

Real Time Artificial Intelligence-Aided Colonoscopy Experience: The Impact on Routine Clinical Practice in a High-Volume Center

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Abstract

Background: Advent of Artificial Intelligence (AI) with the development of computer-aided polyp detection (CADe) could be an important support against colorectal cancer (CRC). Our primary aim was to estimate polyp detection rate (PDR) and adenoma detection rate (ADR) improvement in CADe colonoscopy (CAD-EYE, Fujifilm, Tokyo, Japan) when compared to traditional colonoscopy, and to assess how these results could impact on our clinical activity.

Materials and Methods: We retrospectively collected data from all consecutive 40-to80-years old subjects undergoing colonoscopy for primary CRC screening, post-polypectomy surveillance or the presence of any gastrointestinal symptoms from November 2019 to February 2020 (WL-HD colonoscopy, control arm, 450 patients) and from October 2020 to January 2021 (CAD-EYE colonoscopy, study arm, 250 patients).

Results: Higher PDR (159/250 [63.60%] vs 163/450 [36.22%]; $p < 0,001$) and ADR (115/250 [46%]

vs 138/450 [30,67%]; $p < 0,001$) was found in the CADe group in comparison to the control group. CADe colonoscopy detected more lesions, especially diminutive lesions (RRR 5.07; 95% CI 3.44 - 7.46; $p < 0.001001$) and 6 - 9 mm lesions (RRR 2,75; 95% CI 1.64 - 4.60; $p < 0.001$).

Regarding lesions' histology, CADe is associated to a higher detection of non-advanced adenomas (RRR 2.97; 95% CI 2.02 - 4.38; $p < 0.001$) and serrated lesions (RRR 14.02; 95% CI 5.37 - 36.62; $p < 0.001$), while no significant improvement was found for advanced adenomas (RRR 1.35; 0.34 - 5.34; $p = 0.667$) and adenocarcinomas (RRR 1.3; 95% CI 0.52-3.23; 0.574).

Conclusion: Our study showed a 75,6% and 49,98% relative increase in PDR and ADR in the CADe group (absolute increase of 27,38% and 15,33% respectively). Real-time AI-aided colonoscopy applied in the routine endoscopic activity could significantly improve diagnostic ability especially for diminutive lesions detection. Further studies are needed to evaluate a possible colon cancer incidence reduction following AI-colonoscopy increased ADR.

Keywords: Artificial Intelligence (AI); Computer-Aided Polyp Detection (CADe); Colorectal Cancer (CRC); Polyp Detection Rate (PDR); Adenoma Detection Rate (ADR)

Abbreviations

AI: Artificial Intelligence; CADe: Computer-Aided Detection; CRC: Colorectal Cancer; I-CRC: Interval-Colorectal Cancer; ADR: Adenoma Detection Rate; PDR: Polyp Detection Rate; AA: Advanced Adenomas; SSL: Sessile Serrated Lesions; WL-HD: White Light-High Definition; GI: Gastrointestinal; BMI: Body Mass Index

