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Impact of real-time use of artificial intelligence in improving adenoma detection during colonoscopy: A systematic review and meta-analysis

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ABSTRACT

Background and study aims With the advent of deep neural networks (DNN) learning, the field of artificial intelligence (AI) is rapidly evolving. Recent randomized controlled trials (RCT) have investigated the influence of integrating AI in colonoscopy and its impact on adenoma detection rates (ADRs) and polyp detection rates (PDRs). We performed a systematic review and meta-analysis to reliably assess if the impact is statistically significant enough to warrant the adoption of AI -assisted colonoscopy (AIAC) in clinical practice.

Methods We conducted a comprehensive search of multiple electronic databases and conference proceedings to identify RCTs that compared outcomes between AIAC and conventional colonoscopy (CC). The primary outcome was ADR. The secondary outcomes were PDR and total withdrawal time (WT).

Results Six RCTs (comparing AIAC vs CC) with 5058 individuals undergoing average-risk screening colonoscopy were included in the meta-analysis. ADR was significantly higher with AIAC compared to CC (33.7 % versus 22.9 %; odds ratio (OR) 1.76, 95 % confidence interval (CI) 1.55–2.00; $I^2 = 28\%$). Similarly, PDR was significantly higher with AIAC (45.6 % versus 30.6 %; OR 1.90, 95 %CI, 1.68–2.15, $I^2 = 0\%$). The overall WT was higher for AIAC compared to CC (mean difference [MD] 0.46 (0.00–0.92) minutes, $I^2 = 94\%$).

Conclusions There is an increase in adenoma and polyp detection with the utilization of AIAC.

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer-related death [1], and colonoscopy remains the best modality for CRC screening [2, 3]. Screening colonoscopy not only reduces the incidence of CRC but also reduces CRC-related mortality [4]. This is achieved by the detection and removal of precancerous adenomatous polyps. Adenoma detection rate (ADR) is an important quality indicator of colonoscopy, and increasing ADR by 1.0 % could reduce CRC-related mortality by 3 % and interval cancer by up to 5 % [5]. The quality metric established by the American Society of Gastrointestinal Endoscopy recommends a target ADR of 30 % in men and 20 % in women (25 % average ADR) [6]. However, studies have reported missed adenoma rates of up to 27 % [7]. Several factors could contribute to it, including polyp characteristics (location and size), prep quality,

and inadequate inspection or lack of recognition of sessile polyps by endoscopists.

The inclusion of a second observer has shown to increase ADR [8]. With the advancement in machine learning capabilities over the past decade, multiple studies have investigated the potential of AI to serve as a second observer to help improve quality indicators of colonoscopy, including ADR, poly detection rate (PDR), and withdrawal time (WT) [9–13]. AI, with the use of a deep neural network (DNN), is designed to work like a human brain via multiple layers of neural networks that are stacked onto one another. Each neural network is composed of a computational hub called nodes, and the nodes are interconnected and structured into multiple layers. This multilayered computation structure gives DNN the ability to scan input images and videos (in this case, colonoscopy images/videos) and detect required output (adenoma/polyps). Although we have known about the DNN system since the 1980 s, the recent advances in technology have enabled computers to handle vast amounts of computations data required to establish an effective DNN system [14].

Different DNN systems have been established to aid gastroenterologists in improving quality metrics for colonoscopy, including ADRs. An effective DNN system should have high sensitivity and specificity. Previous retrospective studies have estimated the diagnostic accuracy of DNN systems to detect polyps as 89 % to 95 % [15–17] with a sensitivity of greater than 90 % [17, 18]. Recent RCTs comparing AIAC with CC have investigated the impact of AI on overall ADRs and PDRs [9–13]. We performed a systematic review and meta-analysis with the primary aim to reliably assess if the impact of AIAC on ADR is statistically significant enough that it needs to be adopted in clinical practice. The secondary aim of the meta-analysis was to evaluate the impact of AIAC on PDR and WT.

Materials and methods

This systematic review was performed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. It is reported following Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search strategy

We conducted a comprehensive search of several databases and conference proceedings, including Medline, EMBASE, Scopus, Cochrane Library, and Web of Science databases were searched through April 2020 to identify RCTs that compared outcomes between AIAC and CC. The literature search was performed by an experienced medical librarian using input from the study authors. The details of the search strategy and data sources are reported in **Appendix 1.**

Keywords used in the search included a combination of artificial intelligence (AI), neural networks, deep learning, colonoscopy, colon polyps, polyp detection, and adenoma detection rates. The search was restricted to studies in human subjects published in the English language. Two authors (MA, JSK) independently reviewed the title and abstract of studies identified in the primary search and excluded studies that were not relevant to the research question based on prespecified inclusion and exclusion criteria. The full text of the remaining articles was reviewed to determine whether it reported outcomes of interest. Any discrepancy in article selection was resolved by consensus and in discussion with a co-author. The bibliographic sections of the selected articles, as well as narrative reviews on the topic, were also manually searched for additional relevant studies.

