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Original Article

Impact of endoscopy system, high definition, and virtual chromoendoscopy in daily routine colonoscopy: a randomized trial

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Short title: Impact of imaging modality in routine colonoscopy

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In brief

This comparison between conventional white-light colonoscopy, virtual chromoendoscopy, and high definition versions, using one of the three major endoscopy systems, found no differences in the rates of adenoma detection or adenoma per colonoscopy in 1855 individuals. However, high definition white-light colonoscopy was associated with higher detection rates of serrated adenomas and adenocarcinomas.

Background To improve detection of mucosal lesions during colonoscopy a number of imaging modalities have been suggested, including high definition and virtual chromoendoscopy. Given the theoretical advantage of these new imaging techniques, we aimed to investigate their use for the detection of polyps in patients referred for colonoscopy in a large tertiary hospital.

Methods Demographic, endoscopic, and histological data from 1855 consecutive patients undergoing colonoscopy were collected prospectively. Patients were randomly assigned to three endoscopy systems (Fujinon, Olympus, or Pentax) in combination with four modalities: conventional white-light (n = 505), high definition white-light (n = 582), virtual chromoendoscopy (n = 285) and high definition virtual chromoendoscopy (n = 483).

Results The mean adenoma detection rate (ADR) was 34.9%, and the adenoma per colonoscopy rate (APCR) was 2.1. No significant differences were noted between the three endoscopy systems. Moreover, no differences in ADR or APCR were observed between the four imaging modalities. High definition white-light colonoscopy resulted in a significantly higher detection of sessile serrated adenomas (8.2% vs. 3.8%; $P < 0.01$) and adenocarcinomas (2.6% vs. 0.5%; $P < 0.05$) compared with the conventional procedure.

Conclusions No significant differences in ADR or APCR between different endoscopy systems, high definition, and/or virtual chromoendoscopy could be observed in routine colonoscopies in the general population. High definition endoscopy was associated with a significantly higher detection rate of serrated adenomas and adenocarcinomas.

Trial registered at ClinicalTrials.gov (NCT03243669).

Introduction

Colonoscopy is considered the gold standard for detecting polyps; however, lesions can be missed and may become interval carcinomas. The “miss rate” ranges from 2% for large adenomas (>10 mm) to 26% for very small adenomas (1–5 mm) [1]. Carcinomas are estimated to be missed in 2%–6% of patients during routine colonoscopy [2]. It has been known that early detection of adenomatous polyps leads to a decreased mortality from colorectal cancer [3–5]. A recent prospective cohort study confirmed that an increased adenoma detection rate (ADR) is associated with a reduced risk of interval colorectal cancer [6].

Over recent years, a number of new endoscopic imaging modalities have been introduced that provide a theoretical advantage in the detection of mucosal lesions such as polyps. This is achieved by altering the light wavelength in order to enhance the visibility of superficial structures. Narrow-band imaging (NBI; Olympus, Tokyo, Japan) involves the selective use of certain wavelengths of the visible light spectrum, wherein a shift in the excitation spectrum to the blue light takes place in combination with a higher intensity of the blue “bandwidth.” As a result, the light penetrates less deeply into the intestinal wall, affording better visualization of mainly superficial mucosal structures (such as irregularities, polyps) and the small superficial blood vessels, which are a first sign of neoplasia [7]. Multiband imaging or flexible spectral imaging color enhancement (FICE; Fujinon Corp., Saitama, Japan) is based on a similar principle to NBI, wherein post hoc computer algorithms are used to filter certain wavelengths from the endoscopic image [8]. The Pentax I-SCAN system (Pentax Medical, Tokyo, Japan) is based on an adaptation of the superficial contrast (so called surface enhancement) and, similarly to FICE, a post hoc modification of certain wavelengths of the reflected light. A specific “c-mode” is available for use in

the colon [9]. Fujinon and Pentax use charge-coupled devices with megapixel resolution of 1.3 million and 1.4 million pixels, respectively. Olympus, however, opted for a higher video resolution based on the high definition television.

