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Lower Adenoma Miss Rate of Computer-Aided Detection-Assisted Colonoscopy vs Routine White-Light Colonoscopy in a Prospective Tandem Study

Pu Wang,[1] Peixi Liu,[1] Jeremy R. Glissen Brown,[2] Tyler M. Berzin,[2] Guanyu Zhou,[1] Shan Lei,[1] Xiaogang Liu,[1] Liangping Li,[1] and Xun Xiao[1]

[1]*Department of Gastroenterology, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Chengdu, China; and* [2]*Center for Advanced Endoscopy, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts*

See Covering the Cover synopsis on page 1193.

Keywords: AMR; Artificial Intelligence; Early Detection; Neoplasm.

BACKGROUND AND AIMS: Up to 30% of adenomas might be missed during screening colonoscopy—these could be polyps that appear on-screen but are not recognized by endoscopists or polyps that are in locations that do not appear on the screen at all. Computer-aided detection (CADe) systems, based on deep learning, might reduce rates of missed adenomas by displaying visual alerts that identify precancerous polyps on the endoscopy monitor in real time. We compared adenoma miss rates of CADe colonoscopy vs routine white-light colonoscopy.
METHODS: We performed a prospective study of patients, 18–75 years old, referred for diagnostic, screening, or surveillance colonoscopies at a single endoscopy center of Sichuan Provincial People's Hospital from June 3, 2019 through September 24, 2019. Same day, tandem colonoscopies were performed for each participant by the same endoscopist. Patients were randomly assigned to groups that received either CADe colonoscopy (n=184) or routine colonoscopy (n=185) first, followed immediately by the other procedure. Endoscopists were blinded to the group each patient was assigned to until immediately before the start of each colonoscopy. Polyps that were missed by the CADe system but detected by endoscopists were classified as missed polyps. False polyps were those continuously traced by the CADe system but then determined not to be polyps by the endoscopists. The primary endpoint was adenoma miss rate, which was defined as the number of adenomas detected in the second-pass colonoscopy divided by the total number of adenomas detected in both passes.
RESULTS: The adenoma miss rate was significantly lower with CADe colonoscopy (13.89%; 95% CI, 8.24%–19.54%) than with routine colonoscopy (40.00%; 95% CI, 31.23%–48.77%, $P<.0001$). The polyp miss rate was significantly lower with CADe colonoscopy (12.98%; 95% CI, 9.08%–16.88%) than with routine colonoscopy (45.90%; 95% CI, 39.65%–52.15%) ($P<.0001$). Adenoma miss rates in ascending, transverse, and descending colon were significantly lower with CADe colonoscopy than with routine colonoscopy (ascending colon 6.67% vs 39.13%; $P=.0095$; transverse colon 16.33% vs 45.16%; $P=.0065$; and descending colon 12.50% vs 40.91%, $P=.0364$).
CONCLUSIONS: CADe colonoscopy reduced the overall miss rate of adenomas by endoscopists using white-light endoscopy. Routine use of CADe might reduce the incidence of interval colon cancers. chictr.org.cn study no: ChiCTR1900023086

Adenomas are routinely missed during colonoscopy by individual endoscopists.[1] Although colonoscopy remains the gold standard for screening cancer and precancerous lesions in the colon,[2] colonoscopy can be technically demanding because it requires both manipulation and observation at the same time, and there is significant variation in how colonoscopy is performed and how lesions are detected between individual endoscopists.

Nonvisualization is a major cause of missed diagnosis, because lesions may remain hidden behind folds or debris during colonoscopy. Such lesions could be better exposed by means of high-quality bowel cleansing, endoscopic cameras with wider viewing angles, and meticulous mucosal inspection techniques.[1] However, the adenoma miss rate (AMR) still ranges from 6% to 41% using white-light colonoscopy.[1,3] Studies using full-spectrum colonoscopy (FUSE), which provides 330° angle of view, show an AMR of between 7.0%[4] and 20.5%.[3] This indicates that lesions within the visual field may still be missed due to failure of identification by the human eye.

For those polyps that are technically in the visual field, such lesions may be nonobvious, briefly visible, partially obscured, or appear on the edge of the screen.[5] Second observer strategies that use nurse observers or trainees during colonoscopy may increase the polyp detection rate (PDR), but use of a second observer may or may not increase the adenoma detection rate (ADR).[5–9] In addition, it is likely that adding additional human observers may not

Abbreviations used in this paper: **ADR, adenoma detection rate; AMR, adenoma miss rate; AMR-INV, invisible adenoma miss rate; AMR-V, visible adenoma miss rate; APC, adenoma per colonoscopy; BBPS, Boston bowel preparation scale; BMI, body mass index; CAD, computer aided diagnosis; CADe, computer aided detection; CI, confidence interval; CRC, colorectal cancer; FC, fold change; GI, gastrointestinal; IBD, inflammatory bowel disease; NA, not applicable; NSAID, nonsteroidal anti-inflammatory drug; PMR, polyp miss rate; PMR-INV, invisible polyp miss rate; PMR-V, visible polyp miss rate; PPC, polyp per colonoscopy; SSA/P, sessile serrated adenoma/polyp.**

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WHAT YOU NEED TO KNOW

BACKGROUND AND CONTEXT

Up to 30% of adenomas might be missed during screening colonoscopy. Computer-aided detection (CADe) systems, based on deep learning, might reduce rates of missed adenomas by displaying visual alerts that identify precancerous polyps on the endoscopy monitor in real time.

NEW FINDINGS

CADe colonoscopy reduced the overall miss rate of adenomas by endoscopists performing white-light endoscopy.

LIMITATIONS

Larger studies are needed to provide external validation of these findings.