Selection criteria

In the meta-analysis, we included studies that met the following inclusion criteria (1) RCTs that compared AIAC vs. CC for the screening of CRC; and (2) reported ADR and/or PDR for the two groups. We excluded; (1) computations analysis studies (which involved retrospective analyses of colonoscopy images/videos to generate a DNN system with the assessment of ADR based on image analysis without patient enrollment or control arm); (2) studies in which an AI system was used for histopathological characterization of polyps rather than ADR; (3) that were in the non-English languages; (4) non-human studies; and (5) letters to editors, case reports, retrospective studies, review articles and editorials, and duplicate studies.

Data abstraction and quality assessment

After identifying relevant studies, data on the study characteristics, patient characteristics, and outcomes of interest (ADR, PDR, adenoma location and size, and WT) were abstracted independently by two authors (MA, JSK) onto a standardized form. The quality of evidence was assessed using Grading of Recommendation Assessment, Development, and Evaluation (GRADE) approach. The assessment was performed by two authors (MA, JSK) independently. Overall quality was then deemed as very low, low, moderate, and high using the GRADE Tool [19].

Assessment of risk of bias

The Cochrane tool was used to assess for risk of bias [20, 21]. Two authors (MA, JSK) independently assessed each RCT for the risk of bias. The risk in each study was rated as high, low, or unclear for each of the five domains of the tool: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), and selective reporting (reporting bias).

Outcome assessed

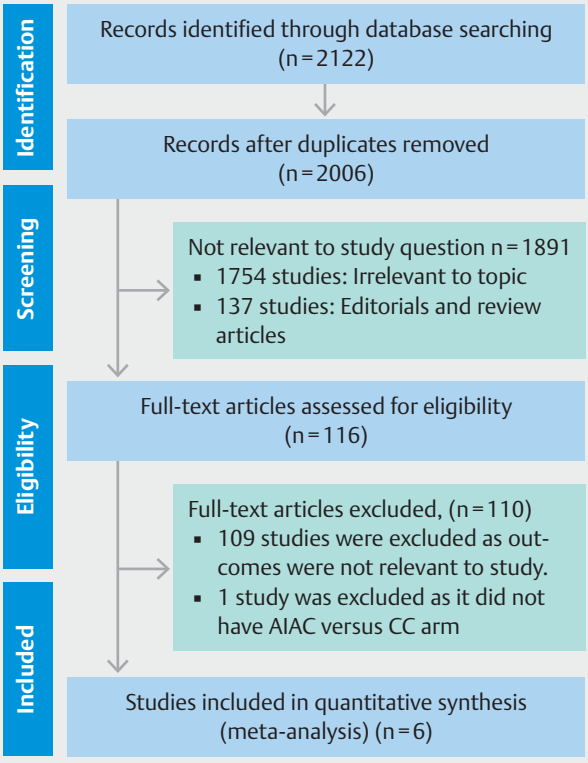
The primary outcome of the study was to assess the impact of AI on ADR. The secondary outcomes included PDR and total WT. We also performed a separate analysis to assess the impact of AIAC in detecting adenomas stratified by their location (in proximal versus distal colon with the splenic flexure being the cutoff) and size (0–5 mm, 6–10 mm, and > 10 mm).

Statistical analysis

Pooled odds ratio (OR) for dichotomous variables and mean differences (MD) for continuous variable and their 95 % confidence intervals (CI) were calculated for the outcomes of interest. The Mantel-Haenszel method was used to calculate the OR, and the inverse variance method was used to calculate the MD. The X^2 test (Cochran Q statistic) was used to evaluate heterogeneity between studies and was quantified using the i^2 statistic. Heterogeneity was assigned as low, moderate, substantial and high based on i^2 values of < 25 %, 26 % to 50 %, 51 % to 75 % and > 75 %, respectively. We planned to assess for publication bias qualitatively by visual inspection of a funnel plot, and quantitatively by the Egger test (**Supplementary Fig. 1** and **Supplementary Fig. 2**) [22]. All analyses were performed using the Review Manager 5.3 (The Cochrane Collaboration, Oxford, UK). Two-sided testing was used. $P < 0.05$ was considered significant.