Theoretically, smaller lesions with a smaller dot resolution should be more easily detected using the abovementioned type of virtual chromoendoscopy compared with the conventional white-light colonoscopy. Meta-analysis shows that NBI might be better than conventional colonoscopy in detecting colorectal polyps and adenomas [10]. However, no difference in polyp or adenoma detection was observed between high definition white-light and high definition NBI [11]. Similarly, FICE and I-SCAN could also not demonstrate improvement of ADR [12]. Other drawbacks are the existence of a learning curve and the time-consuming aspect of chromoendoscopy, hampering its routine use in daily practice [13].

As the different modalities (white-light, virtual chromoendoscopy, and high definition versions) have not been compared head-to-head in a prospective way, we aimed to investigate their influence on ADR in a prospective, randomized, parallel study in a patient population referred for colonoscopy in a large tertiary hospital.

Methods

Trial design and participants

Consecutive patients presenting to the endoscopy unit of the University Hospitals Leuven, Belgium, between December 2010 and June 2014 were enrolled. Both outpatients and inpatients aged ≥ 18 years referred for colonoscopy were eligible for participation regardless of the indication. Based on referral indication, colonoscopies were divided into diagnostic (e.g. abdominal pain, iron deficiency, red blood per

rectum, diarrhea, constipation), screening (e.g. positive occult blood test, familial history of colorectal cancer), and surveillance colonoscopies.

Exclusion criteria were known subtotal colectomy (remaining colon <50 cm), colorectal polyp/malignancy before the start of the colonoscopy, polyposis syndromes (i.e. familial adenomatous polyposis, Lynch syndrome, hyperplastic polyposis syndrome, juvenile polyposis, Peutz–Jeghers syndrome), inflammatory bowel disease, and primary sclerosing cholangitis.

Written informed consent was obtained from all participants. The study protocol S52580 was approved by the local Ethics Committee (B32220109433 30 September 2010), registered at ClinicalTrials.gov (NCT03243669), and conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Interventions

Patients participating in this randomized study underwent colonoscopy that did not differ fundamentally from conventional colonoscopy except for the imaging modality. Classic bowel preparation with a polyethylene glycol solution was given, either in the hospital or as a home preparation. The endoscopes did not differ in design or size from a conventional colonoscope and were all commercially available. Settings for Fujinon and Pentax virtual chromoendoscopy were respectively FICE 4 and i-scan SE4+TE-c. All processors were connected to high definition monitors (NDS Surgical Imaging, San Jose, California, USA).

All colonoscopies were performed by 24 endoscopists, including permanent staff members and consultant gastroenterologists at University Hospitals Leuven. All endoscopists had a minimum of 3 years' colonoscopy experience and were

individually trained by an expert in (virtual) chromoendoscopy. Endoscopists were equally distributed within the different study arms.

During colonoscopy, the following parameters were recorded: bowel preparation by segment using the Boston Bowel Preparation Scale (BBPS) [14], total procedure time (insertion time plus withdrawal time), presence and number of polyps. Adequate bowel cleansing was defined as a BBPS score of 6 or more. Time registration was performed manually by the endoscopy nurse using a stopwatch.

All polyps were resected (or biopsied in cases of endoscopic signs of submucosal invasion), retrieved, and sent for histopathological analysis. Histopathological samples were analyzed by two specialist pathologists according to World Health Organization classification [15].

End points

The primary end point was the histologically proven ADR, defined as the percentage of colonoscopies with at least one adenoma identified, between the different endoscopic systems and imaging modalities.

Secondary end points were: 1) adenoma per colonoscopy rate (APCR), defined as the number of adenomas divided by the number of colonoscopies with at least one adenoma identified; 2) histological adenomatous subtypes (tubulo[villous] adenoma, sessile serrated adenoma, and adenocarcinoma); 3) bowel preparation; and 4) total, insertion and withdrawal time.