IMPACT

Routine use of CADe might reduce the incidence of interval colon cancers.

completely overcome the deficiencies of human attention and human visualization in the identification of subtle colonic lesions.[5,9]

Thanks to the breakthrough of artificial intelligence,[10,11] computer-aided detection (CADe) systems have been developed that show high accuracy, fidelity, and consistency and in prospective randomized trials have shown promise as a standardized second observer. Such a system may help to avoid missed diagnoses for any visible lesions that appear ever briefly in the visual field by providing real-time visual alerts during colonoscopy.[12] The positive impact of CADe on ADR has been demonstrated prospectively in the clinical setting.[5,13]

Although previous prospective studies have shown a clear increase in ADR, relatively little is known about the exact contribution of the CADe system to the increase in detection rate. In addition, AMR, another important indicator that reflects the quality of colonoscopy, has not been specifically examined. Such a variable can directly reflect the impact of CADe by using a back-to-back comparison.[4] We therefore investigated the impact of CADe on AMR by means of a tandem study. Furthermore, by comparing video records of first and second pass, the direct contribution of the CADe system may be better demonstrated.

Methods

Study Design and Patients

This study was a single-center, open-labeled, prospective, randomized, tandem study that was conducted in the endoscopy center in Caotang Branch Hospital of Sichuan Provincial People's Hospital, China, between June 3, 2019, and September 24, 2019. We recruited patients aged 18 to 75 years who had been referred for diagnostic, screening colonoscopy or surveillance colonoscopy (for patients who underwent previous polypectomy). We excluded patients with a history of inflammatory bowel disease, colorectal cancer, colorectal surgery, or contraindication for biopsy. Also excluded were patients in whom the cecum was not reached and who were at high suspicion for polyposis syndromes, inflammatory bowel disease, and colorectal cancer. In addition, we excluded cases of difficult insertion, defined as insertion time >7 minutes in first pass, because of safety considerations for an already prolonged tandem procedure.

The protocol was approved by the Institutional Review Board of Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital. Written informed consent was obtained from all participants before the colonoscopy examination.

Randomization and Masking

All eligible patients were randomized via computer-generated stratified randomization to CADe colonoscopy or routine colonoscopy, followed immediately by the other procedure. Block randomization with a block size of 4 was used to determine the assignment (1:1) of each participant. The randomization was performed using a digital random number generator before the procedure to CADe white-light colonoscopy first vs routine white-light colonoscopy first. Patients were blinded to the grouping. Operating endoscopists were told the group allocation by a research assistant before the start of the colonoscopy procedure.

Interventions

The CADe system (EndoScreener, Shanghai Wision AI Co, Ltd, Shanghai, China) is a real-time automatic polyp detection system (Supplementary Figure S1) developed on a deep learning architecture. In a preliminary study, the system was validated to have a per-image sensitivity of 94.38%, per-image specificity of 95.92%, and an area under the receiver operating characteristic curve of 0.984 to detect colon polyps in colonoscopy report images. In addition, the system was also validated to have a per-polyp sensitivity of 100.00% (per-image sensitivity of 91.64%) and a per-image specificity of 95.40% in real-world colonoscopy videos.[12] The system processes >30 frames/s with a latency of 46.56 ± 2.79 milliseconds on GeForce-1080ti (Nvidia, CA), an imperceptible latency[14] for most human endoscopists. The CADe system was integrated into the endoscopy model by means of synchronously capturing and analyzing the video stream from the endoscopy processor and displaying alert boxes directly into the primary endoscopy monitor. This CADe colonoscopy works in an augmented-reality way to assist endoscopists to detect polyps[1] (Video S1).

Procedures

A same-day back-to-back tandem colonoscopy was performed for each eligible patient by the same endoscopist to assess AMR. All polyps underwent a biopsy or were removed by cold forceps biopsy once verified by the operating endoscopist. Larger polyps identified during colonoscopy underwent biopsy and were referred for later complete resection, as is typical of the endoscopy workflow for a large referral center in China. A biopsy was not performed for diminutive (≤2 mm) rectal polyps deemed by the endoscopist to be hyperplastic in nature[4] by use of blue laser imaging or Fuji Intelligent

Chromoendoscopy mode according to type 1 of Narrow-band imaging International Colorectal Endoscopic Classification.[15] The location, size, and morphologic features according to the Paris classification of each detected polyp were recorded by the research assistant.

Colonoscopies were performed with latest-generation model (Fujifilm LASEREO and VP4450HD), high-definition colonoscopes (EC-L590, EC-580, EC-590; Fujifilm, Tokyo, Japan) and high-definition monitors. All colonoscopy examinations were done with white light only, except for Narrow-band imaging International Colorectal Endoscopic Classification for an identified polyp when blue laser imaging or Fuji Intelligent Chromoendoscopy mode was used in a short interval at the discretion of the colonoscopists. Anesthesia, including midazolam, fentanyl, or propofol, was delivered and supervised by an anesthesiologist during the colonoscopy examination for each participant. Bowel preparation method was 2 L of polyethylene glycol with 6 mL simethicone solution, given in split doses.

Three experienced endoscopists from the division of gastroenterology participated as colonoscopy performers in this study.

In the routine pass, a routine white-light colonoscopy was performed. In the CADe pass, the CADe system processed each frame of the video stream synchronously and reported the detected polyp location with a hollow blue alert box directly in the endoscopy monitor with a simultaneous sound alarm (Video S2). The system was activated during withdrawal only. For any area alerted by the CADe system, the endoscopist was required to check and verify the area within the box based on his or her own clinical judgment.

All polyps detected during first-pass colonoscopy underwent biopsy or were removed using cold forceps biopsy. During the second-pass colonoscopy, any additional polyps detected were underwent biopsy or were removed by cold forceps biopsy. The residue of polyp that underwent biopsy during the first pass was a mark that demonstrated the polyp had been identified during the first pass, and these lesions were not counted as detected during the second pass. Repeat biopsies of lesions that had already undergone biopsy were not taken during the second pass. All biopsy tissue was sent for pathologic examination.

We measured the level of bowel cleanliness during colonoscopy with the Boston Bowel Preparation Scale. Insertion time to the cecum, withdrawal time for each pass, and biopsy time for each lesion were all recorded with a stopwatch during each colonoscopy procedure by a staff assistant. The endoscopist estimated polyp size with an open biopsy forceps.

In the CADe colonoscopy pass, missed polyps by the CADe system and consistent false detections by the CADe system were recorded. A missed polyp by the CADe system was defined as a polyp verified by the endoscopist but undetected by the system. A consistent false detection by the CADe system was defined as a detected area that was continuously tracked by the system but deemed by the endoscopist not to be a polyp. Any complication during the procedure or recovery was also recorded.