Results

A total of 2122 studies were identified by our search criteria; 116 studies were identified after removing duplicate records, animal studies, retrospective studies, and computational analysis. After full-text review of 116 studies, 109 studies were excluded as outcomes reported were not relevant to the current meta-analysis. One additional study was excluded, as it was not a comparative study between AIAC and CC [23]. A total of six studies with a total of 5058 patients that met our inclusion criteria were included in the meta-analysis. The schematic diagram of study identification and selection is illustrated in ▶ **Fig. 1**.



▶ **Fig. 1** Flowchart summarizing the study selection process.

Characteristics and quality of the studies

The study characteristics of individual studies are summarized in ▶ **Table 1** and ▶ **Table 2**. All six studies were RCTs. All the included studies were from China except one by Recipi et al [24], which was done in Italy. All studies were single-center except for the study by Recipi et al [24], which was a multicenter study. There was no difference in the adequacy of bowel prep (based on the Boston Bowel Preparation Scale) between the two groups (AIAC vs CC) in the individual studies (▶ **Table 2**). Colonoscopes from different manufacturers were used in the individual studies. A summarized assessment of the risk of bias in each study using the Cochrane tool is illustrated in **Supplementary Table 1**. **Supplementary Table 2** summarizes the assessment of quality of evidence using the GRADE approach [19].

Adenoma detection rate

ADRs in the six included studies (AIAC vs CC) are summarized in ▶ **Table 2**. On pooled analysis, the ADR was significantly higher with AIAC compared to CC (33.7 % vs 22.9 %; OR 1.76; 95 %CI, 1.55–2.00; $P < 0.001$) (▶ **Fig. 2**, ▶ **Table 3**). There was moderate heterogeneity ($I^2 = 28$ %) in the analysis. GRADE analysis indicated the quality of evidence supporting higher ADR with AIAC was moderate (**Supplementary Table 2**).

Polyp detection rate

The PDRs in the five included studies (AIAC vs CC) are summarized in ▶ **Table 2**. The PDR was significantly higher with AIAC as compared to CC (45.61 % vs 30.69 %; $P < 0.001$; OR 1.90; 95 %CI, 1.68–2.15) (▶ **Fig. 3**, ▶ **Table 3**). There was no heterogeneity ($i^2 = 0$ %) in the analysis. GRADE analysis indicated the quality of evidence supporting higher PDR with AIAC was moderate (**Supplementary Table 2**).

Withdrawal time

Five studies [9, 10,12,13,24] were included in this pooled analysis as one of the studies [11] did not report data on overall WT. Overall WT was higher with AIAC as compared to CC (MD 0.46; 0.00–0.92 minute; $P < 0.001$, $i^2 = 94$ %) (▶ **Fig. 4**). The mean (SD) WT with AIAC was 6.92 (1.99) minutes. However, no polyp WT was similar between the two groups in the three studies [10, 12,13] that reported these data (MD 0.05; –0.03–0.12 minute; $P = 0.21$, $i^2 = 0$ %) (▶ **Fig. 4**).

ADR by adenoma location

The ADRs based on adenoma location in the five included studies (AIAC vs CC) are summarized in ▶ **Table 2**. AIAC identified significantly more adenomas in the proximal colon compared to CC (23.1 % vs 14.5 %, OR 1.81, 95 %CI, 1.57–2.10; $P < 0.001$). Similarly, AIAC identified significantly more polyps in the distal colon compared to CC (OR 2.00 [1.71–2.35]; $P < 0.001$). There

▶ **Table 1** Patient demographics of individual studies.

Study details/ year of publication	Country	Study design	Total number of patients	Screening modality		Mean age in years (SD)		Sex ratio (M:F)	
				Artificial intelligence-aided colonoscopy (AIAC)	Conventional colonoscopy (CC)	AIAC	CC	AIAC	CC
Wang Pu et al (2019)	China	RCT	1058	522	536	51.07 (13.15)	49.94 (13.79)	263:259	249:287
Gong et al (2020)	China	RCT	704	355	349	50 (37–58)	49 (36–57)	187:168	158:191
Wang Pu et al (2020)	China	RCT	1010	508	502	49 (39–60)	49 (40–56)	241:243	254:224
Liu et al (2019)	China	RCT	1026	508	518	51.02 (12.26)	50.13 (12.68)	264:244	287:231
Su et al (2020)	China	RCT	659	308	315	50.54 (10.28)	51.63 (9.04)	159:149	148:167
Recipi et al	Italy	RCT	685	341	344	61 (9.7)	61.1 (0.44)	172:169	165:179

RCT, randomized clinical trial.

was low heterogeneity in both analyses ($i^2 = 22\%$ and $i^2 = 0\%$ respectively) (▶ **Fig. 5** and **Supplementary Table 2**).