Sample size

The sample size was calculated to detect an absolute difference in ADR of 10% between subgroups (power 80%). When using a two-tailed test with an expected ADR difference of 40% vs. 30%, 461 patients per group would have been required (total

5071 patients), whereas using a one-tailed test with an expected ADR difference of 30% vs. 20% resulted in 287 patients per group (total 3157 patients).

Randomization

Patients were first randomized to one of the three available endoscopy systems: Fujinon (processor EPX-4450HD, colonoscopes EC-250WM5, EC-590WI, EC-590WM, and EC-590ZW/M); Olympus (processor Evis Exera II CV-180, colonoscopes CF-Q160AI, CF-Q180AI, and CF-H180AI); and Pentax (processor EPK-i, colonoscopes EC-3870FK2, EC-3870LK, EC-3810F, EC-3890F12, and EC-3890Fi). Within each group, patients were further randomized to: standard resolution white-light colonoscopy; high definition white-light colonoscopy; standard resolution virtual chromoendoscopy (although this is technically impossible with the Fujinon system); or high definition virtual chromoendoscopy. For virtual chromoendoscopy, examination with this modality was only performed during withdrawal.

Based on routine weekly patient numbers, approximately 50% of colonoscopies were being performed with Olympus, followed by 30% Fujinon, and 20% Pentax. Randomization was performed by a dedicated study nurse using sealed envelopes in batches of 40 patients. Every cluster for randomization contained 40 envelopes: 10 Olympus and 10 Olympus high definition (total Olympus 20 out of 40), 4 Fujinon and 8 Fujinon high definition (total Fujinon 12 out of 40), and 2 Pentax and 6 Pentax high definition (total Pentax 8 out of 40); this distribution represented the real-life distribution in the Endoscopy Unit. All of the 40 envelopes were drawn before a new cluster for randomization was started.

Statistical methods

The significance level was calculated using Fisher's exact test and Student's *t* test when appropriate for both primary and secondary end points, as well as exploratory analyses, and adjusted to $\alpha = 0.0269$ based on rough false discovery rate. Calculations were performed using SAS software (version 9.2 of the SAS System for Windows). Results are depicted as mean with 95% confidence interval (CI), calculated as published previously [16].

Results

A total of 2145 patients were eligible for participation in the study. A total of 10 patients refused to participate, leaving 2135 colonoscopies to be performed according to the protocol (Fig. e1, available online). Owing to slow recruitment and technology update, the study was terminated after 42 months before complete recruitment had been achieved.

As no reliable ADR could be obtained from inadequately cleansed or incomplete colonoscopies, 141 colonoscopies with BBPS <6 and 87 incomplete colonoscopies were excluded from the analysis. In addition, 52 files were excluded post-procedure owing to incomplete or incorrect registration, resulting in a total of 1855 colonoscopies available for analysis (Fig. e1, available online).

Of the 1855 patients in the final analysis, the mean age was 60.5 years (95%CI 60.0–61.1 years), with equal sex distribution (female/male 49.6%/50.4%). The majority of colonoscopies were performed for screening purposes (38.7% screening colonoscopy), followed by diagnostic colonoscopy (32.1%) and surveillance colonoscopy (29.3%). These distributions were observed within all groups of systems and modalities (Table 1). White-light colonoscopy was performed in 505 procedures (27.2%), high definition white-light in 582 colonoscopies (31.4%), virtual

chromoendoscopy in 285 colonoscopies (15.4%), and high definition virtual chromoendoscopy in 483 colonoscopies (26.0%).

Adequate bowel cleansing was achieved in 1994/2135 patients undergoing colonoscopy (93.4%), 95.6% of whom also achieved cecal intubation. The cecal intubation rate was similar between the three endoscopy systems (Fig. e1, available online).

Correct time registration was missing for 12 colonoscopies (0.6%); therefore withdrawal time is calculated for 1843 colonoscopies. Mean withdrawal time was 10:27 min:s (95%CI 10:08–10:46; median withdrawal time 8:42; interquartile range 6:12–12:31). The mean ADR was 34.9% (95%CI 32.8–37.1) and the APCR was 2.1 (95%CI 2.0–2.2). Only 78.0% of the colonoscopies were performed with a withdrawal time of more than 6 minutes.

