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Can technology increase adenoma detection rate?

Wee Sing Ngu and Colin Rees

Abstract: Colorectal cancer is the third most common cancer worldwide and the second most common cause of cancer-related death in Europe and North America. Colonoscopy is the gold standard investigation for the colon but is not perfect, and small or flat adenomas can be missed which increases the risk of patients subsequently developing colorectal cancer. Adenoma detection rate is the most widely used marker of quality, and low rates are associated with increased rates of post-colonoscopy colorectal cancer. Standards of colonoscopy and adenoma detection vary widely between different endoscopists. Interventions to improve adenoma detection rate are therefore required. Many devices have been purported to increase adenoma detection rate. This review looks at current available evidence for device technology to improve adenoma detection rate during colonoscopy.

Keywords: adenoma detection rate, colonoscopy, colorectal cancer, colorectal polyps, post-colonoscopy colorectal cancer

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Correspondence to:
Colin Rees
Department of Gastroenterology, South Tyneside District Hospital, South Shields, NE34 0PL, UK
colin.rees@stft.nhs.uk

Wee Sing Ngu
Department of Gastroenterology, South Tyneside District Hospital, South Shields, UK

Introduction

Colorectal cancer is the third most common cancer in the world, with 1.4 million new cases diagnosed in 2012.[1] In the United States, 134,784 cases of colorectal cancer were diagnosed in 2012, with 70,204 men and 64,580 women affected.[2] In Europe, there were 477,000 new cases of colorectal cancer, with the United Kingdom accounting for 41,581 of these.

The majority (90%) of colorectal cancers arise from colorectal adenomas which are present in a third of European and American populations.[3] The adenoma–carcinoma sequence is a well-established pathway by which adenomatous polyps develop into colorectal cancer.[4,5]

Adenoma detection rate (ADR) is defined as the proportion of colonoscopies in which at least one adenoma is found. As a surrogate marker of mucosal visualization, it is regarded as the most important indicator of quality in colonoscopy.[6–8] Low ADR is implicated as one of the primary reasons for post-colonoscopy colorectal cancers (PCCRC). Acceptable levels of ADR will depend upon the population colonoscoped but minimal standards should be defined.[8]

A Polish screening study demonstrated that low ADRs were associated with higher rates of PCCRC ($p = 0.008$). In this study, colonoscopists with an ADR of <20% had a hazard ratio for PCCRC that was 10 times that of colonoscopists with an ADR of >20% (absolute risk for ADR ⩾20% 0.011% *versus* ADR <20% 0.115%).[9] Another large American study of over 300,000 screening, surveillance and diagnostic colonoscopies found an inverse relationship between ADR and the risk of PCCRC, advanced-stage PCCRC and fatal PCCRC. A 1% increase in ADR was associated with a 3% reduction in the risk of PCCRC and a 5% reduction in risk of a fatal PCCRC.[10]

A wide variability in ADR has been reported in both screening and non-screening populations.[11,12] Many factors may be responsible for the variation in ADR, including; suboptimal technique; shorter withdrawal time; inadequate bowel preparation; presence of flat, depressed or subtle lesions; and the inability to visualize the proximal side of haustral folds, flexures (blind spots), rectal valves and ileocaecal valves.[13,14] It has been estimated that 10% of the colonic surface is poorly seen using a standard forward-viewing colonoscope even with good bowel preparation.[15]

Other measures used to assess diagnostic quality are polyp detection rate (PDR), advanced

adenoma detection rate (AADR), adenoma miss rate, mean adenomas per procedure (MAP) and mean adenomas per positive procedure.

PDR is easier to measure compared to ADR and correlates well with ADR in colonic segments proximal to the splenic flexure.[16] The application of a conversion factor to the PDR may be used to accurately estimate the ADR.[17]

AADR measures adenomas more or equal to 10 mm in size with or without the presence of villous components or high-grade dysplasia. Advanced adenomas occur less frequently but have a higher malignant potential. An American observational cohort study of 1933 colonoscopies from 14 colonoscopists reported significant variations in ADR and AADR but found no correlation between them.[18] This may be a result of an increase in small non-advanced adenomas that are counted towards ADR, as demonstrated by a German study analysing trends in ADR in a screening programme.[19]

Missed lesions are polyps or adenomas that are missed during index colonoscopy. Adenoma miss rate is calculated by dividing the total number of adenomas found on repeat examination by the total number of adenomas found on initial and repeat examination. Data show that experienced endoscopists miss up to 6% of adenomas larger than 1 cm in size and 30% of all adenomas.[20] The miss rate for adenomas have been quoted at up to 24%.[14] Small adenomas (<10 mm in size) have a significantly higher miss rate compared to larger adenomas (>10 mm).[14] Adenoma miss rate can be difficult to calculate as it requires tandem colonoscopy; therefore most studies use the ADR rate as a measure of quality in identifying and removing adenomas.