ADR by adenoma size

On stratification of adenomas by size, AIAC was superior to CC in identification of adenomas of 0–5 mm (OR 2.07, 1.81–2.36; $P < 0.001$, $i^2 = 27\%$), 6–10 mm (OR 1.47, 1.19–1.82; $P = 0.004$, $i^2 = 0\%$) and > 10 mm (OR 1.79, 1.27–2.53; $P < 0.001$, $i^2 = 12\%$) (**Supplementary Fig. 3**).

Publication bias

Assessment for publication bias was not performed because there were < 10 studies included in the meta-analysis.

Discussion

With the advent of effective screening modalities, the overall incidence of colon cancer has been decreasing over the past two decades [25]. Nevertheless, CRC remains the third most common cancer worldwide [1]. Colonoscopy is regarded as a gold standard test for CRC screening and is routinely performed for both screening and surveillance of CRC. Development of CRC before the recommended follow-up colonoscopy, also known as "interval cancer" accounts for up to 9% of all colon cancers in Canada and the United States. Almost 85% of these interval cancers are thought to have developed because of either missed polyp or incomplete polyp resection [26]. The overall effectiveness of screening colonoscopy in decreasing CRC incidence can be operator dependent [27] as there is still a substantial variation in performance statistics between physicians. ADR is a well-accepted quality indicator for colonoscopy, but there is a wide variation in reported rates (7 to 53%) [28]. Various newer modalities have been studied to help increase ADR. Some of these interventions include changes in procedure techniques like water immersion and water exchange, add-on devices like Endo-Cuff, cap-assisted colonoscopy, image enhancement with narrow-band imaging (NBI) or chromoendoscopy [29–32] and DNN based computer learning capabilities. While AIAC has shown promising results in improving ADR in the recent RCTs, it is unclear if the impact is significant enough to warrant changes in clinical practice.

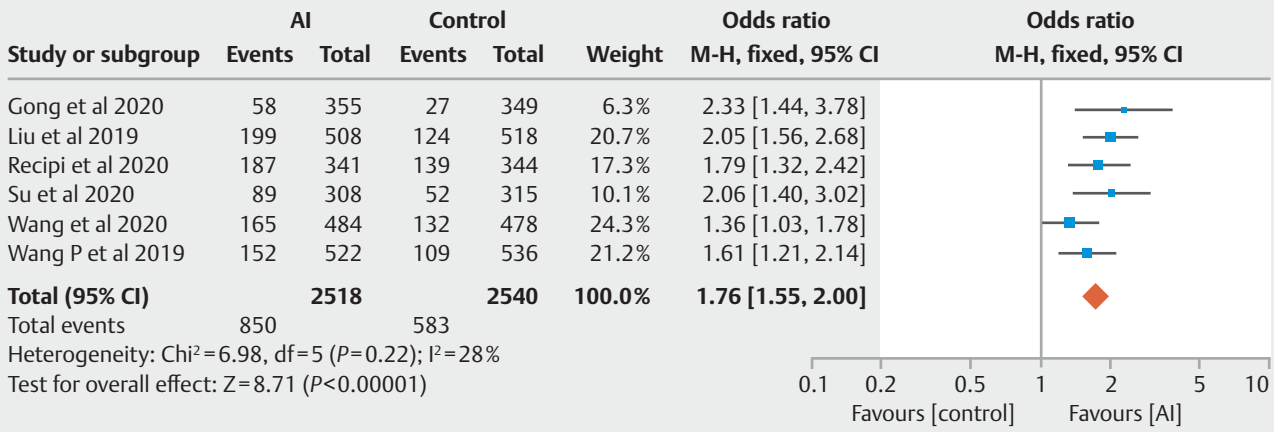
In the current meta-analysis of five RCTs with 5058 patients that compared AIAC vs CC, the use of AIAC was associated with significantly higher ADR (33.7% versus 22.9%; OR 1.76; 95%CI, 1.55–2.00; $P < 0.001$, I2 = 28%) and PDR (45.61% versus 30.69%; OR 1.90; 95%CI, 1.68–2.15; $P < 0.001$, $I^2 = 0\%$). Comparing specific ADRs based on adenoma location and size, AIAC was associated with significantly higher ADRs compared to CC. While there was an increase in the mean WT with AIAC, this was minimal (46 seconds). To the best of our knowledge, this is the first meta-analysis of randomized controlled trials (RCTs) evaluating the impact of AIAC on improving adenoma and PDRs in screening colonoscopy.