Despite a significant difference in withdrawal time, no significant differences in ADR or APCR were noted between the three systems (Table 2, Table e3, available online). Moreover, no significant differences in ADR or APCR were observed between the four imaging modalities (Table e3, Table 4).

To validate the database, variables known to influence ADR, such as sex, smoking habits, and insertion time were analyzed, and were found to affect the ADR, whereas optimal bowel cleansing (BBPS 8 or 9) did not lead to significantly higher ADR compared with adequate bowel cleansing (BBPS 6 or 7) (Table e5, available online).

Endoscopists were classified according to age (< or >45 years) as a surrogate marker for their experience level, and a trend toward higher ADR in the senior group (ADR 36.2% vs. 32.4% in the junior group) was detected but this difference was not significant (Table e6, available online).

No significant difference in adenoma subtypes (Fig. 2) was detected between the three endoscopy systems (Table 2). High definition white-light colonoscopy resulted in a significantly different distribution of adenoma subtypes, with significantly increased detection of sessile serrated adenomas (8.2% vs. 3.8%) and adenocarcinomas (2.6% vs. 0.5%) compared with conventional white-light colonoscopy. No difference in adenoma subtypes was observed between virtual chromoendoscopy and the high definition version (Table 4). Surprisingly, high definition white-light colonoscopy and high definition virtual chromoendoscopy were associated with a significantly lower detection of diminutive (≤ 5 mm) adenomas compared with conventional white-light colonoscopy (62.9% and 61.6% vs. 70.7%, respectively) (Table 4). When hyperplastic polyps were included (because at the time of colonoscopy, histopathological analysis had not yet been performed), this difference in polyp size remained (Table e7, available online).

Discussion

Accurate bowel cancer screening programs rely on excellent quality colonoscopies, using ADR as one of the most valuable quality markers. Longer withdrawal time correlates significantly with increasing detection rate of polyps and lower incidence of interval colon cancer [17,18]. It was shown recently that the endoscopist characteristics of experience and fatigue were associated respectively with increased and decreased detection rate [19,20]. In the current prospective study, we aimed to analyze the influence of endoscopy systems (FICE, NBI, I-SCAN) and imaging modalities (conventional, high definition, and virtual chromoendoscopy) on endoscopy quality parameters such as ADR and APCR.

Bowel preparation is crucial for an adequate ADR [21]; therefore, in the current study, poorly cleansed colonoscopies were documented for quality purposes but not included

in further analysis. In general, no difference in ADR or APCR was observed between the different combinations of endoscopy systems and imaging modalities, confirming previously published analyses [22–24] in a prospective study. Recently it was shown that the quality of bowel preparation could also influence ADR [25]; however, this could not be demonstrated in our study. Another recent study found an association between prolonged cecal insertion time and lower adenoma detection [26]. This difference was also observed in our study. Possible explanations could be suboptimal bowel preparation, decreased colon expansion, or endoscopist experience and/or fatigue.

Sessile serrated adenomas were detected in 5.2% to 6.3%, depending on the endoscopy system used, which is comparable to the suggested serrated polyp detection rate of 5% in average-risk patients [27]. However, detection of serrated adenomas was significantly higher with high definition colonoscopy but not in the virtual chromoendoscopy subgroups. Our results on a general population excluding inflammatory bowel disease and polyposis syndromes are in line with recent studies and European guidelines restricting the routine use of virtual chromoendoscopy to specific risk groups [13,28,29]. One might expect a higher detection rate for diminutive adenomas with high definition colonoscopy; surprisingly, however, a significantly lower detection rate was found with this modality. At the time of colonoscopy, all polyps and not only adenomas were detected by the endoscopist. Therefore, hyperplastic polyps were included in the subanalysis, but again high definition colonoscopy was associated with significantly lower detection of diminutive polyps, whereas virtual chromoendoscopy was associated with significantly higher detection of hyperplastic polyps (Table e7, available online). One explanation could be that in the case of high definition imaging, the borders of the

polyps appear more clearly and therefore endoscopists may overestimate the size of the polyps.