A population-based study in the Netherlands found that 57.8% of patients who had interval cancers had missed lesions at colonoscopy.[21] In addition, they suggested that 86% of interval cancers were preventable and were due to missed lesions, inadequate examinations or surveillance. A majority of the lesions that were missed were proximally located, small in size and had a flat appearance. Variation is also seen in adenoma miss rates. One systematic review analysed six studies in which participants underwent tandem colonoscopy.[14] The miss rate for all adenomas was 22%. Adenoma miss rates for polyps <10 mm in size were significantly higher than for adenomas measuring >10 mm.

MAP is the total number of adenomas detected divided by the number of procedures performed. Mean adenomas per positive procedure (MAP+) is the total number of adenomas detected divided by the number of procedures in which one or more adenomas have been detected. A recent study in a screening population demonstrated that ADR and MAP were positively correlated, mostly due to the fact that 53% of procedures in which adenomas were found only demonstrate one adenoma.[6] MAP+ correlated less well with ADR.

Quality in colonoscopy

Despite variation in ADR, there has been an improving trend worldwide, with studies showing an increase in ADR in Europe, the United States and the United Kingdom.[11,12,19,22] This is attributed to a number of interventions, with the first being improved endoscopy training. A study investigating adenoma miss rates in patients undergoing tandem colonoscopy by a trainee followed immediately by an experienced endoscopist indicated that adenoma miss rates improved with experience of the trainee.[23]

There is also an increased awareness of quality improvement measures that can be utilized to improve AADR as a whole. These measures may include improving bowel preparation,[24] having longer withdrawal times,[25] using hyoscine-n-butylbromide,[26] performing rectal retroflexion and utilizing dynamic patient position changes.[27] The introduction of a simple bundle of measures (withdrawal time of ⩾6 min, use of hyoscine butylbromide, position change and rectal retroflexion) into colonoscopy practice has been shown to increase ADR by 2.1%.[28]

Endoscopy technology

Optical imaging innovations and technological developments in the field of colonoscopy have attempted to increase ADRs with the introduction of high-definition endoscopes, electronic chromoendoscopy (including narrow-band imaging), wide-angle colonoscopies and retrograde viewing devices.[29,30] However, lesions located on the proximal sides of colonic folds can still be missed during standard conventional colonoscopy.[31] Although these views may be improved with dynamic patient position change and routine retroflexion, these manoeuvres may not be effective, particularly in

narrower colonic segments, even with the use of a paediatric colonoscope or gastroscope.[27,32] Colonoscopy with right-side retroflexion has been shown to increase ADR in the right colon with a small risk of adverse events.[33] Transparent caps and hoods that attach to the tip of the scope have been created to hold down folds and improve visualization in the forward view. However, they can make the tip of the scope more rigid and longer, which may impair insertion in an angulated sigmoid colon.[34,35]

This review considers the advances in endoscopy technology surrounding colonoscopy and current available evidence for these.

Methods

A literature search was performed using PubMed and the terms ADR, high definition colonoscopy, chomoendoscopy, narrow band imaging, Fuji Intelligent Color Enhancement, autofluorescence imaging, i-SCAN, endoscopic trimodal imaging, cap-assisted colonoscopy, Endocuff, Endocuff Vision, Full Spectrum Endoscopy, Third-Eye Retroscope, NaviAid G-EYE Balloon Colonoscope, Aer-O-Scope colonoscope, water immersion and water exchange colonoscopy. Reference lists of the resultant articles were inspected for additional relevant papers. Only systematic reviews that were published in the Cochrane library were included. Searches were carried out on all data up to June 2017. The search only included English-language articles. The authors are aware of abstract studies but these were excluded for the purposes of this review. Where possible, the highest levels of evidence have been used. Levels of evidence are graded based on 'The Oxford Levels of Evidence 2'.[36] Table 1 illustrates the highest level of evidence available for each modality.

Imaging

High-definition colonoscopy

High-definition colonoscopy is the use of a high-definition monitor and colonoscope resulting in more images per second being shown with a higher resolution compared to standard colonoscopy, thus improving image quality and potentially identifying more pathology.

Early studies did not report a significant difference in ADR when comparing high-definition colonoscopy with standard colonoscopy.[37–39,41–43] The earliest positive result was a cohort study in which the total number of non-flat, >6 mm adenomas was higher in the high-definition group compared to standard colonoscopy.[41] A retrospective study reported a significant increase of 4.5% in ADR in patients with high-definition colonoscopy with an up to 3% increase found in adenomas <5 mm in size. However, confounding factors such as withdrawal time and quality of bowel preparation were not standardized.[40]

Two recent studies have reported a significant increase in ADR (8.2% $p = 0.02$, 12.6% $p = 0.007$) with high-definition colonoscopy.[44,45] However these were retrospective cohort studies. In conclusion, high-definition colonoscopy appears to improve ADR. However, prospective studies are required to further confirm this.