As AIAC is associated with significantly higher ADR compared to CC, it is possible that the risk of interval cancers could be lower with use of AIAC given that ADR is inversely proportional to the incidence of interval cancers. While CRC screening with colonoscopy significantly decreases the overall incidence of CRC and related mortality, it has been ineffective in decreasing the incidence of proximal colon cancers and mortality [33, 34]. This could be explained by higher missed proximal (right-sided) adenoma detection [33]. In the current meta-analysis, we noted that AIAC significantly increases ADR in the proximal colon compared to CC (23.1% vs 14.5%; OR 1.81; 95%CI, 1.57–2.10; $P < 0.001$) and hence could potentially decrease the incidence of proximal interval cancers.

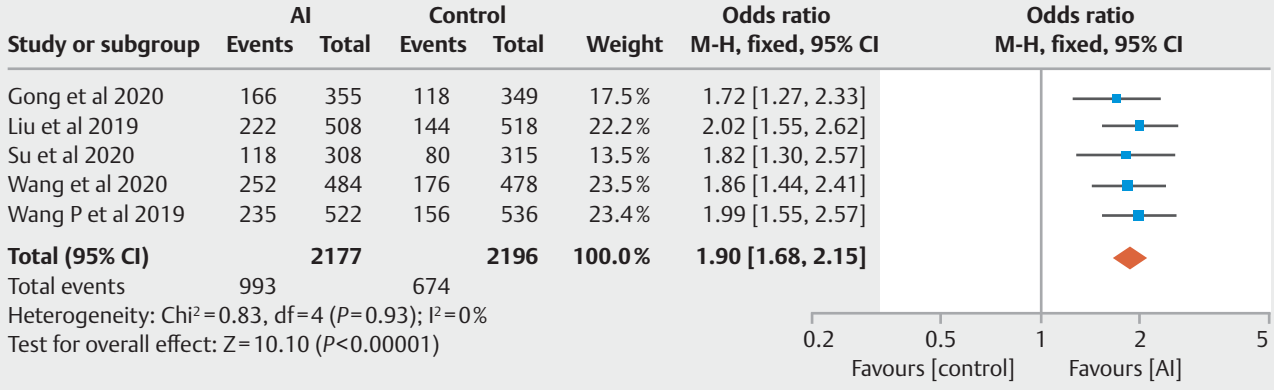
▶ **Table 2** Characteristics of individual studies.

