr>
<tr>
<td>Flexible Intelligent Color</td>
<td>No evidence that FICE improves adenoma detection compared to white light endoscopy</td>
</tr>
<tr>
<td>Enhancement (FICE)</td>
<td></td>
</tr>
<tr>
<td>Auto Fluorescence Imaging (AFI)</td>
<td>AFI does not improve adenoma detection compared to white light endoscopy</td>
</tr>
<tr>
<td>Cap-assisted colonoscopy (CAC)</td>
<td>No evidence that CAC improves adenoma detection compared to white light endoscopy</td>
</tr>
<tr>
<td>Endocuff</td>
<td>Preliminary results appear promising, large trials are currently being performed</td>
</tr>
<tr>
<td>Wide View Endoscopy</td>
<td>Preliminary results appear promising, large trials are currently being performed</td>
</tr>
<tr>
<td>Third Eye Retroscopy (TER)</td>
<td>TER improves detection rate, however impractical in daily practice</td>
</tr>
</tbody>
</table>

**Chromoendoscopy**

Chromoendoscopy (CE) is an imaging technique in which a blue dye stain is sprayed onto the colonic mucosa (Figure 1). This dye can be either absorptive, which is taken up by the epithelial cells (methylene blue), or nonabsorptive, which only attaches superficially to epithelial cells (indigo-carmine). CE enhances mucosal structures and can therefore be used for both detection and differentiation of colonic lesions. For pan-CE, a spray catheter is advanced through the working channel and the dye is sprayed during withdrawal of the colonoscope. One of the first studies assessing the use of CE for detection of colorectal lesions was performed in Japan and showed that especially the detection of small flat and depressed neoplastic lesions was enhanced by CE.61 Comparable results were found in the
study by Kiesslich and colleagues in 2001. Recently, Omata and colleagues showed in their meta-analysis an overall increase in ADR of 1.36 (95% CI 1.23–1.51; I² = 16%) by CE compared to standard colonoscopy.

Although CE has proven to increase adenoma detection, it is a labor-intensive technique which hinders its routinely use in daily practice. Another limitation of CE is that the dye especially attaches to residual feces, impairing the view when bowel preparation is not optimal. Several solutions for these practical hurdles are currently under investigation, such as capsules containing methylene blue that have to be taken by the patient along with the bowel preparation. Another potential solution is adding the dye to the rinse water to stain the colon while rinsing to clean it.

**Digital CE – narrow band imaging**

Compared to CE, narrow band imaging (NBI) is an image-enhancing technique that does not make use of a dye but uses light filters instead (Figure 2). Switching between white light and NBI is electronically activated by a switch on the colonoscope handle. NBI makes use of ambient light of wavelengths of 440–460 nm (blue) and 540–560 nm (green). Because the peak light absorption of hemoglobin occurs at these wavelengths, blood vessels will appear darker compared to the surrounding, allowing for their improved visibility and improved identification of other surface structures. Since the introduction of NBI, several systematic meta-analyses have been published addressing the detection of colorectal adenomas using NBI. Although NBI looked promising for improved detection of adenomas in the beginning, the majority of these meta-analyses did not show any increase in detection compared to conventional white light endoscopy.

The most recent meta-analysis published by Omata assessed the performance of NBI from 14 studies and also did not show significant improvement: 1.03 (95% CI 0.96–1.11; I² = 0%). A possible explanation for the promising results in the beginning could be that during the introduction of NBI endoscopists were looking more accurately during colonoscopy than before, which they also started doing during their white light endoscopies.
Figure 1 Chromoendoscopy (CE)

Figure 2 Narrow Band Imaging (NBI)

Figure 3 Autofluorescence Imaging (AFI)
Flexible intelligent color enhancement (FICE) is developed by Fujinon and makes use of post-process spectral image technology for high-contrast imaging. FICE converts images into spectral images with individual wavelengths and reconstructs them to generate high-contrast images. A xenon light source is incorporated in the endoscopic device producing white light with a spectrum from 400 to 700 nm and is captured by a charge coupled device (CCD). In contrast to NBI, where optical filters are used, FICE can select various combinations of wavelengths from all the light captured by the CCD and display different images.