Outcomes

The primary outcome was AMR, which was defined as the number of adenomas detected in the second-pass colonoscopy divided by the total number of adenomas detected in both passes. The secondary outcome was PMR, which was defined as the number of polyps detected in the second-pass colonoscopy divided by the total number of polyps detected in both passes, in which the hyperplastic polyps in the rectum that had not undergone biopsy were included. The miss rate of advanced adenomas and sessile serrated adenoma/polyps (SSA/Ps) was calculated with the same definitions as AMR and PMR. Patient miss rate was defined as the number of patients in whom adenomas were detected in second pass for the first time divided by the total number of patients with at least one adenoma detected. ADR for the first pass was defined as the proportion of individuals with at least 1 adenoma detected in the first pass procedure. Adenoma per colonoscopy (APC) or polyp per colonoscopy (PPC) was defined as the total number of adenomas or polyps divided by the total number of patients of each group. We defined advanced adenomas as any adenoma of $\geq$10 mm in size, or containing villous histology, or with high-grade dysplasia.[16,17]

Additionally, because the CADe system is felt to help with missed polyps that appear in the visual field but remain unrecognized,[1] but not those that fail to appear in the visual field, to further scrutinize the contribution of the CADe system, 3 senior expert endoscopists reviewed all video records and excluded polyps that did not appear in the visual filed during the first pass. We defined visible AMR (AMR-V) and visible PMR (PMR-V) as the proportion of missed adenomas or polyps among all detected adenomas or polyps that were visible in first pass and the invisible AMR (AMR-INV) and invisible PMR (PMR-INV) as the proportion of missed adenomas or polyps among all detected adenomas or polyps that were invisible in first pass.

Statistical Analysis

We prospectively designed this study to allow for $\geq$80% power to detect a 15% difference (30% vs 15%) in AMR, per lesion analysis, between colonoscopy procedures with a 2-group χ^2 test with a 2-sided α level of 0.05. Thus, the overall participant enrollment goal was 392 to allow for potential exclusions or dropouts of 10%, with each participant undergoing same-day, back-to-back colonoscopy (784 tandem colonoscopies in total). Descriptive statistics were calculated for all measured variables and derived parameters. For continuous variables, time to reach the cecum, colonoscope withdrawal time, and total procedure time, we calculated means, medians and interquartile ranges (IQRs), SDs, and minimums and maximums. For categorical variables, summary statistics are counts and percentages. We used t tests to compare continuous variables. For categorical variables, we used Fisher's exact test or the χ^2 test to compare detection rates between groups. For estimates of proportions, we calculated 95% exact binomial confidence intervals. All tests applied were 2-tailed. We analyzed data with R 3.4.4 software (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline and Demographic Data

The study enrolled 386 patients, and 4 patients withdrew consent before grouping. We randomized 382 patients into the routine-first (n = 190) group or CADe-first group (n = 192). There were 13 patients excluded during colonoscopy due to exclusion criteria. A total of 369 eligible patients were analyzed, with 185 patients in routine-first group and 184 in the CADe first group (Figure 1). The total withdrawal time of routine-first and CADe first groups

was 7.14 minutes vs 7.85 minutes ($P = .001$) in the first pass and 6.73 minutes vs 6.34 minutes ($P = .001$) in the second pass, respectively, possibly due to more polyps detected and more biopsy procedures performed in the CADe colonoscopy. However, when biopsy time was excluded from analysis, the clean withdrawal time was 6.51 minutes vs 6.55 minutes ($P = .745$) in the first pass and 6.04 minutes vs 6.14 minutes ($P = .146$) in the second pass, respectively (Supplementary Table S1).

There were no statistically significant differences between the 2 groups in demographic data, insertion time, bowel preparation level, indication for colonoscopy (Table 1) and adenoma risk factors (Supplementary Table S2). No complications were reported.

Miss Rate of Polyps, Adenomas, Advanced Adenomas, and SSA/P

Table 2 reports the miss rate of polyps, adenomas, and major polyp subtypes. The AMR was significantly lower with CADe colonoscopy than with routine white-light colonoscopy (13.89% vs 40.00%, $P < .0001$). The PMR was also lower with CADe colonoscopy than with routine white-light colonoscopy (12.98% vs 45.90%, $P < .0001$). There were no statistical differences in the miss rate of advanced adenomas and SSAs/Ps.

Table 3 reports the clinicopathologic characteristics of the missed adenomas in routine white-light colonoscopy and CADe colonoscopy. The AMRs for diminutive (<5 mm) adenomas were significantly lower with CADe colonoscopy than with routine white-light colonoscopy (13.11% vs 39.66%, $P = .0015$), as well as for small (5–9 mm) adenomas (13.75% vs 46.94%, $P < .0001$). Regarding morphology, AMR was significantly lower with CADe colonoscopy than with routine white-light colonoscopy in nonpedunculated types (14.18% vs 42.45%, $P < .0001$). AMR was lower with CADe colonoscopy than with routine white-light colonoscopy in the ascending, transverse, and descending colon (Table 3).

Miss Rate of Visible Adenomas and Polyps

AMR-V was 24.21% vs 1.59% ($P < .001$) in the routine-CADe group and CADe-routine group, respectively, and PMR-V was 30.89% vs 2.36% ($P < .001$) in the routine-CADe group and CADe-routine group, respectively (Table 4). Of 23 missed visible adenomas and 59 polyps during the first pass, there were 10 of 23 adenomas (48%), and 22 of 59 polyps (37.29%) recorded in video files being detected by the CADe system in post hoc video analysis.

Miss Rate of Invisible Adenomas and Polyps

AMR-INV was 25.00% vs 12.68% ($P = .016$) in the routine-CADe group and CADe-routine group, respectively, and the PMR-INV was 27.07% vs 11.11%($P < .001$) in the routine-CADe group and CADe-routine group, respectively (Table 4).