Study details			Wang Pu et al (2019)	Gong et al (2020)	Wang Pu et al (2020)	Liu et al (2019)	Su et al (2020)	Recipi et al (2020)
Primary outcome								
Adenoma detection rate (%)	AIAC		29	16	34	39	28.9	54.8
	CC		20	8	28	23	16.5	40.4
Secondary outcomes								
Polyp detection rate (%)	AIAC		45	47	52	44	38.3	–
	CC		29	34	37	28	25.4	–
Adenoma size (in mm)	AIAC	0–5	185	46	211	166	–	115
		6–10	61	4	60	63	–	36
		>10	16	10	10	21	–	36
	CC	0–5	102	25	128	89	–	91
		6–10	50	1	46	43	–	20
		>10	8	1	7	10	–	28
Location of adenoma	AIAC	Cecum, n (%)	3 (1.15)	1 (0.6)	5 (2)	6 (2.4)	3 (2.65)	–
		Ascending, n (%)	47 (17.94)	10 (3)	62 (22)	50 (20)	17 (15.04)	–
		Transverse, n (%)	72 (27.48)	15 (4)	65 (23)	75 (30)	28 (24.78)	–
		Descending, n (%)	44 (16.79)	7 (2)	46 (16)	48 (19.2)	21 (18.58)	–
		Sigmoid, n (%)	64 (24.43)	19 (5)	70 (25)	35 (14)	29 (25.66)	–
		Rectum, n (%)	32 (12.21)	9 (3)	33 (12)	36 (14.4)	15 (13.27)	–
	CC	Cecum, n (%)	1 (0.62)	2 (1)	5 (3)	3 (2.11)	1 (1.79)	–
		Ascending, n (%)	39 (24.38)	4 (1)	41 (23)	40 (28.17)	6 (10.71)	–
		Transverse, n (%)	36 (22.50)	6 (2)	39 (22)	38 (26.76)	11 (19.64)	–
		Descending, n (%)	20 (12.50)	2(1)	31 (17)	22 (15.49)	10 (17.86)	–
		Sigmoid, n (%)	41 (25.62)	9 (3)	44 (24)	20 (14.09)	16 (28.57)	–
		Rectum, n (%)	23 (14.37)	4 (1)	21 (12)	19 (13.38)	12 (21.43)	–
Colon prep	AIAC	Inadequate Boston Prep Scale n (%)	73 (13.98)	21 (6)	71 (15 %)	66 (12.9)	NR	2 (1 %)
		Adequate Boston Prep Scale n (%)	449 (86.02)		413 (85 %)	442(87.1)	NR	339 (99.4)
	CC	Inadequate Boston Prep Scale n (%)	79 (14.74)	22 (6)	65 (14 %)	71 (13.71)	NR	2 (<1)
		Adequate Boston Prep Scale n (%)	457 (85.26)		413 (86 %)	447 (86.29)	NR	342 (99.4)
Total withdrawal time (SD) in min	AIAC		6.89 (1.79)	6.38 (2.48)	7.46 (2.02)	6.82 (1.78)	NR	6.95 (1.68)
	CC		6.39 (1.21)	4.76 (2.54)	6.99 (1.57)	6.74 (1.62)	NR	7.25 (2.48)
No polyp withdrawal time (SD)	AIAC		6.18 (1.38)	NR	6.48 (1.32)	6.37 (0.98)	7.03 (1.01)	–
	CC		6.07 (1.11)	NR	6.37 (1.09)	6.32 (1.09)	5.68 (1.26)	–

AIAC, artificial intelligence-aided colonoscopy; CC, conventional colonoscopy; NR, not rated.



▶ **Fig. 2** Forest plot for studies assessing the effect on artificial intelligence-aided colonoscopy compared to control (conventional colonoscopy) on adenoma detection rate. CI, confidence interval.



▶ **Fig. 3** Forest plot for studies assessing the effect on artificial intelligence-aided colonoscopy compared to control (conventional colonoscopy) on polyp detection rate. CI, confidence interval.

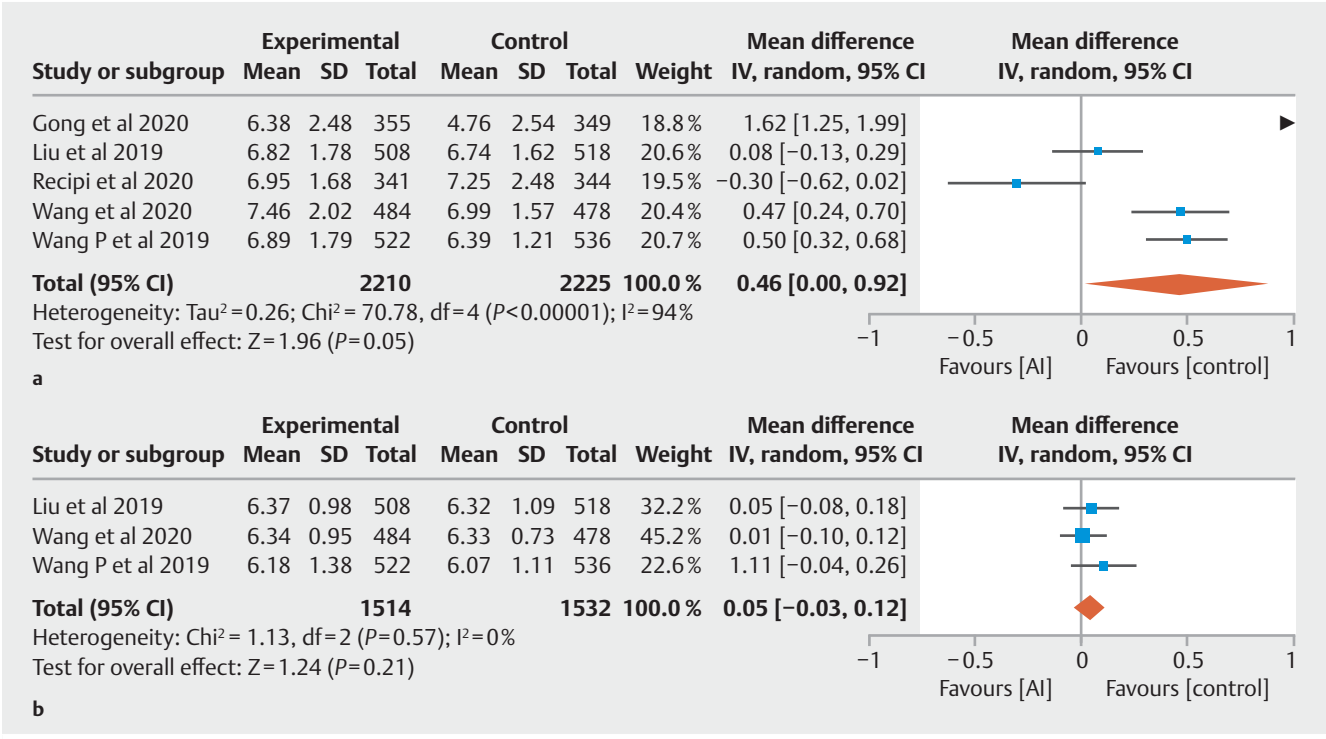
▶ **Table 3** Outcomes of pooled analysis comparing AIAC vs CC.