Conventional chromo-endoscopy

Conventional chromo-endoscopy utilizes contrast dyes that allow for enhancement of the colonic mucosa, thus improving visualization and highlighting surface contours. In conventional pan-colonic chromo-endoscopy, dye in the form of indigo carmine or methylene blue is sprayed with a catheter or is applied directly through the working channel of the endoscope in a segmental fashion onto the entire colorectal mucosa.

A Cochrane systematic review analysed seven randomized controlled trials (RCTs) with a total of 2727 participants and assessed the role of conventional chromo-endoscopy compared to standard colonoscopy in polyp detection and found that chromo-endoscopy generated more participants with at least one neoplastic lesion (OR 1.53, 95% CI 1.31–1.79) and at least one diminutive neoplastic lesion (OR 1.51, 95% CI 1.19–1.92).[46] They concluded that conventional chromo-endoscopy improved the detection rate of small polyps by 90%.[46] Thus, chromo-endoscopy may have a role in improving ADR.

Virtual chromo-endoscopy

Virtual chromo-endoscopy utilizes a narrow spectrum of wavelengths with a decreased penetration depth to enhance visualization of the colonic mucosa. These narrow wavelengths increase the vascular contrast of the mucosa and allow for improved visualization of the colonic mucosal

Table 1. Levels of evidence for devices in colonoscopy.

Study	Level of evidence	Measures used	Primary outcome	Patients (*n*)	Main outcomes
High-definition colonoscopy					
Pellisé and colleagues[37]	2	SD *versus* HDWE	ADR	620	No significant difference in ADR in both groups
Tribonias and colleagues[38]	2	SD *versus* HDWE	PDR	390	Overall polyp rate higher in HDWE group (SD 1.31 ± 1.90; HDWE 1.76 ± 2.31, $p = 0.03$) No significant difference in ADR in both groups
Longcroft-Wheaton and colleagues[39]	2	SD *versus* HD	ADR (<10 mm in size)	170	No significant difference in ADR in both groups
Buchner and colleagues[40]	3	SD *versus* HD	ADR	2430	ADR 4.5% higher in HD group ($p = 0.012$) Adenomas (1–5 mm) up to 3% increase ADR ($p = 0.024$) Adenomas (6–9 mm) 2.5% increase ADR ($p = 0.031$)
East and colleagues[41]	3	SD *versus* HD	ADR	130	No significant difference in ADR in both groups Total number of non-flat, small adenomas (<6 mm) higher in HD group – 78 *versus* 60, $p = 0.03$
Burke and colleagues[42]	3	SD *versus* HDWE	ADR	852	No significant difference in ADR in both groups
Erim[43]	3	SD *versus* HD	PDR	900	No significant difference in ADR in both groups
Jrebi and colleagues[44]	3	SD *versus* HD	ADR, PDR	1268	ADR higher in HD group (30.4% *versus* 22.2%, $p = 0.02$) PDR higher in HD group (48.2% *versus* 35.6%, $p < 0.001$)
Bond and colleagues[45]	3	SD *versus* HD	ADR, MAP	395	ADR 12.6% higher with HD ($p = 0.007$) MAP 0.5 higher with HD ($p = 0.01$) Screening patients
Conventional chromo-endoscopy					
Brown and colleagues[46]	1	CE *versus* SD	PDR, diminutive lesions, number of participants with multiple neoplastic lesions	2727	CE group found more people with at least one neoplastic lesion [odds ratio (OR) 1.53, 95% confidence interval (CI) 1.31–1.79; 7 trials; 2727 participants], and at least one diminutive neoplastic lesion (OR 1.51, 95% CI 1.19–1.92; 4 trials; 1757 participants)

Table 1. (Continued)

Study	Level of evidence	Measures used	Primary outcome	Patients (*n*)	Main outcomes
Narrow-band imaging					
Nagorni and colleagues[47]	1	NBI *versus* SD	PDR	3673	No significant difference in both groups
Senore and colleagues[48]	2	NBI *versus* SD	ADR	117	No significant difference in both groups
East and colleagues[49]	2	NBI *versus* SD	ADR	214	No significant difference in both groups
Ikematsu and colleagues[50]	2	NBI-SD *versus* SD-NBI	ADR/AMR	813	No significant difference for ADR in both groups Lower adenoma miss rate proximal colon for NBI (21.3% *versus* 27.8%, $p = 0.03$)
Adler and colleagues[51]	2	NBI *versus* SD	ADR	401	No significant difference in both groups
Gilani and colleagues[52]	2	SD-NBI *versus* NBI-SD *versus* SD-SD	ADR	300	No significant difference in both groups
Gross and colleagues[53]	2	SD-HDNBI *versus* HDNBI-SD	PMR	96	Polyp miss rates lower with HDNBI-SD (31% *versus* 57%, $p = 0.005$)
Rastogi and colleagues[54]	2	SDWL *versus* HDWL *versus* NBI	ADR	630	No significant difference in ADR in both groups NBI picked up more flat adenomas 11.4% *versus* 2.4% $p < 0.001$
Fuji Intelligent Color Enhancement					
Chung and colleagues[55]	2	NBI *versus* FICE *versus* WL	ADR	1650	No significant difference in all three groups for ADR
Chung and colleagues[56]	2	FICE-SDWL *versus* SDWL-FICE	AMR	359	No significant difference in both groups
Yoshida and colleagues[57]	2	NBI-FICE *versus* FICE-NBI	AMR	55	No significant difference in both groups
Kang and colleagues[58]	2	NBI *versus* FICE	ADR	955	No significant difference in both groups
Autofluorescence imaging					
Zhao and colleagues[59]	1	WL-AFI *versus* AFI- WL	ADR, PDR, AMR, PMR	1199	No significant difference in both groups for ADR and PDR AFI decreases AMR and PMR significantly compared to WL (OR 0.62; 95% CI 0.44–0.86, OR 0.64; 95% CI 0.48–0.85)