ADR, PDR, APC, and PPC

The overall ADR (42.39% vs 35.68%, $P = .186$), overall PDR (63.59% vs. 55.14%, $P = .099$), overall APC (0.78 vs. 0.65, $P = .129$), and overall PPC (1.55 vs. 1.32, $P = .065$) were different between the CADe colonoscopy-first group and the routine colonoscopy-first group. There was no statistical difference found in ADR in the first pass (34.78% vs 26.49%, $P = .085$) in CADe colonoscopy and routine white-light colonoscopy, although the trend was toward a higher ADR in the CADe-first group. The PDR, APC, and PPC in the first pass were significantly higher in CADe colonoscopy than in routine white-light colonoscopy; that is, PDR was 55.98% vs 37.84% ($P = .001$), APC was 0.67 vs 0.39 ($P < .001$), and PPC was 1.35 vs 0.71 ($P < .001$). Similar findings were found when analyzing the second pass: all ADR and PDR and APC and PPC in the second pass were significantly higher in CADe colonoscopy than in routine white-light colonoscopy; that is, ADR was 18.38% vs 10.87% ($P = .043$), PDR was 37.84% vs 19.02% ($P < .001$), APC was 0.26% vs 0.11% ($P = .001$), and PPC was 0.61% vs 0.20% ($P < .001$; Table 5).

Patient Miss Rate

The patient miss rate was lower with CADe colonoscopy than with routine white-light colonoscopy, but without a statistically significant difference (17.95% vs 25.76%, $P = .258$; Table 6.

Consistent False Detections With the CADe System

There were 67 consistent false detections in the CADe colonoscopy. Most consistent false detections were wrinkled mucosa. None was missed by the CADe system among all detected polyps by the endoscopists in the CADe colonoscopy (Supplementary Table S3).

Discussion

In this single-center, open-labeled tandem study, we found AMR and PMR were significantly lower with CADe colonoscopy than routine colonoscopy. AMR obtained from tandem colonoscopy is a more representative parameter to reflect the performance of an individual endoscopist with and without CADe than ADR. In previous tandem studies using traditional colonoscopes, the reported AMR for a single standard colonoscopy has been estimated to be 10% to 30%.[18–21] However, if a wide-viewing angle colonoscope is used for the second pass, AMR may be as high as 31%[3] to 41%.[4] This high miss rate is thought to translate into a higher risk of developing interval cancers for patients who undergo routine colonoscopy. By enlarging the visual field, using technology such as FUSE colonoscopy, AMR may be reduced to 7% to 20%.[3,4] Nevertheless, subtle polyps on the endoscopy screen can still be missed by the endoscopist, which is self-evident by the non-0 miss rate of the wide viewing angle colonoscopies and similar devices.[22–26] Furthermore, it can be challenging for an endoscopist to be fully vigilant to every section of the monitors in a multiscreen setting in colonoscopy.[27,28] In addition, visual gaze patterns differ between endoscopists, and it has been shown that endoscopists with a wider visual gaze pattern or center-looking visual gaze pattern may have a higher adenoma or polyp detection rate than endoscopists with other visual gaze patterns.[29,30]

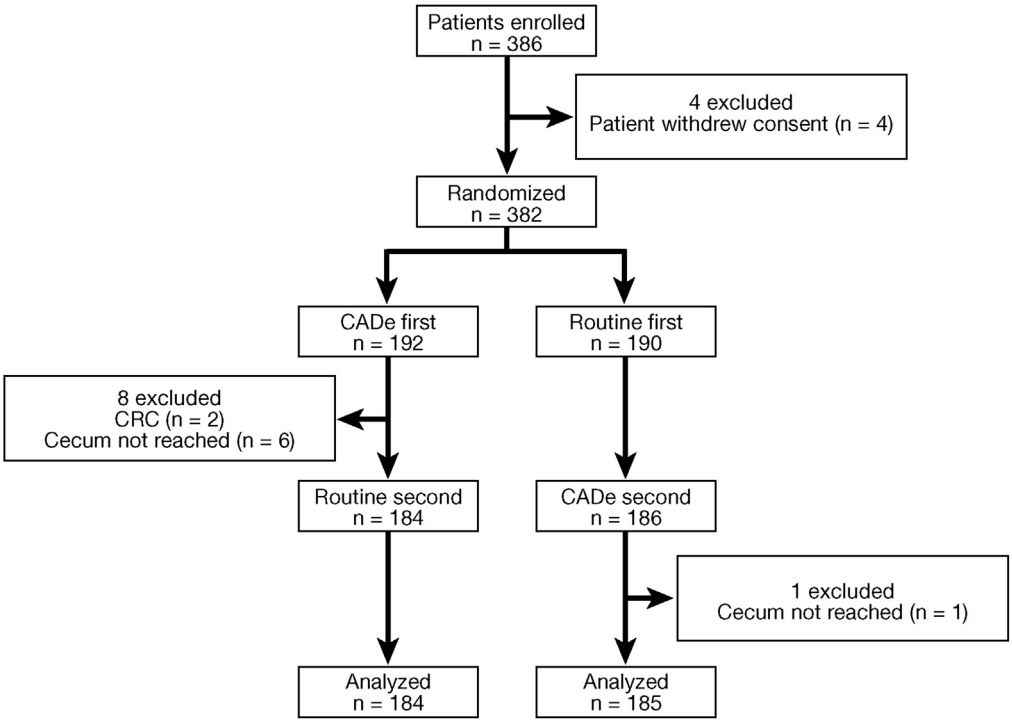

Figure 1. Flow diagram of enrollment.

Finally, "inattentional blindness"[31,32] and "change blindness"[33] phenomena may add to intraproceduralist variability, and neither wider-viewing colonoscopes nor second observer strategies may completely address these issues. Therefore, high-performance CADe may serve as a more standardized "second eye" in assisting the endoscopist to avoid missing any lesion.

In this study, overall AMR was significantly lower in the CADe colonoscopy arm (13.89% vs 40.00%, $P < .0001$). This AMR is comparable to the reduction in AMR seen when FUSE technology is used (7%–20%).[3,4] This indicates missed diagnosis by lack of recognition might be an equally important issue as nonvisualization. Moreover, results in this study are comparable with those of Western and Japanese studies, which similarly show a 30% to 41% AMR[3,4] in the routine colonoscopy groups compared with an AMR of 40% in our white-light–first group.