Introduction

Globally colorectal cancer (CRC) is the third most commonly diagnosed malignancy and the second leading cause of cancer death [1]. CRC has a heterogeneous etiology including both genetic and modifiable environmental risk factors [2]. Screening program, and specifically screening colonoscopy, can reduce CRC incidence by allowing early removal of precancerous lesions (adenomas and serrated polyps) [3,4]. The effectiveness of screening colonoscopy depends on the execution of a high-quality colonoscopy and the “gold standard” predictor of quality is a high adenoma detection rate (ADR), defined as the proportion of individuals undergoing to complete colonoscopy who had at least 1 adenoma [5]. The benchmark for ADRs is $\geq 25\%$ overall ($\geq 30\%$ for men, $\geq 20\%$ for women) [5,6]. Considering that each 1.0% increase in the ADR predicted a 3.0% decrease in the risk of interval cancer (I-CRC, defined as a CRC diagnosed within 60 months after a negative colonoscopy) [7], it is mandatory to identify the highest number of adenomas during colonoscopy. However, a recent meta-analysis showed a miss rate of 26% for adenomas [8]. The main cause is represented by overlooked lesions that may be referred to recognition failure or incomplete mucosal exposure depending on multiple factors such as complexity of the colorectal anatomy, inadequate bowel preparation and/or suboptimal technique in the withdrawal phase of colonoscopy. Advent of Artificial Intelligence (AI) with the development of computer-aided polyp detection (CADe) could be an important support against colorectal cancer (CRC). AI is expected to improve endoscopist adenoma detection rate resulting in the reduction of miss rate and consequently of I-CRC. Initial studies have demonstrated promising results, especially on detection [9,10]. According to a recent meta-analysis, ADR was higher in the CADe group (36,6%) than in the control group (25,2%), gaining 11,4% of ADR [11]. Nevertheless, considering the recent AI introduction in the endoscopy field and lack of data, more studies are needed in real-life situations. Our primary aim was to estimate polyp detection rate (PDR: proportion of individuals undergoing a complete colonoscopy who had at least 1 polyp detected) and adenoma detection rate (ADR) improvement in artificial intelligence-aided colonoscopy (CAD-EYE, Fujifilm, Tokyo, Japan) when compared to traditional colonoscopy, and to assess how these results could impact on our clinical activity. Secondary aims were the evaluation of serrated lesions (SSL: total number of sessile serrated lesions), advanced adenomas (AA: number of advanced adenomas) and non-neoplastic lesions (at least one and total number per patient) among all excised lesions.

This study represents a preliminary real-time routine AI-colonoscopy experience in our high-volume Endoscopy Center due to the recent introduction of advanced technology equipment - CAD-EYE system.

Materials and Methods

Study design and population

This is a single-center cross-sectional study conducted in an open access high volume Endoscopic Unit. We retrospectively collected data from all consecutive 40- to 80-years old subjects undergoing colonoscopy for primary CRC screening, post-polypectomy surveillance or the presence of any gastrointestinal symptoms from November 2019 to February 2020 (traditional colonoscopy, control arm, 450 patients) and from October 2020 to January 2021 (CAD-EYE colonoscopy, study arm, 250 patients). Other inclusion criteria were a Boston Bowel Preparation Scale ≥ 6 , the execution of a complete colonoscopy and a 6 minutes minimal withdrawal time. We excluded all subjects with personal or family history of hereditary colorectal cancer, with personal history of previous any colonic resection, subjects affected by inflammatory bowel diseases and those under antithrombotic therapy precluding polyp's resection.

The research project was approved by the Ethics Board (Prot. 20210027846). This study was conducted according to Helsinki declaration.

Colonoscopy procedures:

- Control group: All patients underwent to high definition (HD) with light (WL) colonoscopy (ELUXEO 760 Fujifilm series videos colonoscopies-Fujifilm Co, Tokyo, Japan).
- Study group (computer-aided detection, CAdE group): All patients underwent to HD- WL colonoscopy with CAD-EYE (ELUXEO 760 Fujifilm series videos colonoscopes; Fujifilm, Tokyo, Japan).

All the procedures were performed under conscious sedation (midazolam, with or without meperidine) and, in a minority of cases, under deep sedation (propofol). Patients were monitored throughout the examination. All patients had signed an informed consent before undergoing colonoscopy. All colonoscopies were performed by the whole endoscopists staff (cecal intubation > 95% and ADR > 25%). Adenomas were all removed with either biopsy forceps, cold snare, hot snare, or endoscopic mucosal resection, depending on the type, size and location of the lesion.

All resected lesions and biopsies were fixed in 10% buffered formalin solution in separate jars and were classified according to Vienna classification [12].

CAD-EYE, Fujifilm, Tokyo, Japan artificial intelligence-aided colonoscopy

Artificial intelligence-aided colonoscopy CAD-EYE by Fujifilm was recently installed in our Endoscopic Unit.

Furthermore, it is the first commercially available system with no-magnified image to allow both Colonic Polyp Detection and Characterization ("Hyperplastic" and "Neoplastic").

Artificial intelligence is a type of machine learning known since 1950 that in medicine can support physicians in diagnosis. AI utilizes a type of machine learning-deep learning model based on deep neural/convolutional neural networks, which mimics the structure of the human brain. This system in colonoscopy is based on an algorithm, derived from a lot of data sets made by a group of specialists, that allows to detect and analyze lesions.

