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Linked-color imaging with or without artificial intelligence for adenoma detection: a randomized trial

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received 18.5.2023
accepted after revision 3.1.2024
accepted manuscript online 8.1.2024
published online 1.2.2024

Bibliography
Endoscopy 2024; 56: 376–383
DOI 10.1055/a-2239-8145
ISSN 0013-726X

Georg Thieme Verlag KG, Rüdigerstraße 14,
70469 Stuttgart, Germany

Supplementary Material
Supplementary Material is available under
https://doi.org/10.1055/a-2239-8145

Scan this QR-Code for the author commentary.

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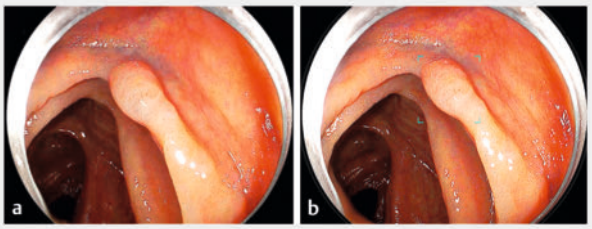
ABSTRACT

Background Adenoma detection rate (ADR) is an important indicator of colonoscopy quality and colorectal cancer incidence. Both linked-color imaging (LCI) with artificial intelligence (LCA) and LCI alone increase adenoma detection during colonoscopy, although it remains unclear whether one modality is superior. This study compared ADR between LCA and LCI alone, including according to endoscopists' experience (experts and trainees) and polyp size.

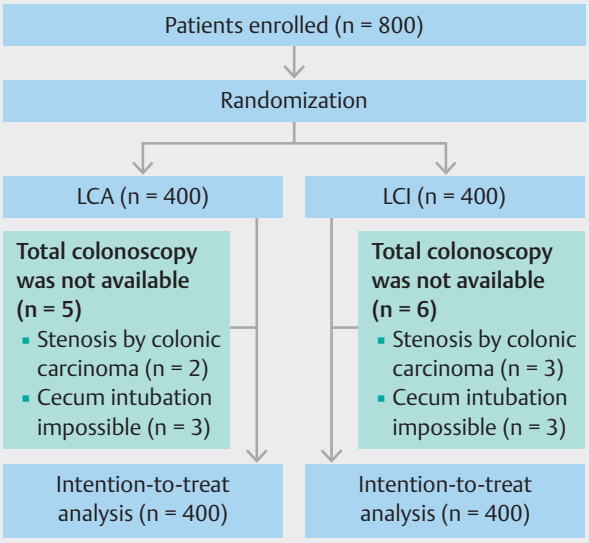
Methods Patients undergoing colonoscopy for positive fecal immunochemical tests, follow-up of colon polyps, and abdominal symptoms at a single institution were randomly assigned to the LCA or LCI group. ADR, adenoma per colonoscopy (APC), cecal intubation time, withdrawal time, number of adenomas per location, and adenoma size were compared.

Results The LCA (n = 400) and LCI (n = 400) groups showed comparable cecal intubation and withdrawal times. The LCA group showed a significantly higher ADR (58.8% vs. 43.5%; P<0.001) and mean (95%CI) APC (1.31 [1.15 to 1.47] vs. 0.94 [0.80 to 1.07]; P<0.001), particularly in the ascending colon (0.30 [0.24 to 0.36] vs. 0.20 [0.15 to 0.25]; P = 0.02). Total number of nonpolypoid-type adenomas was also significantly higher in the LCA group (0.15 [0.09 to 0.20] vs. 0.08 [0.05 to 0.10]; P = 0.02). Small polyps (≤5, 6–9 mm) were detected significantly more frequently in the LCA group (0.75 [0.64 to 0.86] vs. 0.48 [0.40 to 0.57], P<0.001 and 0.34 [0.26 to 0.41] vs. 0.24 [0.18 to 0.29], P = 0.04, respectively). In both groups, ADR was not significantly different between experts and trainees.

Conclusions LCA was significantly superior to LCI alone in terms of ADR.



▶ **Fig. 1** Sessile serrated lesion detection by linked-color imaging (LCI). a LCI alone. b LCI assisted by artificial intelligence.



▶ **Fig. 2** Patient enrollment flow chart. LCA, linked-color imaging with artificial intelligence; LCI, linked-color imaging alone.