(Continued)

Table 1. (Continued)

Study	Level of evidence	Measures used	Primary outcome	Patients (*n*)	Main outcomes
Moriichi and colleagues[60]	3	Back-to-back SD and AFI	ADR	88	ADR increase by 8% $p < 0.05$ in AFI group ADR increase in AFI 30.3% ($p < 0.05$) but only for inexperienced endoscopists (<500 SD and <10 AFI) Only looked at sigmoid and rectum
i-SCAN™					
Hoffman and colleagues[61]	2	SD *versus* i-SCAN	ADR	220	ADR 38% i-SCAN *versus* 13% SD $p < 0.0001$
Hong and colleagues[62]	2	HDWL-HDWL, i-SCAN1-HDWL, i-SCAN2-HDWL	ADR	389	No improvement in ADR but i-SCAN effective for real-time histologic prediction of polyps
Chan and colleagues[63]	3	HDWL *versus* i-SCAN	Predicting polyp histology	75	No significant difference in both groups
Pigò and colleagues[64]	3	HDWL *versus* histology	Predicting polyp histology	78	i-SCAN helps assist in real-time prediction of histology with 95% sensitivity, 82% specificity and 92% accuracy
Basford and colleagues[65]	3	HDWL *versus* i-SCAN	Predicting polyp histology	84	No significant difference in both groups
Bowman and colleagues[66]	3	HDWL *versus* i-SCAN	ADR	1936	ADR higher with i-SCAN (618 *versus* 402, $p < 0.01$) Advanced adenomas (⩾10 mm) higher with i-SCAN (79 *versus* 47, $p = 0.021$)
Kim and colleagues[67]	3	HDWL *versus* i-SCAN	PDR	501	PDR higher with i-SCAN (52% *versus* 38.1%, $p = 0.004$)
Rodríguez-D'Jesus and Saperas[68]	3	HDWL *versus* i-SCAN	Diagnostic yield	155	No significant difference
Endoscopic trimodal imaging					
Kuiper and colleagues[69]	2	ETMI (HRE-AFI) *versus* SD-SD	ADR	234	No significant difference in both groups
Van den Broek and colleagues[70]	2	HRE-AFI *versus* AFI-HRE	AMR	100	No significant difference in both groups
Rotondano and colleagues[71]	2	HRE-AFI *versus* AFI-HRE	AMR	94	No significant difference in both groups

Table 1. (Continued)

Study	Level of evidence	Measures used	Primary outcome	Patients (*n*)	Main outcomes
Cap-assisted colonoscopy					
Morgan and colleagues[72]	1	CAC *versus* SD	Efficacy of colonoscopy as diagnostic tool	5932	May improve caecal intubation time, PDR and pain
Pohl and colleagues[73]	1	CAC *versus* SD	ADR	1113	No significant difference in ADR
Desai and colleagues[74]	1	CAC *versus* SD	Right-sided ADRs	686	Improvement in right-sided ADR with CAC (23% *versus* 17%, $p = 0.01$) Improvement in flat ADRs with CAC (OR 2.08, 95% CI 1.3–3.20, $p < 0.01$)
Rastogi and colleagues[35]	2	CAC *versus* SD	ADR	420	Higher ADR with CAC 69% *versus* 56%, $p = 0.009$
De Wijkerslooth and colleagues[75]	2	CAC *versus* SD	ADR	1380	No change in ADR but improve patient comfort scores
Othman and colleagues[76]	2	CAC *versus* SD	ADR	440	No improvement in ADR Improvement in AADR with CAC (9.9% *versus* 4.6%, $p = 0.049$)
Hewett and Rex[77]	2	CAC-SD *versus* SD-CAC	AMR	67	CAC lower miss rate 21% *versus* 33%, $p = 0.039$ especially in diminutive adenomas ⩽5 mm 22% *versus* 35%, $p = 0.037$
Horiuchi and colleagues[78]	2	CAC *versus* SD	ADR	107	No significant difference in ADR
Harada and colleagues[34]	2	CAC *versus* SD	PDR, CIT, patient comfort	592	No significant change in PDR but lower patient discomfort scores
Tee and colleagues[79]	2	CAC *versus* SD	CIT	400	No change in PDR or caecal intubation time
Frieling and colleagues[80]	2	CAC *versus* SD	PDR	504	No significant difference in PDR
Endocuff™/Endocuff Vision™					
Floer and colleagues[81]	2	EAC *versus* SD	ADR	500	ADR significantly increased 35.4% *versus* 20.7%, $p < 0.0001$
Biecker and colleagues[82]	2	EAC *versus* SD	PDR	498	PDR increased with EAC (56% *versus* 42%, $p = 0.0001$)