AMR was significantly lower for both diminutive (<5 mm) and small adenomas (5–9 mm) in the CADe colonoscopy group compared with the routine colonoscopy group in this tandem study. Notably, CADe here is shown to reduce the miss rate in the ascending, transverse, and descending colon, whereas FUSE and similar approaches, which aim at enlarging the visual field, mainly seem to primarily provide benefits in the right colon where the folds are deeper.[1,3,4] Consistent with our previous studies, CADe reduces the miss rate of nonpedunculated adenomas. However, there was no statistical difference in the miss rate of large adenomas, advanced adenomas, and SSAs/Ps, a fact likely due to limited sample size and corresponding low statistical power for these specific groups of polyps. Similar findings were seen in the J-FUSE study.[3]

Moreover, no difference in miss rates of SSAs/Ps is suggested due to low numbers and insufficient powering. It is also possible that the learning images used to train the CADe system were limited by the experience of average endoscopists. An exclusive study demonstrated the per-image sensitivity of this CADe system on small SSAs/Ps was 80%, which is <94%, the per-image sensitivity of the conventional adenomas and non-neoplastic polyps.[34] Future improvement in CADe should be directed to sensitively and specifically detect hard-to-detect SSAs/Ps collected among more extensive sources. Further studies should also look at AMR for advanced adenoma and SSAs/Ps, with a larger sample size aimed at detecting a statistically significant difference.

In this study, some missed adenomas did not appear on the screen during the first pass and were detected due to additional exposure during the second pass, a situation that cannot be counted as a contribution from the CADe system. We therefore performed a post hoc video analysis and tried to measure a more "specific" AMR for only visible polyps, which we defined as AMR-V. Hence, we could compare CADe and the naked human eye exclusively on visible lesions. AMR-V represents the maximal possibility that the CADe could help to decrease the miss rate. Only 1.59% visible adenomas were missed by CADe colonoscopy, whereas 24.21% of visible polyps were missed in the routine colonoscopy group ($P < .001$). Furthermore, among the 23 initially missed visible adenomas by endoscopists, 10 (43.48%) were successfully detected by the CADe system in the post hoc video analysis. These data indicate that half of the initially missed visible adenomas could be addressed directly by CADe's alert.

Table 1. Baseline Information

Characteristics	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
Age, mean (SD), *y*	47.19 (10.38)	47.72 (10.82)	.628
BMI, mean (SD), *kg/m²*	23.21 (3.15)	23.19 (3.02)	.939
Indication, n (%)			.42
Screening	55 (29.73)	58 (31.52)	
Symptomatic	117 (63.24)	107 (58.15)	
Surveillance	13 (7.03)	19 (10.33)	
Sex, n (%)			.467
Female	99 (53.51)	91 (49.46)	
Male	86 (46.49)	93 (50.54)	
BMI category, n (%)			.593
<25 kg/m²	132 (71.35)	135 (73.37)	
25 to <30 kg/m²	51 (27.57)	45 (24.46)	
≥30 kg/m²	2 (1.08)	4 (2.17)	
Procedure time, n (%)	.831		
AM	96 (51.89)	98 (53.26)	
PM	89 (48.11)	86 (46.74)	
Endoscope, n (%)[b]			.5
EC-590ZW/M	2 (1.08)	0 (0.00)	
EC-L590WM	17 (9.19)	19 (10.33)	
EC-580RD/M	1 (0.54)	0 (0.00)	
EC-590WM	2 (1.08)	1 (0.54)	
EC-L590ZM	163 (88.11)	164 (89.13)	
Anesthesia, n (%)[c]	NA		
No	0 (0.00)	0 (0.00)	
Yes	185 (100.00)	184 (100.00)	
Boston Score, mean (SD)	7.19 (1.42)	7.11 (1.40)	.563
Boston Score rank, n (%)			.846
Inadequate (sum <6.0 or anyone <2.0)	24 (12.97)	25 (13.59)	
Adequate (sum ≥6.0 and everyone ≥2.0)	161 (87.03)	159 (86.41)	

BMI, body mass index; NSAID, nonsteroidal anti-inflammatory drug.
[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.
[b]Fujifilm, Tokyo, Japan.
[c]Anesthesia was administered with midazolam fentanyl or propofol by an anesthesiologist there to monitor for complications.

This study is the first study to analyze a specific AMR for visible lesions, which overcomes a common limitation of previous FUSE tandem studies,[3,4] which did not distinguish whether the additional detection of specific polyps was actually due to its wider viewing angle cameras. Noticeably, the miss rate is higher in the routine-CADe group not only of visible adenomas/polyps but also of invisible adenomas/polyps. To further break down this analysis on each operating endoscopist (Supplementary Table S4), the result is very similar among them. This indicates that endoscopists can focus more on exposing colon mucosa because of the enhanced CADe signal on the exposed polyps. Thus, it indicates that CADe not only increased polyps detection in the visual field but also increased the exposure of more polyps.

PDR, APC, and PPC were significantly higher in the CADe colonoscopy group compared with routine white-light colonoscopy in both first and second passes. These findings are consistent with previous comparative studies, which demonstrated the positive impact of CADe. The 67 total consistent false detections in the CADe colonoscopy was consistent with our previous studies, in which wrinkled mucosa consisted of the largest portion of false-positive lesions. Moreover, the similar withdrawal time (excluding the biopsy time) further demonstrated that the false alarm rate is low enough that withdrawal times are not affected during CADe withdrawal (Supplementary Table S1).

It should be noted that to alert visible lesions is only one of application scenarios of computer vision technology. Only with high-level manipulation of endoscopists can this technology play its best role. Therefore, another important application of artificial intelligence during colonoscopy is to alert suboptimal inspection,

Table 2. Analysis of Per-Lesion Miss Rate

Variable	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
Adenoma			
Detected at first pass	72	124	
Detected at second pass	48	20	
Miss rate, %	40.00 (31.23–48.77)	13.89 (8.24–19.54)	<.0001
Polyp			
Detected at first pass	132	248	
Detected at second pass	112	37	
Miss rate, %	45.90 (39.65–52.15)	12.98 (9.08–16.88)	<.0001
Advanced adenoma			
Detected at first pass	9	1	
Detected at second pass	3	1	
Miss rate, %	25.00 (0.50–49.50)	50.00 (−19.30 to 119.30)	>.99
SSAs/Ps			
Detected at first pass	1	0	
Detected at second pass	2	1	
Miss rate, %	66.67 (13.33–120.01)	100.00 (100.00–100.00)	.9978

NOTE: Data are presented as n or median (interquartile range).
[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or the *t* test.

including endoscopists' ignorance to inspect the back of folds and flexures, to fully inflate the lumen, to clean the lens and absorb the liquid, as well as unstable manipulation and too fast withdraw. Thus the CADe system, with a combination of a suboptimal inspection alert system as well as new optical models or accessories (such as FUSE and Endocuff), which enlarge the visual filed, can further increase the detection of colon cancer and any precancerous lesions.