Introduction

Colorectal cancer is the second leading cause of cancer-related deaths worldwide, with an estimated 1.9 million new cases and 930 000 deaths annually [1]. The adenoma detection rate (ADR) for the large intestine is associated with the colorectal cancer rate and is an important indicator of colonoscopy quality. The American Society for Gastrointestinal Endoscopy and the American College of Gastroenterology set the target ADR at ≥25% for patients with average risk aged ≥50 years [2]. Corley et al. reported a significant discrepancy of 7.4%–52.5% in the ADR among endoscopists, and showed that a 1% increase in the ADR leads to a 3% decrease in the colorectal cancer rate and a 5% decrease in the colorectal cancer mortality rate [3]. Furthermore, Kaminski et al. reported that the risk of interval cancer diagnosed between regular screenings is 10 times greater in patients whose endoscopist has an ADR of <20% than in those whose endoscopist has an ADR of ≥20% [4]. More than half of colorectal cancer cases are reportedly missed despite regular endoscopic examinations [5].

Image-enhanced endoscopy has recently been developed to improve the ADR in daily practice, and linked-color imaging (LCI) has attracted particular attention (▶ **Fig. 1**). The LASEREO laser endoscope (Fujifilm, Tokyo, Japan) combines two short-wavelength laser beams (410 nm and 450 nm) and a phosphor excited by a 450-nm laser output to enable white-light imaging, blue-laser imaging, and LCI observations [6]. Recent studies have indicated that using LCI increases background blood vessel visibility and enhances reddish hues; therefore, redness associated with inflammation, polyps, and cancer is enhanced, improving the ADR [7, 8]. In a systematic review and meta-analysis, Shinozaki et al. reported that, compared with white-light imaging, LCI had a greater ADR and polyp detection rate [9].

In recent years, the usefulness of artificial intelligence (AI) has been reported in solving complex multinomial problems in various fields, including computer-aided detection (CADe) in medicine. Large prospective trials have been conducted on colonoscopy AI, and a meta-analysis of these studies was recently published [10]. The authors reported that the ADR associated with CADe had 95% sensitivity and good discrimination ability [10]. Other meta-analyses of randomized controlled trials (RCTs) also reported that the ADR was significantly higher with the use of CADe [11, 12, 13]. The EC-02 CADe system, trained using >250 000 colonoscopy images, was developed to detect and characterize colorectal polyps. This CADe system is available in two modes, white-light imaging and LCI [14].

To the best of our knowledge, no study has compared the ADR and mean number of adenomas per colonoscopy (APC) between AI-assisted LCI (LCA) and LCI alone during colonoscopy. Therefore, this study aimed to compare the ADR between AI-assisted LCI and LCI colonoscopy in a large patient sample. Furthermore, we evaluated differences in ADRs between the LCA and LCI groups according to endoscopists' experience (experts and trainees) and polyp size.

Methods

Study design

This prospective RCT included patients from Saitama Medical University in Japan and was conducted from February 2022 to March 2023. The study protocol complied with the tenets of the revised Declaration of Helsinki (1989) and was approved by the appropriate institutional review board (2021–115). Written informed consent was obtained from all patients.

Patients

Patients aged ≥20 years undergoing colonoscopy following a positive fecal immunochemical tests, or for evaluation of abdominal symptoms, or follow-up for colorectal polyps were enrolled (▶ **Fig. 2**). The details of this study were explained to the patients orally and in writing. Patients who provided written informed consent were eligible for inclusion. The exclusion criteria were patients who underwent colonoscopy without bowel preparation, and those with intestinal obstruction, stenosis, fistula, a history of colorectal surgery, active inflammatory bowel disease, diverticulitis, or active or suspected colorectal bleeding.

Randomization and blinding

Patients were randomly assigned in a 1:1 ratio to undergo AI-assisted LCI colonoscopy (LCA group) or LCI colonoscopy alone (LCI group) via block randomization using computerized randomization lists. Anonymization was ensured by allocating codes specific to the study instead of using personal information such as patient name or identification. Allocation was concealed and kept in a sealed envelope, which was opened by a nurse just before initiation of scope withdrawal. Until that moment, the endoscopist was blinded to group assignment.