A recent meta-analysis by Omata and colleagues pooled five studies on the detection of colorectal adenomas with FICE. The pooled analysis showed RR estimates of 1.09 (95% CI 0.97–1.23; I² = 5%). A recent study comparing NBI, FICE and white light was not included in this meta-analysis which did not demonstrate an increased detection rate for FICE. In conclusion, there is currently no firm evidence that FICE significantly improves the ADR compared to white light endoscopy.

i-SCAN is another image-enhancing technique that makes use of a post-process tonal contrast of surface filters to highlight vascularity and mucosal details. i-SCAN as a technique is less investigated than all the other imaging modalities addressed in this review. Hoffman and colleagues published the first randomized controlled trial on i-SCAN, demonstrating that (HD) i-SCAN was superior to standard video colonoscopy at detecting patients with at least one colorectal lesion (adenoma or cancer): 38 vs 13% (p < 0.0001) [70]. Conflicting results were shown in a randomized study by Hong and colleagues, which neither showed an increased ADR nor adenoma miss rate for i-SCAN versus HD white light. Due to limited data, no conclusive statements can be made on the performance of i-SCAN concerning improvement of the ADR.

Autofluorescence imaging
Autofluorescence imaging (AFI) makes use of differences in mucosal blood flow and endogenous fluorophores, for example, collagen, flavins and NADPH, which change the autofluorescence signal emitted following short-wavelength illumination (Figure 3). The autofluorescent signal is processed and creates a
false color image in which normal colonic mucosa is green and adenomas and cancer is purple, potentially facilitating the detection of colonic lesions. The only commercially available endoscopic AFI system is the so-called endoscopic trimodal imaging (ETMI) system by Olympus, which combines AFI with both HD white light and NBI. The pilot study by Matsuda and colleagues was positive but the randomized tandem study by van den Broek and colleagues demonstrated no significant beneficial effect of AFI over HD white light endoscopy. \(^{72,73}\) Comparable results were found in the randomized study by Kuiper and colleagues.\(^{74}\) Recently, Omata and colleagues performed a metaanalysis and included five AFI studies.\(^{63}\) They found a pooled RR estimate of 1.04 (95% CI 0.87–1.27; I\(^2\) = 0%) for ADR with AFI compared to white light endoscopy. In conclusion, there seems to be no place for AFI in improving the detection of lesions during colonoscopy.

**Cap-assisted colonoscopy**

One of the tools that is used to visualize the proximal surface of the mucosal folds that could potentially reduce polyp miss rates is the transparent plastic cap (Figure 4). This cap is placed on the tip of the endoscope and aims to keep appropriate vision by keeping distance between the colonoscope and the mucosa while pressing down the mucosal folds. The studies comparing cap-assisted colonoscopy (CAC) with conventional colonoscopy show variable results. Westwood and colleagues published in 2012 a meta-analysis including 12 studies and showed that CAC detected significantly more patients with polyps (odds ratio 1.13; p = 0.030) and had a lower average polyp miss rate (12.2 vs 28.6%) than standard colonoscopy.\(^{75}\) In the same year, another meta-analysis appeared including 16 randomized controlled clinical trials, in which similar results were found. CAC detected a higher proportion of patients with polyp(s) (RR 1.08; 95% CI 1.00–1.17).\(^{76}\) However, a more recent meta-analysis by Omata and colleagues did not show an advantage for CAC, with pooled estimate of RR for ADR of 1.07 (95% CI 0.94–1.23; I\(^2\) = 48%).\(^{63}\) Thus, CAC does not seem to have an irrefutable additive value for detecting more colonic lesions compared to conventional colonoscopy. It might, however, reduce cecal intubation time and improve CIR, as demonstrated by several studies.\(^{77}\)
Figure 4: Cap-assisted colonoscopy (CAC)

Figure 5: EndoCuff

Figure 6: Full spectrum endoscopy (FUSE)

Figure 7: Extra wide angle view endoscopy (EWave)

Figure 8: Third Eye Retroscope (TER)
**EndoCuff**

The EndoCuff is a cap that is designed to straighten colonic folds without blurring the endoscopic view, potentially increasing the detection rate of polyps on the proximal side of folds (Figure 5). The cuff is placed at the tip of the endoscope, distal to the bending section. It is constructed with two rings of soft, flexible slim projections. The projections are hinged at their bases so that during intubation they slip into housings in the cuff, so as to not interfere with forward movement, and on withdrawal the distal row of long projections flares outward and flattens the folds, aiming to enable a more complete view of the bowel wall previously hidden behind the folds. Initially, the EndoCuff was used for complex polyp resection and scar assessment in the sigmoid colon in a case series of 12 patients. More recently, a feasibility study was published on the use of the EndoCuff in complete colonoscopies and a retrospective analysis demonstrated an ADR of 34%, which seems acceptable. Currently, large randomized controlled trials on ADR are being performed and to evaluate its potential additional use.