This study has several limitations. First, AMR obtained in the tandem study cannot reflect the absolute miss rate, because some lesions might have been missed again in the second pass. For those possible missed polyps/adenomas detected by post hoc video analysis with CADe in the first pass, but not detected in the second pass during the study, there is no reliable way to further characterize these lesions without a third colonoscopy. However, the 34.78% and 26.49% ADR in CADe colonoscopy and routine colonoscopy

Table 3. Clinicopathologic Characteristics of Adenomas Missed With Routine and CADe Colonoscopy

Characteristics	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
Size, *mm*			
<5	39.66 (27.07–52.25)	13.11 (4.64–21.58)	.0015
5–9	46.94 (32.97–60.91)	13.75 (6.20–21.30)	<.0001
≥10	15.38 (−4.23 to 34.99)	33.33 (−20.01 to 86.67)	.4842
Morphologic type to			
Pedunculated	23.08 (0.18–45.98)	10.00 (−8.59 to 28.59)	.4241
Not pedunculated	42.45 (33.04–51.86)	14.18 (8.27–20.09)	<.0001
Laterally spreading tumor	0.00 (0.00–0.00)	Not applicable	
Location			
Cecum	50.00 (−19.30 to 119.30)	0.00 (0.00–0.00)	.5473
Ascending colon	39.13 (19.18–59.08)	6.67 (−2.26 to 15.60)	.0095
Transverse colon	45.16 (27.64–62.68)	16.33 (5.98–26.68)	.0065
Descending colon	40.91 (20.36–61.46)	12.50 (−0.73 to 25.73)	.0364
Sigmoid colon	40.62 (23.60–57.64)	18.18 (5.02–31.34)	.0514
Rectum	20.00 (−4.79 to 44.79)	20.00 (−15.06 to 55.06)	>.99

NOTE: Data are presented as the median (interquartile range).
[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.

Table 4. Miss Rate of Visible and Invisible Adenomas and Polyps

Variable	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
AMR-V	0.2421	0.0159	<.001
PMR- V	0.3089	0.0236	<.001
AMR-INV	0.2500	0.1268	.016
PMR-INV	0.2707	0.1111	<.001

[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.

are the highest in Chinese data[35–38] in a population younger than a guideline-recommended screening population; thus, we believe the result is meaningful and representative.

Second, this open-label trial might introduce subjective bias, because endoscopists might put more effort in when being observed or might relax and rely on the CADe in nonblinded trials, leading to an overestimation or underestimation of the effectiveness of CADe system. However, the 34.78% and 26.49% ADR for CADe colonoscopy or routine colonoscopy was consistent with our double-blinded study,[5] in which the same endoscopy models were used, and the withdrawal time was also similar in 2 groups, which could be an indirect marker of attentiveness. In addition, the overall ADR, PDR, APC, and PPC in both passes were not different between the CADe colonoscopy-first group and routine colonoscopy-first group, which indicates that the possibility of missing adenomas or polyps is not biased after 2 passes and is independent of the order. These findings suggest that there is likely minimal subjective bias seen in the endoscopists used in this study.

Third, because tandem colonoscopy in each patient was performed by the same endoscopist, there might be "one and done phenomenon,"[39–41] whereby endoscopists may be less careful when examining the rest of the colon after identifying a single adenoma and might be less attentive in the second pass procedure. However, a single endoscopist design may introduce minimal interobserver variation, which is a goal for this study.

Fourth, we did not restrict the study population to screening-only participants according to guidelines; thus, the results might not generalizable to a typical screening population in which the absolute number of adenomas is higher.

Fifth, only skilled endoscopists were allowed to participate in this study as colonoscopy performers; thus, the results might not be generalizable to junior endoscopists or trainees. How this CADe system will affect AMR as a clinical routine in practice is less clearly demonstrated in this study, because only 3 endoscopists participated. Reproducing the findings among more endoscopists of varying experience would appear warranted.

Sixth, the judgments made by the panel of 3 experts who reviewed the video record were not a gold standard as pathology and thus might introduce subjective bias.

Finally, the new-generation models with image enhanced technologies, such as Linked Color Imaging by Fujifilm, could offer better visualization[42] and have the potential to supersede white-light colonoscopy; thus, the effectiveness of CADe using the latest models of endoscope should be further investigated.

Table 5. ADR, PDR, APC, and PPC

Variable	Routine-CADe group (N = 185)	CADe-routine group (N = 184)	*P* value[a]	Odds ratio	95% confidence interval	Interval
Whole process						
PDR	0.5514	0.6359	.099	1.421	0.936–2.157	1.221
ADR	0.3568	0.4239	.186	1.327	0.872–2.018	1.146
Average number of						
Detected polyps	1.3189	1.5489	.065	1.174	0.990–1.393	0.403
Detected adenomas	0.6486	0.7826	.129	1.207	0.947–1.537	0.59
First Pass						
PDR	0.3784	0.5598	.001	2.089	1.378–3.167	1.789
ADR	0.2649	0.3478	.085	1.48	0.948–2.312	1.364
Average number of						
Detected polyps	0.7135	1.3478	<.001	1.889	1.529–2.333	0.804
Detected adenomas	0.3892	0.6739	<.001	1.732	1.295–2.315	1.02
Second Pass						
PDR	0.3784	0.1902	<.001	0.386	0.240–0.619	0.379
ADR	0.1838	0.1087	.043	0.542	0.299–0.982	0.683
Average number of						
Detected polyps	0.6054	0.2011	<.001	0.332	0.229–0.482	0.253
Detected adenomas	0.2595	0.1087	.001	0.419	0.249–0.706	0.457

[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.