Colonoscopy procedure

Colonoscopy was performed using attached transparent hoods (D-201–12704 and D-201–13404; Olympus Medical Systems, Tokyo, Japan). MoviPrep (EA Pharma Co., Tokyo, Japan) laxative was used for bowel preparation. Either scopolamine butylbromide (10 mg) or glucagon (0.5 mg) was used. Furthermore, midazolam (1–4 mg) was used for conscious sedation only when the patient complained of abdominal discomfort or pain. The colonoscope used in this study was EC-L600ZP7 using the LASEREO 7000 system (Fujifilm Co.). The CAD EYE (EW10-EC02) endoscopic real-time diagnostic support function (Fujifilm Co.) was used to support lesion detection.

Colon cleansing quality was graded as poor, fair, or good according to the criteria reported by Aronchick et al. [15, 16]. Observations were conducted using white-light imaging during anal insertion and LCI during withdrawal. A biopsy or resection, followed by histopathological analysis was performed if polyps were observed. All colonoscopies were performed by one of five endoscopists: three experts (completed >1000 colonoscopies) and two trainees (completed <1000 colonoscopies). No endoscopists had red–green color blindness.

Histopathology

The specimens were fixed in 10% formalin and stained with hematoxylin and eosin for evaluation. The polyps were classified as tubular adenoma, villous adenoma, tubulovillous adenoma, traditional serrated adenoma, sessile serrated lesion (SSL), hyperplastic polyp, juvenile polyp, or tubular adenocarcinoma.

Outcome measurement

Colonic polyps were histopathologically diagnosed. The primary endpoint was the ADR, defined as the percentage of patients in whom adenomas were detected. The secondary endpoints were the APC, cecal intubation time, withdrawal time, cleanliness score (Aronchick scale) [16], APC of diminutive adenomas, APC in each segment, adenoma histopathology and morphology, SSL detection rate, and mean number of SSLs detected per colonoscopy. The cecal intubation time, withdrawal time (excluding treatment time), ADR, and APC were evaluated and compared between the two groups. In addition, data for polyp location, size, and type were compared between experts and trainees.

Sample size calculation and statistical analyses

At our hospital, the ADR was 0.45 on observation using LCI and 0.55 on observation using AI-assisted LCI (0.1 higher than the ADR with LCI alone). We considered α and power values as 0.05 and 0.80, respectively. Enrollment ratio 1 provided 390 patients for each group. Considering a withdrawal rate, the total target sample size was set to 800 patients.

Continuous data are expressed as mean, and categorical data are expressed as number and percentage. Continuous and categorical variables were compared between groups using Student's *t*-test and Pearson's chi-squared test, respectively. The 95%CIs were calculated, and the relative risk (RR) was also calculated for ADR. Furthermore, subgroup analysis was performed according to the indication (fecal immunochemical test and other). All statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, New York, USA). Statistical significance was considered at $P<0.05$, and all tests were two sided.

Results

Among the 800 patients enrolled from Saitama Medical University Hospital, 400 patients were allocated to the LCA group and another 400 patients to the LCI alone group. Five patients in the LCA group and six in the LCI group had colonic stenosis owing to advanced colorectal cancer or difficulty with cecal intubation (difficulty reaching the terminal ileum). All 800 patients were included in the intention-to-treat analysis (▶ **Fig. 2**). The mean patient age was 65.1 years (95%CI 63.7 to 66.5) in the LCA group and 66.1 years (95%CI 64.7 to 67.4) in the LCI group, and there were no significant sex differences between the groups. Overall, 61 patients (7.6%) had a history of abdominal surgery, 115 (14.4%) had diabetes, 89 (11.1%) had diverticulosis, and 56 (7.0%) had ulcerative colitis in remission (mucosal healing). The reasons for colonoscopy were positive fecal immunochemical test results, polyp follow-up, bloody stool, screening, and symptoms such as lower abdominal pain (▶ **Table 1**).

The mean cecal intubation time and withdrawal time were not significantly different between the two groups. Bowel cleanliness and the number of patients between experts and trainees were also not significantly different between the groups (▶ **Table 2**). There was no mucosal injury in either group.