Outcome	No of studies	Odds ratio (AIAC vs CC) (95% CI)	Heterogeneity I^2
Adenoma detection rates	6	1.76 [1.55–2.00]	28%
Polyp detection rates	5	1.90 [1.68–2.15]	0%
Proximal colon ADR	5	1.81 [1.57–2.10]	0%
Distal colon ADR	5	1.96 [1.70–2.27]	0%

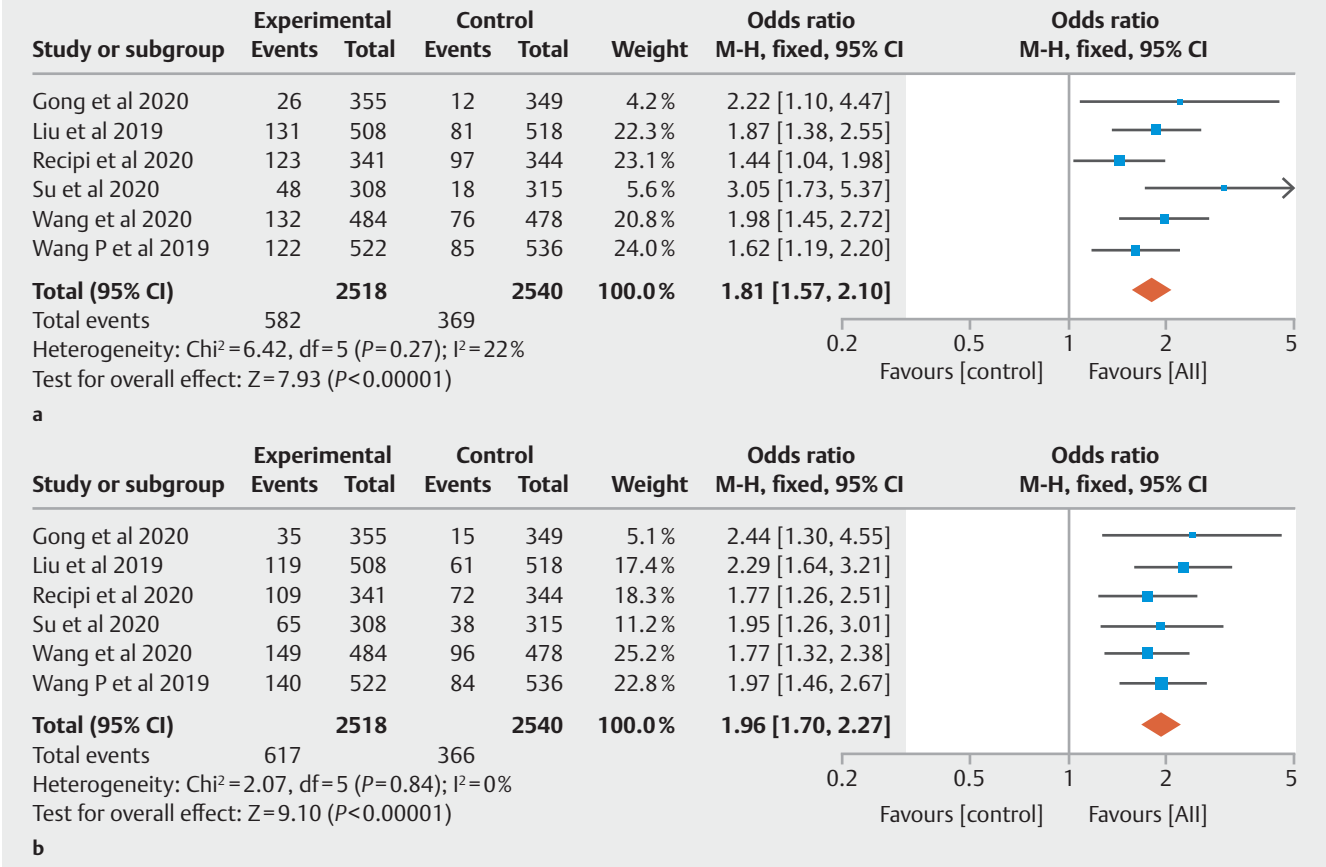
AIAC, artificial intelligence-aided colonoscopy; CC, conventional colonoscopy; ADR, adenoma detection rate;