CAD-EYE-Fujifilm software has learned specific images for detection and characterization by using the latest deep learning technology by FUJIFILM Medical AI Technology "REiLI". Data set includes WLI (White Light Image) and the chromoendoscopic LCI (Linked Color Image) and BLI (Blue Light Image). Learning method is designed based on the technical literature.

Data collection and management

Clinical data were extracted from the endoscopic digital database (medical charts) onto a pre-defined spreadsheet developed with Microsoft Excel®, by dedicated study personnel. All data were irreversibly anonymized, after verifying their completeness.

Sample size and power

We expected to be able to enroll 250 subjects undergoing CAdE-colonoscopy with an expectation of a 30% adenoma detection rate in the control group and a 45% in the CAD-EYE group. To detect this difference with power 90% and alpha error 1%, to take into account the observational nature of the study and the need for adjusted analyses in the secondary objectives, with Fisher exact test, 438 subjects in the

control groups were necessary. Considering the possible missing data due to the retrospective data collection, we enrolled 450 patients in the control group and 250 patients in the CAD-EYE group.

Statistical analysis

The primary endpoint was the proportion of patients with at least one adenoma detected and it was compared between groups by means of the Chi² test. Descriptive statistics were obtained for all variables assessed in the study population. Mean and standard deviation are reported for normally distributed variables, mean and interquartile range for skewed distributions, proportions for categorical variables. For group comparisons, Student t test (rank sum test or Mann-Whitney test for skewed distributions) were used for quantitative variables (ANOVA or Kruskal-Wallis for > 2 groups respectively), and Pearson’s Chi² test (Fisher exact test where appropriate) for categorical variables, at univariable analysis.

For patient-level binary endpoints, univariable and multivariable logistic regression models were applied. Selection of variables in multivariable models were dictated by clinical relevance, with no further selection, and we therefore included, besides group: age (in years), gender, body mass index (BMI)*, smoking status (current, former smoker, never)*, alcohol intake*, primary reason for colonoscopy. (*Definitions reported in supplementary table A).

1. Smoking Status	
Current Smoker	An adult who has smoked 100 cigarettes in his or her lifetime and who currently smokes cigarettes.
Former Smoker	An adult who has smoked at least 100 cigarettes in his or her lifetime but who had quit smoking at the time of interview.
Never Smoker	An adult who has never smoked, or who has smoked less than 100 cigarettes in his or her lifetime.
2. Drinking Status	
Current Light Drinker	At least 12 drinks in the past year but 3 drinks or fewer per week, on average over the past year.
Current Moderate Drinker	More than 3 drinks but no more than 7 drinks per week for women and more than 3 drinks but no more than 14 drinks per week for men, on average over the past year.
Current Heavier Drinker	More than 7 drinks per week for women; more than 14 drinks per week for men, on average over the past year.
Lifetime Abstainer	Fewer than 12 drinks in lifetime
3. Body Mass Index (BMI) Kg/m² - Nutritional Status	
Below 18.5	Underweight
18.5 to 24.9	Normal
25.5 to 29.9	Overweight
30.0 and above	Obese

Supplementary Table A: Definitions of smoking, drinking and nutritional status.

For patient-level count endpoints (number of lesions per patient, number of adenomas per patient), Poisson models were employed. To explore factors associated to higher number of lesions, multilevel mixed ordered logistic regression models were employed, with “patient” as random effect. Analyses were performed with Stata version 16.0 (Stata Corporation, 4905 Lakeway Drive, College Station, Texas 77845, USA).

P value of < 0.05 was considered statistically significant.

Results

Descriptive analysis

From October 2020 to January 2021, we enrolled 250 patients (study arm) and from November 2019 to February 2020 450 patients (control arm). No differences on any characteristics were found between study and control group (Table 1). The number of polyps of any histology per colonoscopy was significantly higher in the CADe group (p50 = 1 [IQR, 0-2]) in comparison to the control group (p50 = 0 [IQR, 0-1]) (p < 0,001). Higher PDR was found in the study arm (159/250 [63.60%] vs 163/450 [36.22%]; p < 0,001) (Table 2). Notably, also ADR was significantly higher in the CADe group than in the control arm (115/250 [46%] vs 138/450 [30,67%]; p < 0,001). Also, hyperplastic and serrated lesions were detected more frequently in the study group (61/313 [19.49] and 40/313 [12.78%] respectively. In the CADe group the total number of diminutive lesions (≤ 5 mm) corresponds to 77% (242/313), with an increase of about 20% compared to the control group (55,56%, 150/270).