The number of detected polyps was 525 and 374 in the LCA and LCI groups, respectively. The ADR was 58.8% (95%CI 53.8 to 63.6) and 43.5% (95%CI 38.6 to 48.5) in the LCA and LCI groups, respectively (RR 1.351, 95%CI 1.176 to 1.551; $P<0.001$) (▶ **Table 3**). The ADR for experts was 56.2% (95%CI 49.9 to 62.3) and 46.2% (95%CI 39.9 to 52.6) in the LCA and LCI groups, respectively (RR 1.216, 95%CI 1.024 to 1.444; $P=0.02$). For trainees, the ADR was 63.4% (95%CI 54.9 to 71.3) and 38.9% (95% CI 31.1 to 47.2) in the LCA and LCI groups, respectively (RR 1.628, 95%CI 1.285 to 2.063; $P<0.001$). Differences in ADRs between experts and trainees in the LCA and LCI groups were as follows: expert vs. trainee, 56.2% (95%CI 49.9 to 62.3) vs.

▶ **Table 1** Clinical characteristics of patients undergoing colonoscopy with linked-color imaging, with and without assistance from artificial intelligence.

	LCA (n = 400)	LCI (n = 400)	*P* value
Age, mean [95%CI], years	65.1 [63.7 to 66.5]	66.1 [64.7 to 67.4]	0.33[1]
Sex, n (%) [95%CI]			0.67[2]
▪ Male	223 (55.8) [50.7 to 60.7]	229 (57.3) [52.2 to 62.2]	
▪ Female	177 (44.3) [39.3 to 49.3]	171 (42.8) [37.8 to 47.8]	
Complications/history, n (%) [95%CI]			0.93[2]
▪ Prior abdominal surgery	31/155 (20.0) [14.0 to 27.2]	30/166 (18.1) [12.5 to 24.8]	
▪ Diabetes	53/155 (34.2) [26.8 to 42.2]	62/166 (37.3) [30.0 to 45.2]	
▪ Diverticulosis	43/155 (27.7) [20.9 to 35.5]	46/166 (27.7) [21.1 to 35.2]	
▪ Ulcerative colitis	28/155 (18.1) [12.4 to 25.0]	28/166 (16.9) [11.5 to 23.4]	
Indication, n (%) [95%CI]			0.94[2]
▪ FIT	136 (34.0) [29.4 to 38.9]	129 (32.3) [27.7 to 37.1]	
▪ Symptoms	83 (20.8) [16.9 to 25.1]	82 (20.5) [16.7 to 24.8]	
▪ Polyp surveillance	75 (18.8) [15.0 to 22.9]	77 (19.3) [15.5 to 23.5]	
▪ Screening	106 (26.5) [22.2 to 31.1]	112 (28.0) [23.7 to 32.7]	

LCA, linked-color imaging with artificial intelligence-assisted colonoscopy; LCI, linked-color imaging-assisted colonoscopy; FIT, fecal immunochemical test.
[1]Student's *t* test.
[2]Chi-squared test.

▶ **Table 2** Colonoscopy details of patients undergoing colonoscopy with linked-color imaging, with and without assistance from artificial intelligence.

	LCA (n = 400)	LCI (n = 400)	Between-group differences[1] [95%CI]	*P* value
Cecal intubation time, mean [95%CI], minutes	6.4 [6.1 to 6.7]	6.8 [6.5 to 7.1]	−0.40 [−0.85 to 0.04]	0.07[2]
Withdrawal time, mean [95%CI], minutes	7.0 [6.8 to 7.2]	7.0 [6.8 to 7.2]	−0.01 [−0.28 to 0.26]	0.96[2]
Cleanliness score, n (%) [95%CI]				0.23[3]
▪ Good	390 (97.5) [95.5 to 98.8]	383 (96.0) [93.6 to 97.7]	1.51 [−0.95 to 3.97]	
▪ Fair	10 (2.5) [1.2 to 4.5]	16 (4.0) [2.3 to 6.4]	−1.51 [−3.97 to 0.95]	
Endoscopist, n (%) [95%CI]				0.61[3]
▪ Expert	258 (64.5) [59.6 to 69.2]	251 (62.8) [57.8 to 67.5]	1.75 [−4.92 to 8.42]	
▪ Trainee	142 (35.5) [30.8 to 40.4]	149 (37.3) [32.5 to 42.2]	−1.75 [−8.42 to 4.92]	

LCA, linked-color imaging with artificial intelligence-assisted colonoscopy; LCI, linked-color imaging-assisted colonoscopy.
[1]LCA – LCI.
[2]Student's *t* test.
[3]Chi-squared test.