In the analyses based on adenoma size (0–5 mm, 6–10, and ≥ 10 mm), AIAC improved ADR in all categories compared to CC. Advanced adenomas (defined as an adenoma that measures 10 mm or more in size, contains a substantial villous component, or exhibits high-grade dysplasia) are associated with an increased risk of CRC. [35]. As AIAC increased the detection of adenomas ≥ 10 mm compared to CC (OR 1.79; 1.27–2.53; P < 0.001, i^2 = 12%), it may further help in reducing interval CRC (**Supplementary Table 1**).

One of the biggest challenges besides cost and logistical consideration to use AIAC is the concern for increased WT. In the current meta-analysis, 1) the increase in total WT with AIAC was minimal, and 2) the no polyp WT was similar between AIAC and CC. WT may be used as a surrogate marker for adequate colon exam, and an increase in total WT with AIAC is



▶ **Fig. 4** Forest plot for studies assessing the effect on artificial intelligence-aided colonoscopy compared to control (conventional colonoscopy) on **a** overall withdrawal time and **b** no polyp withdrawal time. CI, confidence interval.



▶ **Fig. 5** Forest plot for studies assessing the effect on artificial intelligence-aided colonoscopy compared to control (conventional colonoscopy) on **a** proximal colon adenoma detection rate and **b** distal colon adenoma detection rate. CI, confidence interval.

probably related to increased polyp/adenoma detection and subsequent polypectomy compared to the CC group. The U.S. Multi-Society Taskforce (MSFT) on CRC recommends at least a 6-minute WT, but the compliance is not uniform. Although the use of AIAC increased the WT by 47 seconds, the overall WT with AIAC was 6.92 ± 1.99 minutes, which is well within the range of recommended by MSFT.

There are several limitations to the current meta-analysis. All but one study was from China and hence the generalizability of the meta-analysis results in the Western population is uncertain. There was moderate heterogeneity ($I^2 = 28\%$) in the pooled analysis of ADR. However, in the analyses of specific ADR based on location (proximal vs. distal colon) and size (< 5 mm, 5–10 mm, > 10 mm) of polyps, the heterogenicity is low. Different DNN systems were used in the included studies, and it could contribute to heterogeneity. While there was substantial heterogeneity in the pooled analysis of WT ($I^2 = 94\%$), there was no heterogeneity ($I^2 = 0$) in the pooled analysis of no polyp WT. We were unable to assess the impact of AIAC in improving ADR when the prep was inadequate, as individual studies did not report separate ADRs when the prep was inadequate (for both AIAC and CC groups). The included studies did not report data on costs associated with AIAC and cost-effectiveness, which are important considerations in screening programs.

The strengths of this review are as follows: systematic literature search with well-defined inclusion and exclusion criteria, rigorous evaluation of the risk of bias using the Cochrane tool, and assessment of the quality of evidence using the GRADE approach. Only RCTs were included in the meta-analyses to improve the reliability of our pooled estimates for real-time use of AI. In addition to estimating the impact of AIAC on overall ADR, we also performed separate analyses to estimate specific ADRs based on location and size of polyps. There was low heterogeneity noted in analyses of most outcomes.

Conclusion

In conclusion, the use of AIAC significantly improves ADR and PDR compared to CC with minimal increase in WT. AIAC also improves the detection of polyps in the proximal colon and large polyps (> 10 mm). Hence, the use of AIAC could potentially decrease the incidence of interval cancers. Future studies are needed in the Western population to confirm the generalizability of the current meta-analysis results. Further studies are also needed on the cost-effectiveness of AIAC.

Competing interests

The authors declare that they have no conflict of interest.

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