Table 6. Analysis by Patient Findings

Variable	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
Patients with adenoma			
Detected at first pass	49	64	
Detected at second pass	34	20	
Detected at second pass for the first time	17	14	
Detection rate at first pass, %	26.49 (20.13–32.85)	34.78 (27.90–41.66)	.0846
Miss rate, %	25.76 (19.46–32.06)	17.95 (12.40–23.50)	.258

NOTE: Data are presented as n or median (interquartile range).
[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.

Conclusion

The results from this study suggest a significantly lower AMR when a CADe technology is used compared with routine white-light colonoscopy. The detection of diminutive and small adenomas with nonadvanced histology and nonpedunculated shape could be effectively improved by CADe colonoscopy. The CADe colonoscopy has the potential to improve the clinical efficacy of screening and surveillance colonoscopy, with the goal of further decreasing the risk of interval colorectal cancer development.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at https://doi.org/10.1053/j.gastro.2020.06.023.

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Correspondence
Address correspondence to: Xun Xiao, Department of Gastroenterology, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, No. 32 West Second Section, First Ring Rd, Chengdu, Sichuan 610042, China. e-mail: xiaoxun001@outlook.com.

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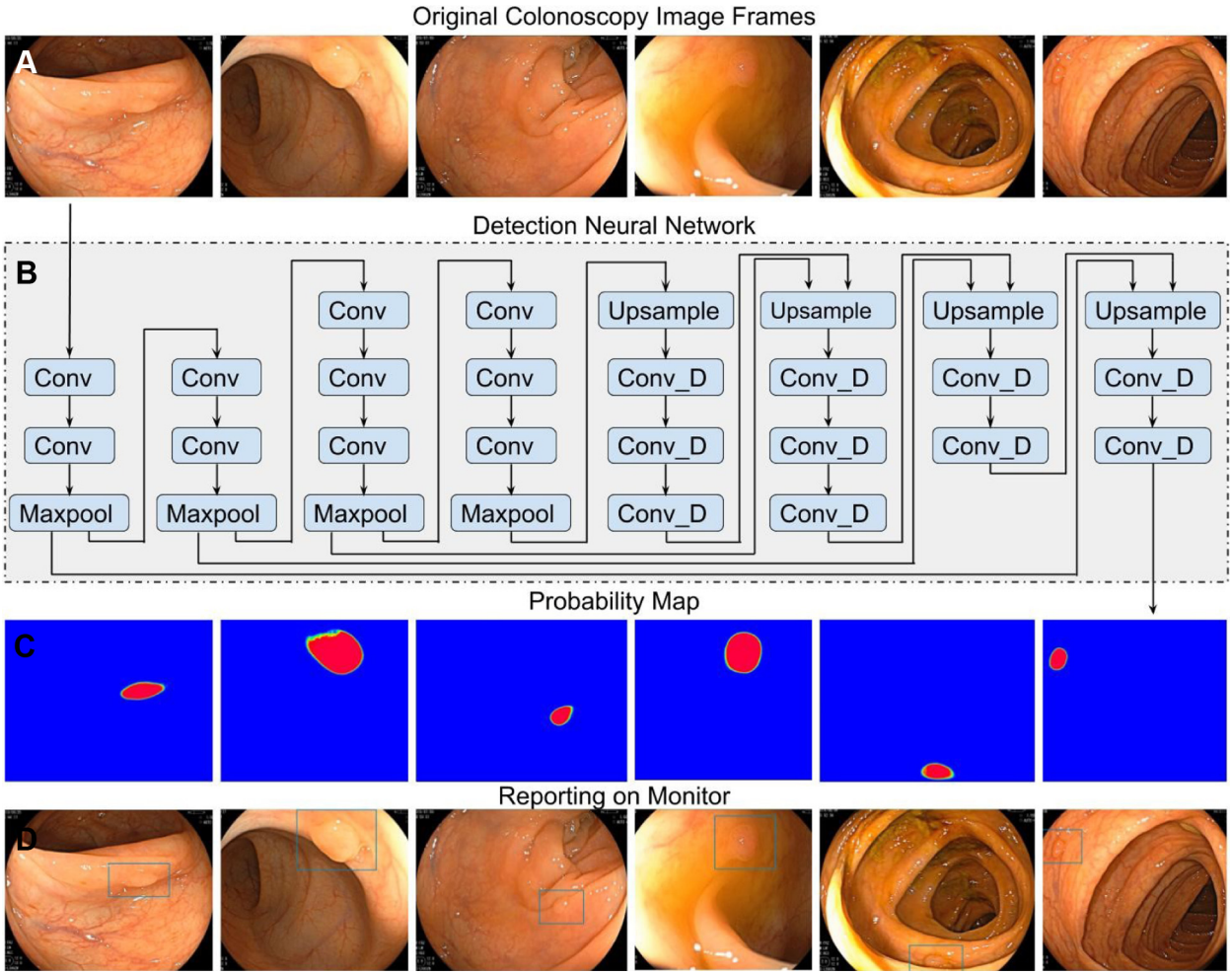
CRediT Authorship Contributions
Pu Wang, M.D (Conceptualization: Lead; Formal analysis: Lead; Methodology: Lead; Project administration: Lead; Writing – original draft: Lead; Writing – review & editing: Lead). Peixi Liu, MM (Conceptualization: Supporting; Data curation: Lead; Investigation: Lead). Jeremy R Glissen Brown, MD (Conceptualization: Supporting; Writing – review & editing: Equal). Tyler M Berzin, MD (Conceptualization: Supporting; Writing – review & editing: Equal). Guanyu Zhou, MM (Conceptualization: Supporting; Investigation: Equal). Shan Lei, MD (Conceptualization: Supporting; Investigation: Equal). Xiaogang Liu, MM (Data curation: Lead; Supervision: Lead). Liangping Li, MM (Data curation: Equal; Supervision: Equal). Xun Xiao, MM (Conceptualization: Equal; Investigation: Equal; Methodology: Supporting).

Conflicts of interest:
The authors disclose no conflicts. The CADe system (EndoScreener) was developed by Shanghai Wision AI Co, Ltd. The system was provided free-of-charge for the purpose of this study. Employees in the company were not involved in the clinical trial in any way, including in study design, statistical analysis, or manuscript writing.