63.4% (95%CI 54.9 to 71.3) (between-group difference −7.18 [95%CI −17.15 to 2.79]; *P* = 0.16) in the LCA group and 46.2% (95%CI 39.9 to 52.6) vs. 38.9% (95%CI 31.1 to 47.2) (between-group difference 7.29 [95%CI −2.68 to 17.26]; *P* = 0.16) in the LCI group (see **Table 1s** in the online-only Supplementary material). No significant difference was found in either of the groups.

The APC was significantly higher in the LCA group than in the LCI group (1.31 [95%CI 1.15 to 1.47] vs. 0.94 [95%CI 0.80 to 1.07]; between-group difference 0.378 [95%CI 0.164 to 0.591]; *P*<0.001) (▶ **Table 4**).

The number of adenomas in the ascending colon was significantly higher in the LCA group than in the LCI group (0.30 [95% CI 0.24 to 0.36] vs. 0.20 [95%CI 0.15 to 0.25]; between-group

▶ **Table 3** Adenoma detection with linked-color imaging, with and without assistance from artificial intelligence.

	LCA (n = 400)	LCI (n = 400)	Between-group differences[1] [95%CI]	*P* value[2]
ADR, n (%) [95%CI]	235 (58.8) [53.8 to 63.6]	174 (43.5) [38.6 to 48.5]	15.25 [8.40 to 22.10]	<0.001
▪ ADR in experts	145/258 (56.2) [49.9 to 62.3]	116/251 (46.2) [39.9 to 52.6]	9.99 [1.34 to 18.63]	0.02
▪ ADR in trainees	90/142 (63.4) [54.9 to 71.3]	58/149 (38.9%) [31.1 to 47.2]	24.45 [13.31 to 35.59]	<0.001
Relative risk [95%CI] (vs. LCI)				
▪ ADR	1.351 [1.176 to 1.551]	–	–	
▪ ADR in experts	1.216 [1.024 to 1.444]	–	–	
▪ ADR in trainees	1.628 [1.285 to 2.063]	–	–	

[LCA, linked-color imaging with artificial intelligence-assisted colonoscopy; LC, linked-color imaging-assisted colonoscopy; ADR, adenoma detection rate.
[1]LCA – LCI.
[2]Chi-squared test.

difference 0.100 [95%CI 0.019–0.181]; *P* = 0.02) (▶ **Table 4**). However, no significant differences were found between the LCA and LCI groups in the number of adenomas in the cecum (0.10 [95%CI 0.07 to 0.14] vs. 0.06 [95%CI 0.03 to 0.08]; between-group difference 0.045 [95%CI 0.000 to 0.090]; *P* = 0.05), transverse colon (0.28 [95%CI 0.21 to 0.34] vs. 0.21 [95%CI 0.15 to 0.26]; between-group difference 0.073 [95%CI –0.011 to 0.156; *P* = 0.09), descending colon (0.19 [95%CI 0.14 to 0.23] vs. 0.13 [95%CI 0.08 to 0.17]; between-group difference 0.058 [95%CI –0.005 to 0.120]; *P* = 0.07), sigmoid colon (0.36 [95%CI 0.29 to 0.43] vs. 0.28 [95%CI 0.22 to 0.33]; between-group difference 0.085 [95%CI –0.002 to 0.172]; *P* = 0.06), or rectum (0.11 [95%CI 0.07 to 0.14] vs. 0.07 [95%CI 0.05 to 0.10]; between-group difference 0.035 [95%CI –0.010 to 0.080]; *P* = 0.13).

Adenomas were classified based on polyp size as follows: ≤5, 6–9, and ≥10 mm. Specifically, adenomas measuring ≤5 mm (0.75 [95%CI 0.64 to 0.86] vs. 0.48 [95%CI 0.40 to 0.57]; between-group difference 0.270 [95%CI 0.129 to 0.411]; *P*<0.001) and 6–9 mm (0.34 [95%CI 0.26 to 0.41] vs. 0.24 [95% CI 0.18 to 0.29]; between-group difference 0.100 [95%CI 0.007 to 0.193]; *P* = 0.04) were detected significantly more frequently in the LCA group than in the LCI group (▶ **Table 4**). No significant difference was found in the detection rate for adenomas ≥10 mm.