(Continued)

Table 1. (Continued)

Study	Level of evidence	Measures used	Primary outcome	Patients (*n*)	Main outcomes
Van Doorn and colleagues[83]	2	EAC *versus* SD	ADR	1063	No significant difference in ADR in both groups MAP was higher in EAC group (1.44 *versus* 1.18%, $p = 0.036$) CIT shorter in EAC group (7 min *versus* 8.3 min, $p < 0.001$)
De Palma and colleagues[84]	2	EAC *versus* SD	ADR	288	ADR improved with EAC (29.6% *versus* 26.3%, $p < 0.01$) Small adenomas (<5 mm) detection rate improved with EAC (129 *versus* 84, $p < 0.01$)
Bhattacharyya and colleagues[85]	2	EAC *versus* SD	ADR	534	No significant difference in ADR Screening patients
Ngu and colleagues[86]	2	EAC *versus* SD	ADR	1772	ADR improved by 4.8% ($p = 0.02$) globally, 10.8% ($p < 0.001$) in patients attending via the English Bowel Cancer Screening Programme.
Sawatzki and colleagues[87]	3	EAC	ADR	104	ADR of 47% screening population by experienced endoscopists
EndoRings™					
Dik and colleagues[88]	2	EndoRings-SD *versus* SD-EndoRings	AMR	116	Adenoma miss rate in EndoRings group lower (10.4% *versus* 48.3%, $p < 0.001$)
Full spectrum endoscopy®					
Gralnek and colleagues[89]	2	SD-FUSE *versus* FUSE-SD	AMR	185	Adenoma miss rate lower in FUSE group 7% *versus* 41%, $p < 0.0001$
Hassan and colleagues[90]	2	FUSE *versus* SD	AMR	658	No significant improvement in ADR
Papanikolaou and colleagues[91]	2	SD-FUSE *versus* FUSE-SD	AMR	215	Adenoma miss rate lower in FUSE group 10.9% (95% CI 3.8–18.1) *versus* 33.7% (95% CI 23.4 *versus* 44.1)
Ito and colleagues[92]	3	FUSE	ADR	130	No significant improvement in ADR
Gralnek and colleagues[93]	3	FUSE	Feasibility, usability, safety	50	Safe to use
Song and colleagues[94]	3	FUSE	Feasibility	262	Safe to use ADR reported 36.3%

Table 1. (Continued)

Study	Level of evidence	Measures used	Primary outcome	Patients (*n*)	Main outcomes
Third-eye ® Retroscope ®					
Leufkens and colleagues[95]	2	Tandem SC-TEC *versus* TEC-SC	ADR	395	Net additional ADRs 23.3% for adenomas
NaviAid™ G-EYE™ balloon colonoscope					
Halpern and colleagues[96]	2	SD-NaviAid *versus* NaviAid-SD	AMR	126	Adenoma miss rate lower in NaviAid group 7.5% *versus* 44.7%, $p = 0.0002$
Gralnek and colleagues[97]	3	NaviAid	Safety and feasibility	47	Safe and feasible
Aer-O-Scope™ colonoscope					
Vucelic and colleagues[98]	4	Aer-o-scope	Extent of colonic intubation	12	83% caecal intubation rate
Water-aided (immersion/exchange) colonoscopy					
Hafner and colleagues[99]	1	Water-aided *versus* air insufflation	Technical quality, screening efficacy, patient acceptance	2933	Main benefit is reduction in procedure-related abdominal pain which may enhance acceptance of screening/ surveillance colonoscopy. Some improvement in ADR likely due to cleansing effects of water
Cadoni and colleagues[100]	2	WE *versus* WI *versus* AICD	To assess ADR in the right colon	1200	Water exchange colonoscopy achieved significantly higher ADR (<10 mm adenomas) in the right colon (WE 11.9% *versus* WI 6.9%, $p = 0.016$, *versus* AICD 7.2%, $p = 0.025$)