During the study period, European guidelines for the monitoring of endoscopy became available [30], and have been updated recently [31]. Rates of adequate bowel preparation (93.4%) and cecal intubation (95.6%) were both above the 90% recommended by the European Society of Gastrointestinal Endoscopy.

Although the withdrawal time was well above the recommended minimum of 6 minutes, the guidelines stipulate a minimum of 90% of colonoscopies with a withdrawal time above 6 minutes rather than a mean or median withdrawal time. Analysis revealed that only 78.0% of the colonoscopies were performed with a withdrawal time of more than 6 minutes. Despite this lower minimal withdrawal time, the ADR (34.9%) was well above the recommended 25% [32].

It is known that colonoscopy withdrawal time is shorter in unmonitored gastroenterologists [33]. As this study was primarily designed to analyze ADR and colonoscopy timing, it is possible that some endoscopists were not always fully aware of being monitored themselves. As monitoring and documenting withdrawal time can improve quality [33], this has now been incorporated into our routine endoscopy practice.

One of the limitations of this study is the fact that recruitment was much slower than expected. After 42 months, the study was terminated to prevent further time and technique discrepancy. Hence, it is possible that small differences between subgroups were not detected (type II error). Post hoc analysis revealed that to claim that the current small differences in ADR were significant, a sample size of more than 20 000 colonoscopies would have been required. To further validate the database, known

variables from the literature, such as sex and smoking, were analyzed [34,35]. Significant differences in ADR could be observed, indicating that the study sample is representative of a real-life situation. Therefore, we think this study contains important data, as it is the first study to compare different systems head-to-head, and despite the low power, we could not find a substantial difference between the different systems that would be clinically relevant.

Another limitation of the study is the different levels of experience of the endoscopists. The use of age as a surrogate marker for experience in colonoscopy showed a higher but nonsignificant ADR in the senior group (36.2% vs. 32.4%), with both values above the recommended 25%. One needs to take into account that the personal experience of the endoscopist also has evolved during the 4 years of the study. This bias is inherent to prospective studies but represents the real-life situation.

Finally, the use of manual time registration by the sole endoscopy nurse has resulted in a number of incorrect time registrations, mainly by not registering the end of the procedure.

In conclusion, our results demonstrated that no significant differences in ADR or APCR were observed between different endoscopy systems and imaging modalities in routine colonoscopy in the general population in a real-life endoscopy unit. However, high definition endoscopy was associated with a significantly higher detection rate of serrated adenomas and adenocarcinomas, suggesting that high definition should be the new minimum standard in colonoscopy. In addition to documenting patient characteristics such as bowel preparation, endoscopist parameters such as cecal intubation rate, and insertion and withdrawal times should also be monitored to maintain good quality in endoscopy.

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Fig. e1 Study flow chart.

Fig. 1 Representative endoscopic images of tubular adenoma, sessile serrated adenoma, and adenocarcinoma using white-light colonoscopy (top row) and virtual chromoendoscopy (bottom row).

Table 1 Patient characteristics (N = 1855*).