Pathological findings differed significantly between the LCA and LCI groups for tubular adenomas (1.03 [95%CI 0.89 to 1.16] vs. 0.79 [95%CI 0.66 to 0.91]; between-group difference 0.238 [95%CI 0.055 to 0.420]; *P* = 0.01) and SSLs (0.05 [95%CI 0.02 to 0.08] vs. 0.02 [95%CI 0.00 to 0.03]; between-group difference 0.035 [95%CI 0.004 to 0.066]; *P* = 0.03) (▶ **Table 4**). However, the SSL detection rate was significantly higher in the LCA group than in the LCI group (4.0% vs. 1.0%; between-group difference 3.00 [95%CI 0.85 to 5.15]; *P* = 0.007) (▶ **Table 5**).

Macroscopic findings for the LCA and LCI groups were sessile, nonpolypoid, and peduncular. The APC for sessile adenomas was significantly higher in the LCA group than in the LCI group (0.98 [95%CI 0.85 to 1.11] vs. 0.60 [95%CI 0.50 to 0.70]; between-group difference 0.378 [95%CI 0.211 to 0.544]; *P*<0.001) (▶ **Table 4**). Additionally, the APC for nonpolypoid adenomas was significantly higher in the LCA group than in the LCI group (0.15 [95%CI 0.09 to 0.20] vs. 0.08 [95%CI 0.05 to 0.10]; between-group difference 0.070 [95%CI 0.012 to 0.128]; *P* = 0.02).

Subgroup analysis by indication (fecal immunochemical test and other) showed a significantly higher ADR in the LCA group (**Table 2s**).

Discussion

In this study, we aimed to compare the ADRs achieved during colonoscopy using LCI with AI assistance and LCI alone to evaluate the usefulness of CADe. The results revealed that incorporation of AI assistance with LCI observations yielded significantly higher ADRs compared with observations using LCI alone. Although improvements in the ADR and APC have been reported with LCI alone or with AI-assisted observation using white-light imaging, to the best of our knowledge, this is the first report of observations with AI-assisted LCI and the first study to compare this modality with LCI alone.

One factor associated with the ADR is endoscopist experience. Significant differences in the ADR have been reported between physicians whose average extraction time was <6 minutes and those whose average extraction time was >6 minutes [17]. Follow-up studies found that an extraction time of 8–10 minutes is essential for achieving a sufficient ADR [18], thus indicating that a longer observation time improves the ADR. In the current study, we examined whether there was a difference in the ADR between the two imaging groups according to endoscopist experience (i.e. experts vs. trainees). The results showed that although the ADR for experts was lower in the LCA group (56.2% vs. 63.4%; *P* = 0.16) and higher in the LCI group (46.2% vs. 38.9%; *P* = 0.16) (**Table 1s**), the difference between experts and trainees was not significant in either group. It is notable, however, that trainees had a better ADR than experts with the use of LCA.

▶ **Table 4** Adenoma detection with linked-color imaging, with and without assistance from artificial intelligence.