ADR, adenoma detection rate; AICD, air insufflation colonoscopy; AMR, adenoma miss rate; CE, conventional chromo-endoscopy; EAC, Endocuff-assisted colonoscopy; ETMI, endoscopic trimodal imaging; EVAC, Endocuff Vision-assisted colonoscopy; FICE, Fuji Intelligent Color Enhancement; FUSE, full spectrum endoscopy; HD, high-definition colonoscopy; HDNBI, high-definition narrow-band imaging colonoscopy; HDWE, high-definition wide-angle colonoscopy; HDWL, high-definition white-light colonoscopy; HRE, high-resolution endoscopy; NBI, narrow-band imaging colonoscopy; PDR, polyp detection rate; SD, standard-definition colonoscopy; SDWL, standard-definition white-light colonoscopy; TEC, Third-Eye Retroscope; WE, water exchange colonoscopy; WI, water immersion colonoscopy.

surface. Different manufacturers have developed their own systems of virtual chromo-endoscopy and the use of such modalities has been proposed for characterization of colonic lesions.[101]

Narrow-band imaging (NBI) (Olympus Inc., Tokyo, Japan)

Narrow-band imaging uses narrow-band filters placed behind the light source to eliminate red light and increase the exposure of blue and green light. Blue light (415 nm) enhances the visualization of superficial mucosal capillaries while green light (540 nm) increases the visibility of submucosal and mucosal vessels.

A Cochrane review of 11 RCTs and 3673 patients in 2012 found no evidence to suggest that NBI was significantly better than standard colonoscopy at improving detection rates in average-risk populations.[47] Six successive RCTs have reflected this and shown no significant increase in ADR with NBI.[48–52,54] In contrast, a single-centre RCT found higher adenoma miss rates in standard colonoscopy compared to high-definition colonoscopy utilizing NBI (49% *versus* 27%, $p = 0.036$).[53] The authors argue that because two different colonoscopes were used in tandem compared to the other previously reported studies – standard colonoscopy followed by another colonoscope with better definition and high contrast – their study was more representative of a true miss rate. There is evidence that NBI may be of benefit in high-risk population groups such as those with Lynch syndrome and hyperplastic polyposis syndrome in ADR.[102,103] In Lynch syndrome, the use of NBI in the proximal colon for surveillance colonoscopies improved ADR by 15%,[102] whereas NBI has been reported to significantly reduce polyp miss rate by 26% in hyperplastic polyposis syndromes.[103]

Current evidence has not demonstrated that NBI significantly improves ADR in normal-risk individuals. However, NBI may be of benefit in high-risk individuals.

Fuji Intelligent Color Enhancement (FICE) (Fujinon Inc., Saitama, Japan)

FICE is a computed spectral estimation technology system that enhances the visibility of mucosal and vascular details by narrowing the bandwidth of light. FICE offers the endoscopist the choice of different wavelengths for optimal views.

Three tandem RCTs and one non-tandem RCT have shown no significant benefit of FICE over standard colonoscopy or NBI[55–58] in improving ADR. However, in the tandem RCT by Chung and colleagues, inadequate bowel preparation in at least 50% of cases may have impacted on ADR.[55] Yoshida and colleagues also reported that poor visibility was noted with FICE for blood visibility, which may affect detection of more vascularated adenomatous lesions.[57] There is no strong evidence that FICE improves ADR.

Autofluorescence imaging (AFI) (Olympus, Tokyo, Japan)

Autofluorescence imaging produces real-time pseudo-colour images by a rotating filter that produces short-wavelength light. Tissue exposure to this light leads to excitation of endogenous substances and subsequent emission of fluorescent light.

A tandem prospective study of 88 patients found an ADR rise of 8% with AFI, which increased to 30.3% when performed by less experienced endoscopists.[60] However, this study only looked at the rectum and sigmoid area. There are no large RCTs available yet for this modality. A recent meta-analysis of six studies with 1199 colonoscopies found no significant differences in ADR or PDR in AFI compared to WLE, but reported that AFI did significantly decrease AMR (OR 0.62; 95% CI 0.44–0.86) and PMR (OR 0.64; 95% CI 0.48–0.85).[59]

More evidence is required from RCTs to determine the role of AFI in improving ADR.

i-SCAN™ (Pentax, Tokyo, Japan)

i-SCAN™ is another virtual chromo-endoscopy system designed to enhance surface and vascular pattern to improve optical diagnostic performance. It has three modes of image enhancement: surface enhancement, contrast enhancement and tone enhancement.

Two RCTs reported conflicting ADR results. One study showed that i-SCAN™ improved ADR by up to 25% compared to standard colonoscopy.[61] However, this study compared high-definition colonoscopy and i-SCAN™ with standard-definition colonoscopy. High-definition colonoscopy has been shown to be more sensitive

in detecting small, flat polyps and therefore this may not be a true representation of i-SCAN™.[38,41] Only one study compared standard colonoscopy with standard colonoscopy and i-SCAN™; this is more representative of the effectiveness of using i-SCAN™ in the average-risk population. This study concluded that there was no improvement in ADR but that i-SCAN™ played a role in real-time histology prediction of polyps.[62]

The largest cohort study of 1936 patients reported higher ADR with i-SCAN™, including higher AADRs.[66] However, the role of i-SCAN™ in improving ADR has not yet been proven conclusively and larger RCTs are required.