**Wide angle colonoscopy**

Currently, standard view colonoscopy provides a 140- to 180-degree forward view. Over the past few years, endoscopes with a view that is wider than 180 degrees have been developed to address the problem of ‘the dead angle’ during colonoscopy. Full spectrum endoscopy (FUSE) is an endoscopic system enabling wide-view imaging developed by EndoChoice (Figure 6). It is a non-HD white light colonoscope which has three video cameras: one on the tip of the endoscope and two on the sides. It has two settings: a 160-degree forward-viewing and a 330-degree ultra-wide-viewing mode (composed of the three cameras). The 330-degree view is processed by three CCD chips, so the endoscopist has to look at three separate display screens at the same time during endoscopy. Recently, the results of a clinical study with the FUSE system were published and demonstrated a 71% increase in ADR. The adenoma miss rate was significantly lower in patients in the full-spectrum endoscopy group than in those in the standard forward-viewing procedure group: 5 (7%) of 67 vs 20 (41%) of 49 adenomas were missed (p < 0.0001). This is the only study showing this remarkably increased ADR with an imperfect design since both investigations were performed by the same endoscopist. More studies are needed to reproduce these results.
Recently, Olympus Medical Systems also developed a wideview colonoscope, the Extra Wide Angle View Endoscope (Figure 7). With this endoscope, the view can be enlarged to 235 degrees and incorporated in one image. Both the forward view and the side views are shown on one display screen because the total view is processed by one CCD chip, so the endoscopist can directly see the enlarged view of the colon. Furthermore, the colonoscope is equipped with NBI and the forward view can be magnified up to 1.5-times. A small feasibility study showed that the mean detection rate for all simulated polyps with the extrawide-angle-view colonoscope was significantly higher than that with the standard colonoscope (68 vs 51%; \( p < 0.0001 \)) [81]. Randomized clinical trials are currently being performed and will evaluate its potential additive effect in increasing ADR.

**Third eye retroscope**

Another way to improve inspection on the proximal side of haustral folds, the inner curve of flexures and ileocecal or rectal valves is the use of the Third Eye Retroscope (Figure 8). This is a thin device with a bend and a small camera on the tip. This device is inserted through the working channel upon withdrawal and extends beyond the tip of the colonoscope, providing a continuous retrograde view. The forward view is displayed on the left side of the split-screen monitor and the retrograde view on the right side. The performance of the Third Eye Retroscope was first described in a simulated setting and showed a significant increase in detecting lesions behind folds compared to only standard forward view (81 vs 12%; \( p < 0.00001 \)) [82]. After these promising ex vivo results, a pilot study (29 patients) followed showing a 11.8% increase in diagnostic yield [83]. A large multicenter trial (TERRACE study) demonstrated an increased PDR as well as an increased ADR [84].

One of the major limitations of the Third Eye Retroscope is that the extra camera occupies the working channel. Upon detection of a polyp the retroscope has to be removed to insert a snare or forceps, increasing the procedural time and effort. Although the first results with this new instrument were quite spectacular, this has not led to its widespread use in clinical practice, probably because of practical disadvantages.
SUMMARY

High-quality colonoscopy depends on both the performance of the endoscopist and the colonoscopic equipment available. To assess its quality, a number of quality indicators have been established in the past decade. These include CIR, withdrawal time, ADR, bowel preparation, sedation and discomfort, and complication registration. Assessment of these quality parameters and benchmarking should induce awareness, training and continuous quality improvement. Other factors that could contribute to further improvement of high-quality colonoscopy are accurate reporting, patient positioning, rectal retroflexion or the use of antispasmodics.