	LCA (n = 400)	LCI (n = 400)	Between-group differences[1] [95%CI]	*P* value[2]
APC, mean [95%CI]	1.31 [1.15 to 1.47]	0.94 [0.80 to 1.07]	0.378 [0.164 to 0.591]	<0.001
Size, mean [95%CI]				
▪ ≤5 mm	0.75 [0.64 to 0.86]	0.48 [0.40 to 0.57]	0.270 [0.129 to 0.411]	<0.001
▪ 6–9 mm	0.34 [0.26 to 0.41]	0.24 [0.18 to 0.29]	0.100 [0.007 to 0.193]	0.04
▪ ≥10 mm	0.23 [0.17 to 0.29]	0.21 [0.15 to 0.27]	0.018 [−0.071 to 0.106]	0.70
Morphology, mean [95%CI]				
▪ Sessile	0.98 [0.85 to 1.11]	0.60 [0.50 to 0.70]	0.378 [0.211 to 0.544]	<0.001
▪ Nonpolypoid	0.15 [0.09 to 0.20]	0.08 [0.05 to 0.10]	0.070 [0.012 to 0.128]	0.02
▪ Pedunculated	0.18 [0.13 to 0.23]	0.26 [0.19 to 0.33]	−0.080 [−0.166 to 0.006]	0.07
Colonic segment, mean [95%CI]				
▪ Cecum	0.10 [0.07 to 0.14]	0.06 [0.03 to 0.08]	0.045 [0.000 to 0.090]	0.05
▪ Ascending colon	0.30 [0.24 to 0.36]	0.20 [0.15 to 0.25]	0.100 [0.019 to 0.181]	0.02
▪ Transverse colon	0.28 [0.21 to 0.34]	0.21 [0.15 to 0.26]	0.073 [−0.011 to 0.156]	0.09
▪ Descending colon	0.19 [0.14 to 0.23]	0.13 [0.08 to 0.17]	0.058 [−0.005 to 0.120]	0.07
▪ Sigmoid colon	0.36 [0.29 to 0.43]	0.28 [0.22 to 0.33]	0.085 [−0.002 to 0.172]	0.06
▪ Rectum	0.11 [0.07 to 0.14]	0.07 [0.05 to 0.10]	0.035 [−0.010 to 0.080]	0.13
Histopathology, mean [95%CI]				
▪ Tubular adenoma	1.03 [0.89 to 1.16]	0.79 [0.66 to 0.91]	0.238 [0.055 to 0.420]	0.01
▪ Tubulovillous adenoma	0.07 [0.03 to 0.10]	0.03 [0.01 to 0.05]	0.035 [−0.007 to 0.077]	0.10
▪ SSL	0.05 [0.02 to 0.08]	0.02 [0.00 to 0.03]	0.035 [0.004 to 0.066]	0.03
▪ Villous adenoma	0.04 [0.02 to 0.06]	0.02 [0.00 to 0.03]	0.020 [−0.004 to 0.044]	0.10
▪ Traditional serrated adenoma	0.06 [0.03 to 0.09]	0.02 [0.01 to 0.04]	0.035 [0.000 to 0.070]	0.049
▪ High grade dysplasia	0.06 [0.03 to 0.09]	0.03 [0.01 to 0.05]	0.030 [−0.005 to 0.065]	0.09
▪ Submucosal adenocarcinoma	0.01 [0.00 to 0.02]	0.01 [0.00 to 0.02]	−0.003 [−0.015 to 0.010]	0.71
▪ Advanced carcinoma	0.03 [0.01 to 0.05]	0.03 [0.01 to 0.05]	0.005 [−0.021 to 0.031]	0.70

LCA, linked-color imaging with artificial intelligence-assisted colonoscopy; LCI, linked-color imaging-assisted colonoscopy; APC, adenomas per colonoscopy; SSL, sessile serrated lesion.
[1]LCA – LCI.
[2]Student's *t* test.

Furthermore, the ADR for trainees was 38.9% with LCI and 63.4% with LCA; this indicated that AI-assisted LCI may be particularly useful for trainees.

Despite physician experience, human error is unavoidable in polyp detection. However, the use of AI is expected to improve the skills of the endoscopist. An RCT comparing the ADR in colonoscopies with and without the use of CADe showed that the ADR was significantly higher in the group using CADe than in the group not using CADe [19]. Further, Luo et al. compared a CADe group with a non-CADe group using 64 134 polyp-positive and 48 065 polyp-negative images, and reported a significant improvement in the polyp detection rate in the CADe group [20]. Hassan et al. analyzed five RCTs with 4354 patients included in the final analysis and found that the pooled ADR was significantly higher in the CADe group than in the control group [21].

Despite this improvement, several studies have reported that there is no significant difference in the detection rate of advanced adenomas [12, 13, 15]. In the current study, we found no significant difference in the detection of polyps ≥10 mm, which is consistent with previous results. This suggests that although CADe colonoscopy has excellent performance in detecting lesions, ADR improvement may be limited to microadenomas. Although the ADR is a colonoscopy quality index, it is unclear whether the overdetection of microadenomas, with a relatively small risk of future cancer development, will reduce

▶ **Table 5** Detection of sessile serrated lesions with linked-color imaging, with and without assistance from artificial intelligence.