Endoscopic trimodal imaging (ETMI) (Olympus, Tokyo, Japan)

ETMI combines the use of high-definition endoscopy, autofluorescence imaging and narrow-band imaging during colonoscopy.

The use of ETMI in tandem colonoscopy RCTs has not been found to significantly reduce adenoma miss rates or improve ADR.[69–71] One study had non-academic endoscopists while the other two RCTs were conducted at expert centres. Two of these RCTs also recruited high-risk patients with a history of previous adenomas, cancer or a positive family history of cancer. ETMI has not yet been demonstrated to improve ADR.

Devices to attach to colonoscope

Cap-assisted colonoscopy

Cap-assisted colonoscopy is the use of a transparent cap attached to the distal tip of the colonoscope to flatten colonic folds to improve mucosal visualization proximally.

There have been mixed results in RCTs evaluating the diagnostic yield of cap-assisted colonoscopy. Initial studies which often included a small sample of endoscopists and had a limited sample size showed no improvement in ADR with cap-assisted colonoscopy.[35,78,77] Some studies utilized PDR instead of ADR as their primary outcome.[80] A Cochrane review also concluded that cap-assisted colonoscopy increased PDR but there was not enough evidence to suggest it increased ADR as well.[72] A further systematic review concluded that there was an improvement in right-sided adenomas with cap-assisted colonoscopy.[74] Other studies have shown equivocal results, but they did show that cap-assisted colonoscopy improved patient comfort compared to standard colonoscopy.[34,75,79] The CAP study utilized a two-centre, multi-endoscopist, RCT approach to determine the role of cap-assisted colonoscopy in adenoma detection.[73] There was no significant difference found with ADR in both groups. Cap-assisted colonoscopy seemed to be of benefit for some endoscopists who experienced an increase in ADR by 20%, whereas for others there was a 15% decrease. This was not related to endoscopist experience.[73]

Cap-assisted colonoscopy has not yet been demonstrated to convincingly improve ADR.

Endocuff™ and Endocuff Vision™ (Arc Medical Design Ltd, Leeds, UK)

Endocuff™ is a disposable cuff that is attached onto the distal end of the colonoscope. The first version of Endocuff™ comprised two rows of backwards-pointing flexible 'finger like' projections at intervals around the device circumference. The second version, called Endocuff Vision™, only has one row of these projections, which are longer.

A multicentre prospective RCT using Endocuff™ with 500 patients in Germany found an absolute increase of 14% in ADR.[81] A Swiss pilot study demonstrated an ADR of 47% in the screening population.[87] A recent large RCT in the Netherlands found no significant difference in ADR in the Endocuff-assisted colonoscopy group. However, MAP was significantly higher and caecal intubation time quicker in the Endocuff-assisted colonoscopy group.[83] A UK study of screening patients using Endocuff-assisted colonoscopy reported no significant difference in ADR.[85]

The ADENOMA study found that Endocuff Vision™ improved ADR globally by 4.7% (p=0.02) which was driven by an increase in ADR of 10.8% (p<0.001) in patients attending for colonoscopy via the English Bowel Cancer Screening Programme.[86]

In conclusion, Endocuff Vision™ may have a role in improving ADR in the Bowel Cancer Screening population.

EndoRings™ (EndoAid Ltd, Caesarea, Israel)
EndoRings™ is a silicone endoscopic add-on device that consists of a short tube-like core with several layers of flexible circular rings. It is attached to the tip of the scope; during scope withdrawal the rings centre the scope and straighten colonic folds, thus enhancing mucosal views.

One multicentre, randomized, tandem study has been completed comparing the use of EndoRings™ with standard colonoscopy and demonstrated a lower adenoma miss rate with EndoRings™ colonoscopy. There was no significant difference in caecal intubation or withdrawal times, although total procedure time was longer in the EndoRings™ colonoscopy group due to removal of more polyps.[88]

The initial study suggests benefits from Endo Rings™. However, further evidence is required from RCTs.

Different types of colonoscopes

Full Spectrum Endoscopy® (FUSE) (EndoChoice Inc., Alpharetta, GA, USA)
FUSE® is a colonoscope that allows for a high-resolution 330° 'full spectrum' view of the colonic lumen. It consists of a main control unit and a video colonoscope with three imagers and LED groups located at front and both sides of the flexible tip. The video images transmitted from the three cameras on the left side, front and right side of the colonoscope are displayed on three continuous monitors. The addition of the two side cameras provides a more comprehensive view of colonic mucosa and visualizes blind spots more easily.

An initial prospective single-centre pilot cohort feasibility study showed that FUSE was feasible, usable and safe.[93] Following this, a multicentre, randomized, tandem colonoscopy trial illustrated that the adenoma miss rate was significantly lower in patients in the FUSE group (7% *versus* 41%, $p < 0.0001$).[89] This result has been mirrored by a Greek tandem study that reported lower miss rates by 23% with FUSE. It is argued that the use of FUSE could lead to an absolute reduction of US$145 dollars per patient due to a significantly higher sensitivity associated with FUSE.[104] However, a recent Italian RCT reported no statistically significant difference in ADR and AADR between FUSE and standard colonoscopy in screening programme patients.[90]

In conclusion, there is inconclusive evidence for the use of FUSE in reducing adenoma miss rates and further RCTs are required.