Supplementary Figure S1. Schematic of the automatic polyp detection algorithm. (*A*) Original colonoscopy image frames generated during regular colonoscopy procedures. (*B*) Deep convolutional neural network: SegNet architecture (http://mi.eng.cam.ac.uk/projects/segnet/), which calculates the probability of belonging to a polyp for each pixel in the input colonoscopy image frame. (*C*) Probability map, which shows the probability of belonging to a polyp (blue represents probability = 0, red represents probability = 1, and color in between represents 0 < probability < 1), for each pixel in the input image frame. (*D*) Based on the probability map, the hollow blue boxes are added to the original image, to highlight the polyp areas for the observing clinicians.

Supplementary Table S1. Time to the Cecum and Withdrawal Time

	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
Time to the cecum at first pass, *min*	3.54 (2.08–4.99)	3.30 (1.96–4.64)	.107
Time to the cecum at second pass, *min*	2.73 (1.00–4.47)	2.42 (1.16–3.68)	.048
Withdrawal time at first pass, *min*	7.14 (5.50–8.79)	7.85 (5.48–10.21)	.001
Withdrawal time except biopsy time at first pass, *min*	6.51 (5.45–7.57)	6.55 (5.34–7.77)	.745
Withdrawal time at second pass, *min*	6.73 (5.36–8.10)	6.34 (5.53–7.15)	.001
Withdrawal time except biopsy time at second pass, *min*	6.04 (5.29–6.79)	6.14 (5.50–6.79)	.146
	Overall routine (n = 369)	Overall CADe (n = 369)	
Time to the cecum, *min*	2.98 (1.51–4.45)	3.02 (1.44–4.59)	.74
Withdrawal time, *min*	6.74(5.39–8.10)	7.29 (5.27–9.30)	<.001

NOTE: Data are presented as the median (interquartile range).
[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.

Supplementary Table S2. Adenoma risk factors

Characteristics	Routine-CADe group (n = 185)	CADe-routine group (n = 184)	*P* value[a]
Family history of adenoma			.723
None	181 (97.84)	179 (97.28)	
Yes	4 (2.16)	5 (2.72)	
Family history of colon cancer	0.977		
None	172 (92.97)	171 (92.93)	
Yes	13 (7.03)	13 (7.07)	
Personal history of adenoma			.296
None	179 (96.76)	174 (94.57)	
Yes	6 (3.24)	10 (5.43)	
Diabetes mellitus			.285
No	176 (95.14)	179 (97.28)	
Yes	9 (4.86)	5 (2.72)	
Coronary artery disease			.084
No	182 (98.38)	184 (100.00)	
Yes	3 (1.62)	0 (0.00)	
Tobacco use			.197
No	129 (69.73)	117 (63.59)	
Yes	56 (30.27)	67 (36.41)	
Alcohol use			.740
No	105 (56.76)	108 (58.70)	
Yes	80 (43.24)	76 (41.30)	
Acetylsalicylic acid use			.986
No	180 (97.30)	179 (97.28)	
Yes	5 (2.70)	5 (2.72)	
NSAID use			.484
No	180 (97.30)	181 (98.37)	
Yes	5 (2.70)	3 (1.63)	
Folate use			.403
No	183 (98.92)	180 (97.83)	
Yes	2 (1.08)	4 (2.17)	
Calcium/vitamin D use			.958
No	147 (79.46)	146 (79.35)	
Yes	38 (20.54)	38 (20.65)	
Hormone replacement therapy use			.314
No	185 (100.00)	183 (99.46)	
Yes	0 (0.00)	1 (0.54)	

NOTE: Data are presented as n (%).
NSAID, nonsteroidal anti-inflammatory drug.
[a]*P* value from χ^2 test or Fisher's exact test, as appropriate, or *t* test.

Supplementary Table S3. Consistent false detections with the CADe system

Variable	CADe group (N = 369)[a]
Consistent false detection, n (%)	67 (100.00)
Bubble	8 (11.94)
Feces	11 (16.42)
Undigested debris	16 (23.88)
Wrinkled mucosa	22 (32.84)
Local inflammation	3 (4.48)
Local bleeding	0 (0.00)
Rounded drug capsules	3 (4.48)
Other (circular blood vessel, scar, diverticulum, etc)	4 (5.97)
Missed polyp, n (%)	0 (0.00)

[a]N (%).

Supplementary Table S4. AMR and PMR of 3 Endoscopists

	Endoscopist 1			Endoscopist 2			Endoscopist 3		
Variable	Routine-CADe group (n = 54)	CADe-routine group (n = 63)	*P* value	Routine-CADe group (n = 78)	CADe-routine group (n = 73)	*P* value	Routine-CADe group (n = 53)	CADe-routine group (n = 48)	*P* value
Adenoma									
Detected at first pass	27	51		25	39		20	34	
Detected at second pass	14	8		19	7		15	5	
Miss rate, %	34.15 (19.63–48.67)	13.56 (4.82–22.30)	.0002	43.18(28.54–57.82)	15.22 (4.84–25.60)	<.0001	42.86 (26.46–59.26)	12.82 (2.33–23.31)	<.0001
Polyp									
Detected at first pass	48	92		54	95		30	61	
Detected at second pass	28	13		40	14		44	10	
Miss rate, %	36.84 (25.99–47.69)	12.38(6.08–18.68)	.0175	42.55(32.55–52.55)	12.84 (6.56–19.12)	.0047	59.46 (48.27–70.65)	14.08 (5.99–22.17)	.0056
Advanced adenoma									
Detected at first pass	3	0		2	0		4	1	
Detected at second pass	0	0		1	1		2	0	
Miss rate, %	0.00 (0.00–0.00)	NA		33.33 (−20.01 to 86.67)	100.00 (100.00–100.00)	>.99	33.33 (-4.39–71.05)	0.00 (0.00–0.00)	NA
SSA/P									
Detected at first pass	0	0		1	0		0	0	
Detected at second pass	0	0		2	0		0	1	
Miss rate, %	NA	NA		66.67 (13.33–120.01)	NA		NA	100.00 (100.00–100.00)	NA

NOTE: Data are presented as n or mean (interquartile range).
NA, not applicable.