	LCA (n = 400)	LCI (n = 400)	Between-group differences[1] [95%CI]	*P* value
SSL detection, n (%) [95%CI]	16 (4.0) [2.3 to 6.4]	4 (1.0) [0.3 to 2.5]	3.00 [0.85 to 5.15]	0.007[2]
SSL, mean [95%CI]	0.05 [0.02 to 0.08]	0.02 [0.00 to 0.03]	0.035 [0.004 to 0.066]	0.03[3]

LCA, linked-color imaging with artificial intelligence-assisted colonoscopy; LCI, linked-color imaging-assisted colonoscopy; SSL, sessile serrated lesions.
[1]LCA – LCI.
[2]Chi-squared test.
[3]Student's *t* test.

future cancer risk and mortality. Additionally, it is unclear whether the overdetection of small lesions may increase the cost of colonoscopy.

Visibility is another factor associated with the ADR. The aim of bowel cleansing in colonoscopy is to reduce both the number of missed lesions and the examination time. The degree of bowel cleansing is an important quality indicator in colonoscopy, despite conflicting results on its correlation with the ADR [22].

Image-enhanced endoscopy is also highly beneficial for visibility. By measuring the color difference, Yoshida et al. demonstrated that tumor visibility was better with LCI than with white-light imaging, reducing polyp oversight in the cecum and ascending colon [23]. We also previously conducted a multicenter RCT with LCI to show improvement in the APC [24]. Furthermore, SSLs have poor vascularization, and LCI facilitates their diagnosis by increasing the whiteness in regions with insufficient vascularization [25, 26]. One study showed that LCI yielded significantly higher visibility scores for both hyperplastic polyps and SSLs compared with white-light imaging [27]. In the current study, LCI was used for both groups; however, there was a significant difference in SSL detection, suggesting they can be missed in endoscopy, even with LCI and improved visibility. Yoshida et al. reported that by observing the cecum and ascending colon for 30 seconds using LCI after white-light imaging, the detection rates for SSL and adenomas increased by 12.4 percentage points, from 30.7% to 43.1% [28]. This further emphasizes the role of time in the ADR. Adding CAD EYE to LCI to improve endoscopist support and visibility may have contributed to the improvement of the ADR in the current study.

The final significant factor associated with the ADR is blind spots specific to the colon. CADe cannot detect polyps in blind spots as they are not visible in the image, and regardless of visibility and AI, they are difficult to detect. Blind spots include the back of the haustra, behind the ileocecal valve, the flexure, and near the anus. Previously, we reported that, compared with a transparent hood, the Endo-wing (Shangxian Minimal Invasive, Inc. Liaoning, China) reduces blind spots and improves APC and polyp detection in the sigmoid colon, where lesions are easily hidden behind the folds of the colon [29]. Moreover, when a wide-angle lens is used, and a cap is attached to the endoscope tip, it is easier to observe behind the folds [30, 31, 32, 33]. A recent prospective multicenter RCT showed that the ADR can be improved using Endocuff Vision (Arc Medical Design Ltd., Leeds, UK), indicating the importance of understanding blind spots [34]. As these studies were not conducted using LCI, further ADR improvement is expected if AI is added to LCI observation and other devices are fitted to reduce blind spots further.

This study has some limitations. First, in nearly one-fifth of the patients, colonoscopy was performed for diagnostic purposes due to abdominal pain; thus, ours was not a pure screening cohort. This means that physicians had some level of expectation with respect to patient findings. Second, double blinding was not feasible because endoscopists could determine whether AI was used during colonoscopies. Third, the endoscopist's skills were not matched. Given that we were unable to randomize the endoscopists (experts and trainees), it was possible that the endoscopist experience may have affected the ADR. However, there was no significant difference in the ADR according to endoscopist experience between the LCA and LCI groups. Finally, most colonoscopies were performed after 2:00 pm and may have resulted in lapsed concentration and lower ADR. Moreover, the attachment of a hood in both groups could have affected the results, particularly during times of lapsed concentration. Fortunately, this would have affected both groups evenly. In the future, multicenter trials with a larger sample size are needed to compare the ADR and APC between LCA and LCI. In addition, we would like to evaluate whether the time of day the endoscopy is performed impacts the ADR.

In conclusion, this prospective RCT demonstrated that LCA was significantly superior to LCI in terms of the ADR.

Conflict of Interest

The authors declare that they have no conflict of interest.

Clinical Trial

Trial Registration: UMIN Japan (http://www.umin.ac.jp/english/) | Registration number (trial ID): UMIN000046361 | Type of study: Randomized control trial

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