	Fujinon (n = 530)			Olympus (n = 954)				Pentax (n = 371)			
	WLC	HD-WLC	HD-VC	WLC	HD-WLC	VC	HD-VC	WLC	HD-WLC	VC	HD-VC
Patients, n	172	197	161	263	256	213	222	70	129	72	100
Sex, female:male, n	81:91	98:99	87:74	134:129	120:136	95:118	121:101	38:32	62:67	31:41	54:46
Age, mean (SD), years	59.3 (11.5)	61.4 (12.6)	61.3 (11.5)	60.1 (12.1)	60.2 (11.8)	60.8 (12.6)	59.6 (13.5)	60.7 (12.8)	60.9 (12.1)	62.4 (11.8)	61.3 (13.0)
Smoking, n (%)	91 (52.9)	95 (48.2)	89 (55.3)	143 (54.4)	116 (45.3)	102 (47.9)	110 (49.5)	34 (48.6)	55 (42.6)	32 (44.4)	45 (45.0)
Indication, n (%)											
Screening	63 (36.6)	76 (38.6)	60 (37.3)	101 (38.4)	98 (38.3)	78 (36.6)	79 (35.6)	27 (38.6)	65 (50.4)	28 (38.9)	42 (42.0)
Diagnostic	45 (26.2)	69 (35.0)	58 (36.0)	78 (29.7)	79 (30.9)	68 (31.9)	86 (38.7)	18 (25.7)	36 (27.9)	26 (36.1)	32 (32.0)
Surveillance	64 (37.2)	52 (26.4)	43 (26.7)	84 (31.9)	79 (30.9)	67 (31.5)	57 (25.7)	25 (35.7)	28 (21.7)	18 (25.0)	26 (26.0)

HD, high definition; VC, virtual chromoendoscopy; WLC, white-light colonoscopy.

*Data on 1855 patients after exclusion of patients with inadequate bowel preparation (n = 141), incomplete colonoscopy (n = 87) or other reasons (n = 52).

Table 2 Procedure characteristics and findings by endoscopy system (N = 1855*).

	Fujinon (n = 530)	Olympus (n = 954)	Pentax (n = 371)
ADR, % (95%CI)	35.8 (31.8–39.9)	33.1 (30.3–36.3)	37.7 (32.8–42.7)
APCR, n (95%CI)	2.0 (1.9–2.2)	2.2 (2.1–2.3)	2.0 (1.9–2.2)
Withdrawal time, mean (SD), min:s	10:00 (7:21)	10:19 (6:25)	11:25 (7:26) [†]
Number of adenomas, n (%)	385	706	284
TA and TVA	357 (92.7)	658 (93.2)	259 (91.2)
SSA	24 (6.2)	37 (5.2)	18 (6.3)
Adenocarcinoma	4 (1.0)	11 (1.6)	7 (2.5)

ADR, adenoma detection rate; APCR, adenoma per colonoscopy rate; CI, confidence interval; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma.

*Data on 1855 patients after exclusion of patients with inadequate bowel preparation (n = 141), incomplete colonoscopy (n = 87) or other reasons (n = 52).

[†] $P < 0.005$ vs. Fujinon; $P < 0.01$ vs. Olympus.

Table e3 Procedure characteristics and findings by endoscopy system (N = 1855*).

	Fujinon (n = 530)			Olympus (n = 954)				Pentax (n = 371)			
	WLC n = 172	HD-WLC n = 197	HD-VC n = 161	WLC n = 263	HD-WLC n = 256	VC n = 213	HD-VC n = 222	WLC n = 70	HD-WLC n = 129	VC n = 72	HD-VC n = 100
Endoscopists, n	19	20	16	24	24	20	23	19	19	15	19
ADR, %	33.1	37.6	36.6	33.6	37.1	30.5	30.2	37.1	32.6	43.1	41.0
APCR, n	2.3	1.9	1.9	2.4	2.5	2.2	1.8	2.0	1.9	2.1	2.2
Withdrawal time, mean, min:s	10:05	9:58	9:57	10:04	10:06	10:57	10:14	10:54	10:57	12:24	11:50
Number of adenomas, n (%)	133	141	111	214	233	141	118	51	79	65	89
TA and TVA	129 (97.0)	125 (88.7)	103 (92.8)	202 (94.4)	214 (91.8)	131 (92.9)	111 (94.1)	50 (98.0)	65 (82.3)	63 (96.9)	81 (91.0)
SSA	3 (2.3)	13 (9.2)	8 (7.2)	11 (5.1)	15 (6.4)	8 (5.7)	3 (2.5)	1 (2.0)	9 (11.4)	1 (1.5)	7 (7.9)
Adenocarcinoma	1 (0.8)	3 (2.1)	0 (0.0)	1 (0.5)	4 (1.7)	2 (1.4)	4 (3.4)	0 (0.0)	5 (6.3)	1 (1.5)	1 (1.1)
Size of adenomas, n (%)											
Diminutive (≤ 5 mm)	88 (66.2)	95 (67.4)	76 (68.5)	155 (72.4)	152 (65.2)	92 (65.2)	74 (62.7)	38 (74.5)	38 (48.1)	43 (66.2)	46 (51.7)
Small (6–10 mm)	34 (25.6)	30 (21.3)	27 (24.3)	50 (23.4)	59 (25.3)	37 (26.2)	35 (29.7)	6 (11.8)	25 (31.6)	18 (27.7)	34 (38.2)
Large (>10 mm)	11 (8.3)	16 (11.3)	8 (7.2)	9 (4.2)	22 (9.4)	12 (8.5)	9 (7.6)	7 (13.7)	16 (20.3)	4 (6.2)	9 (10.1)