Third-eye® Retroscope® (TEC) (Avantis Medical Systems, Inc., Sunnyvale, CA, USA)
Third-eye® Retroscope® was invented to enhance the visualization of proximal colonic folds. It is a device that consists of a video processor, a single-use polarizing filter cap for colonoscope light source and a 3.5 mm flexible single-use catheter with a camera and diode light source at the tip. The TER is retroflexed at 180° after being inserted through the working channel of the colonoscope, and provides a 135° retrograde view of the colon. The TERRACE study, which was the only randomized back-to-back study of TER, found a net additional detection rate of 30% for polyps and 23% for adenomas.[95]

RCTs are required to assess the role of TEC in ADR improvement.

NaviAid™ G-EYE™ Balloon Colonoscope (SMART Medical Systems, Ra'anana, Israel)
The NaviAid™ G-EYE™ colonoscope comprises a standard colonoscope with a permanently integrated, reusable balloon at the distal end of the colonoscope. It allows for the colonoscope to be withdrawn with the balloon partially inflated, thus allowing for straightening of haustral folds and improving mucosal views. In addition, the balloon can be inflated to help anchor and stabilize the colonoscope when required.

A prospective cohort study of 50 patients identified an ADR of 45% with no major complications.[97] A recent tandem RCT found that the adenoma miss rate of NaviAid™ G-EYE™ colonoscopy was significantly lower (7.5% *versus* 44.7%, $p = 0.0002$) compared to standard colonoscopy.[96] This was a relatively small trial of 106 patients and the same colonoscopist performed both tandem procedures and was not blinded to the technology used.

In conclusion, large RCTs are required to further investigate the role of NaviAid™ G-EYE™ Balloon Colonoscope in ADR improvement.

Aer-O-Scope™ colonoscope (GI-View Ltd, Ramat Gan, Israel)

The Aer-O-Scope™ consists of a disposable scanner, which is the colonoscope component, and a workstation. The disposable scanner is made up of a soft multi-lumen tube with a unique pneumatic self-propulsion system that utilizes balloons and low-pressure carbon dioxide gas. This system maximizes the views of the entire colonic mucosa, including behind haustral folds. The lens head enables 360° panoramic, omni-directional visualization on a single screen.

A pilot study of 12 patients found a promising caecal intubation rate of 83% with no complications observed.[98]

Larger studies are required to assess the safety and accessibility of Aer-O-Scope™ before considering its role in ADR improvement.

Others

Water immersion and water exchange colonoscopy

Water immersion colonoscopy can be used as an adjunct to air insufflation to aid insertion, and is characterized by the removal of infused water during the withdrawal phase of colonoscopy. Water exchange colonoscopy is the infusion of water during the insertion of the colonoscope without air insufflation. It is a technique in which water-containing faeces are removed and exchanged for clean water in the absence of air insufflations.

A Cochrane review of 16 RCTs and 2933 patients found the main benefit of water immersion and water exchange colonoscopy to be reduction in pain scores.[99] There was also a small improvement in ADR (RR 1.16, 95% CI 1.04–1.30, $p = 0.007$).[99] A recent RCT of 1200 patients reported that water exchange colonoscopy achieved higher ADR (adenomas <10 mm) in the right colon of 5% compared to water immersion and 4.7% compared to air insufflation colonoscopy.[100] The results are promising but further evidence for the benefit of water-aided colonoscopy from RCTs is required.

Summary

Optimizing mucosal visualization is fundamental to ensuring high-quality colonoscopy. High ADRs are associated with better outcomes. ADR can be improved by improving technique but may also be improved by utilizing technology. It is important that this technology is studied properly and that it can be utilized by a wide range of endoscopists, not just experts. The majority of studies for devices currently reported focus on the use of devices in procedures undertaken by expert colonoscopists and may not truly reflect all groups of colonoscopists. Some studies show a significant improvement in ADR, and it is important that ongoing research involves RCTs and focuses on the learning curves for each device and the generalizable nature of findings. As evidence for the use of devices grows, it is also important that studies comparing the various devices are undertaken to establish which are most effective and in what clinical setting. Although it is important to optimize the use of new technology, the cost and time required to train endoscopists must be considered. The learning curve to use novel approaches correctly must be understood as well as the potential for increased time to undertake procedures. Additionally, health economics analyses should be undertaken to establish the cost-effectiveness of each device. The wide range of technology may be confusing to general colonoscopists and decisions regarding application of technology should be based on high-quality evidence. Specialist and national societies have an important role in supporting clinicians as they work out the optimal technology to deliver the best outcomes for their patients.

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Conflict of interest statement

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