Advances in colonoscopic equipment can also contribute to improved colonoscopic quality. Most techniques focus either on highlighting mucosal structure or enlarging the endoscopic view. For highlighting mucosal structures, several imaging techniques are available: HD colonoscopy, CE, digital CE (NBI, FICE, i-SCAN) and AFI. Of all these techniques, CE is the only technique that shows significant improvement in ADR compared to standard white light endoscopy. However, the technique is laborious and time consuming, and therefore not applicable for routine daily practice. Techniques that focus on enlarging the endoscopic view are CAC, EndoCuff, wide-view endoscopy and Third Eye Retroscopy. To date, only a few studies have been published on these techniques and more research is needed to ultimately demonstrate its potential positive effect on ADR.

EXPERT COMMENTARY

It is known that suboptimal detection of colonic lesions during colonoscopy is one of the major risk factors for postcolonoscopy CRC. Therefore, it is important to have adequate information on the factors that contribute to high quality for each colonoscopy. Previously, a practicing endoscopist was not equipped with tools to measure his/her own quality. Today, a number of quality indicators have not only been established to measure but also to benchmark and hopefully improve the quality of colonoscopy. This suggests that routine registration of colonoscopy details through a reporting system that contains complete data on quality
indicators should be advocated. This will create awareness among endoscopists and will also help establish new quality parameters in the future.

Increasing ADR does not explicitly result in improved patient care, but detecting lesions with significant malignant potential does. So an increase in ADR should not be the result of detecting more diminutive adenomas in a medium risk population, but also by detecting subtle lesions that were previously not detected (e.g., flat adenomas, sessile serrated adenomas). This goal can be reached by performing colonoscopy according to the quality indicators, the awareness of the malignant potential of serrated lesions and potentially also by advanced imaging techniques. Currently, CE is the only technique with a proven additive value in detecting adenomas but not feasible for daily practice of routine patients. However, advanced endoscopic imaging is a quickly developing field of research and the quality of colonoscopy will probably improve rapidly because of these developments.

The English ‘Joint Advisory Group in GI Endoscopy’ created a teaching system to optimize colonoscopy performance: the Direct Observation of Procedure or Skills (DOPS). DOPS is an assessment tool that is designed to evaluate the performance of an endoscopist performing a colonoscopy. It consists of a structured checklist, and after the colonoscopy the endoscopist receives immediate feedback to identify strengths and areas of development. DOPS is used to test performance of trainees as well as registered endoscopists. In several countries such as the UK and the Netherlands, DOPS is also used to test an endoscopist for accreditation in the national bowel cancer screening programs. Additionally, the Direct Observational Polypectomy Skills (DOPyS) was developed, a tool designed to measure competence in polypectomy. The DOPyStool is also currently being used for accreditation in bowel cancer screening programs, and increasingly during the training of GE fellows to measure their competence.

FIVE-YEAR VIEW

CRC is one of the major causes of cancer-related death in the Western world. To reduce this mortality rate, multiple CRC screening programs have been introduced. Individuals at high risk for CRC should have the best test available, which is
colonoscopy. However, for average-risk persons another screening test with less burden and potentially higher participation rates should be considered. Such screening programs, for example, FOBT- or sigmoidoscopy-based screening programs, aim to select a population with a chance of having CRC or advanced lesions.

Ideally, all groups at risk for CRC should be tested with an accurate noninvasive test before being subdued to an invasive colonoscopy. As rough estimates suggest that only 1 in 20 adenomas develop into cancer and that generally takes 10 to 15 years, ideally the noninvasive test would only detect lesions that are actually close to becoming invasive/malignant, preventing needless colonoscopies and polypectomies for less relevant lesions.

Now that a set of scientific-based quality indicators has been established, and that much attention is given in medical literature, courses and conferences, it seems only a matter of time before measurement of the quality data becomes daily practice. Implementation and benchmarking in routine daily practice will certainly further increase the quality of colonoscopy. Hopefully, the systematic collection of all data on colonoscopy and the coupling of these databases with national cancer registries will help establish new and potentially more accurate quality indicators.

Endoscopists should be aware of their endoscopic technique and try to optimize. Endoscopic equipment will also continue to improve. Alongside commercial developments in advanced imaging, endoscopic research is currently performed in many countries worldwide. At the moment, CE is the only technique that increases ADR but impractical for daily practice, and digital CE has not yet proven its benefit for this purpose. Although wide-view colonoscopy shows promising results, more data on its potential to increase ADR and feasibility are needed. Theoretically, a technique that combines highlighting of the mucosal structures with an enlarged endoscopic view would provide the optimal colonoscopy equipment.
CHAPTER 1

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