ADR, adenoma detection rate; APCR, adenoma per colonoscopy rate; HD, high-definition; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma; VC, virtual chromoendoscopy; WLC, white-light colonoscopy.

*Data on 1855 patients after exclusion of patients with inadequate bowel preparation (n = 141), incomplete colonoscopy (n = 87) or other reasons (n = 52).

Table 4 Procedure characteristics and findings by imaging modality (N = 1855*).

	WLC	HD-WLC	VC	HD-VC
Number of patients, n	505	582	285	483
ADR, % (95%CI)	33.9 (30.3–38.6)	36.3 (32.3–40.2)	33.7 (28.2–39.2)	34.5 (30.3–38.8)
APCR, n (95%CI)	2.3 (2.1–2.5)	2.1 (2.0–2.3)	2.1 (1.9–2.3)	1.9 (1.8–2.0)
Withdrawal time, mean (SD), min:s	10:11 (6:52)	10:15 (7:25)	11:19 (6:57) ^{†,‡}	10:25 (6:17)
Total adenomas, n (%)	398	453	206	318
TA and TVA	381 (95.7)	404 (89.2) ^{‡,§}	194 (94.2)	295 (92.8)
SSA	15 (3.8)	37 (8.2) [¶]	9 (4.4)	18 (5.7)
Adenocarcinoma	2 (0.5)	12 (2.6) [‡]	3 (1.5)	5 (1.6)
Size of adenomas, n (%)				
Diminutive (≤ 5 mm)	281 (70.6)	285 (62.9) [‡]	135 (65.5)	196 (61.6) [‡]
Small (6–10 mm)	90 (22.6)	114 (25.2)	55 (26.7)	96 (30.2) [‡]
Large (>10 mm)	27 (6.8)	54 (11.9) [‡]	16 (7.8)	26 (8.2)

ADR, adenoma detection rate; APCR, adenoma per colonoscopy rate; CI, confidence interval; HD, high definition; SSA, sessile serrated adenoma; TA, tubular adenoma; TVA, tubulovillous adenoma; VC, virtual chromoendoscopy; WLC, white-light colonoscopy.

*Data on 1855 patients after exclusion of patients with inadequate bowel preparation (n = 141), incomplete colonoscopy (n = 87) or other reasons (n = 52).

[†]P < 0.05 vs. HD-WLC.

[‡]P < 0.05 vs. WLC.

[§]P < 0.05 vs. VC.

[¶]P < 0.01 vs. WLC.

Table e5 Variables known to influence adenoma detection rate.

ADR, %	Total (n = 1855), % (95%CI)	<i>P</i>	Fujinon (n = 530)			Olympus (n = 954)			Pentax (n = 371)			
			WLC	HD-WLC	HD-VC	WLC	HD-WLC	HD-VC	WLC	HD-WLC	HD-VC	
Patients, n			172	197	161	172	197	161	172	197	161	1
Sex		0.0010										
Male	41.1 (38.0–44.3)		31.9	44.4	41.9	48.1	45.6	34.7	30.7	40.6	40.3	5
Female	28.7 (25.7–31.6)		34.6	30.6	32.2	21.6	27.5	25.3	29.8	34.2	24.2	2
Smoking		0.0088										
Smoking	37.6 (34.5–40.8)		35.2	37.9	40.4	35.0	44.0	33.3	33.6	44.1	36.4	4
Nonsmoking	32.3 (29.4–35.3)		30.9	37.3	31.9	34.2	31.4	27.9	26.8	30.6	29.7	4
Insertion time*		0.0249										
Fast	42.2 (41.5–42.9)		40.5	51.0	45.0	36.9	48.4	37.7	32.7	52.9	35.5	5
Slow	34.2 (33.6–34.9)		33.3	34.7	29.3	29.2	33.3	26.4	32.7	29.4	32.3	5
Bowel cleansing		0.7663										
Optimal	34.6 (32.1–37.1)		33.1	39.7	37.8	32.6	35.2	31.4	29.6	37.0	28.3	4
Adequate	35.9 (31.7–40.2)		33.3	29.3	33.3	40.0	43.9	28.8	31.7	37.5	43.2	3

ADR, adenoma detection rate; CI, confidence interval; HD, high definition; VC, virtual chromoendoscopy; WLC, white-light colonoscopy.

*Fast, mean 3:20 min:s (SD 0:31); Slow, mean 16:16 min:s (SD1:58); *P* < 0.001.

Table e6 Procedure characteristics and findings by endoscopist group*.

	Total (n = 1855)	<i>P</i>	Fujinon (n = 530)				Olympus (n = 954)					Pentax (n = 371)				
			Overall	WLC	HD- WLC	HD- VC	Overall	WLC	HD- WLC	VC	HD- VC	Overall	WLC	HD-WLC	VC	HD-VC
Patients, n																
Junior	629		166	60	66	40	278	71	63	69	75	185	32	67	31	55
Senior	1226		364	112	131	121	676	192	193	144	147	186	38	62	41	45
ADR, % (95%CI)		0.1109														
Junior	32.4 (28.8–36.1)		30.1 (23.1–37.1)	26.7	33.3	30.0	30.9 (25.5–36.4)	31.0	28.6	31.9	32.0	36.8 (29.8–43.7)	25.0	31.3	51.6	41.8
Senior	36.2 (33.5–38.9%)		38.5 (33.5–43.5)	36.6	39.7	38.8	34.3 (30.7–37.9)	35.9	39.9	29.9	29.3	38.7 (31.7–45.7)	47.4	33.9	36.6	40.0

ADR, adenoma detection rate; CI, confidence interval; HD, high-definition; VC, virtual chromoendoscopy; WLC, white-light colonoscopy.

*Junior <45 years; Senior, >45 years.

Table e7 Polyp subtypes per imaging modality.

	WLC	HD-WLC	VC	HD-VC
Polyp detection rate, % (95%CI)	51.1 (46.7–55.4)	51.0 (47.0–55.1)	49.1 (43.3–54.9)	47.4 (43.0–51.9)
Total polyps, n (%)	619	711	374	498
Hyperplastic polyps	221 (35.7)	258 (36.3)	168 (44.9)*	180 (36.1)
Adenomas	398 (64.3)	453 (63.7)	206 (55.1)*	318 (63.9)
Size of polyps, n (%)				
Diminutive (≤ 5 mm)	481 (77.7)	510 (71.7) [†]	279 (74.6)	347 (69.7) [†]
Small (6–10 mm)	109 (17.6)	142 (20.0)	79 (21.1)	124 (24.9) [†]
Large (>10 mm)	29 (4.7)	59 (8.3) ^{†,‡}	16 (4.3)	27 (5.4)

CI, confidence interval; HD, high-definition; VC, virtual chromoendoscopy; WLC, white-light colonoscopy.

* $P < 0.01$ vs. WLC, vs. HD-WLC, and vs. HD-VC.

[†] $P < 0.05$ vs. WLC.

[‡] $P < 0.05$ vs. VC.