Variables	CADe Group (n = 250)	Control Group (n = 450)	p-value
Mean age (SD)y	62 (10.3)	63.2 (9.9)	0.209
Gender n (%)			0.752
Female	113 (45.2)	210 (46.7)	
Male	137 (54.8)	240 (53.3)	
BMI (SD)	25.8 (4.6)	25.5 (4.1)	0.474
Alcohol intake n (%)			0.624
Never	113 (45.20)	199 (44.22)	
Occasional	73 (29.20)	136 (30.22)	
Moderate	49 (19.60)	97 (21.56)	
Unknown	15 (6)	18 (4)	
Smoking n (%)			0.376
Never	185 (74)	355 (74.44)	
Previous	7 (2.80)	9 (2)	
Current	42 (16.80)	88 (19.56)	
Unknown	16 (6.40)	18 (4)	
Indication for colonoscopy n (%)			0.136
Screening	68 (27.20)	153 (34.00)	
Surveillance	44 (17.60)	81 (18.00)	
GI symptoms	138 (55.20)	216 (48.00)	
Polyps per Colonoscopy (SD)	1.25 (1.44)	0.6 (1.06)	< 0.001

Table 1: Demographic and clinical characteristics of the study population.

	CADe group (n = 250)	Control group (n = 450)
Subjects with at least one lesions	159	163 (36.22%)
Of any histology n (%)	(63.60%)	
Subjects with at least one adenoma n (%)	115 (46%)	138 (30,67%)
Lesions of any size and histology n	313	270
Histological classification n (%)		
Hyperplastic	61(19.49)	28 (10.37)
Serrated lesions without Dysplasia	32 (10.22)	8 (2.96)
Serrated lesions with dysplasia	8 (2.56)	1 (0,37)
Tubular Adenoma LGD	187 (59.74)	191 (70.74)
Tubular Adenoma HGD	3 (0.96)	7 (2.59)
Villous-Tubular Adenoma LGD	10 (3.19)	18 (6.67)
Villous- Tubular Adenoma HGD	3 (0.96)	5 (1.85)
Adenocarcinoma	4 (1.28)	12 (4.44)
Inflammatory	2 (0.96)	0 (0)
Normal mucosa	3 (0.96)	0 (0)

Table 2: Lesions and histological classification.

Univariable analysis

At univariable analysis, CADe colonoscopy was associated to a higher adenoma detection; interestingly, at multivariable analysis the association was even stronger (OR 2.57; 95% CI 1.80 - 3.67; p = < 0.001) (Table 3). Other independent factors were age (OR 1.72 per each 10- year increase; 95% CI 1.43 - 2.93; p = < 0.001) and BMI (OR 1.06; 95% CI 1.02 - 1.11; p = 0.003), whereas to undergo to colonoscopy for the presence of GI symptoms is associated to a lower finding of adenomas (OR 0.50; 95% CI 0.33 - 0.74; p < 0.001).

Variables	OR [95% CI]	p-value
Control	1.00	
CADEYE	2.57 [1.80 - 3.67]	< 0.001
Age (per 10 year increase)	1.72 [1.43 - 2.08]	< 0.001
BMI	1.06 [1.02 - 1.11]	0.003
Smoking		
Never	1.00	
Previous	0.97 [0.32 - 2.93]	0.957
Current	1.81 [1.16 - 2.80]	0.008
Alcohol intake		
Never	1.00	
Occasional	0.95 [0.64 - 1.42]	0.813
Moderate	1.12 [0.72 - 1.75]	0.612
Clinical Indication		
Screening	1.00	
Surveillance	0.69 [0.42 - 1.14]	0.150
Symptoms	0.50 [0.33 - 0.74]	< 0.001

Table 3: Multivariable logistic regression model for adenomas (defined as at least one adenoma per patient).

Multivariable analysis

CADe colonoscopy detected more lesions (Table 4), especially diminutive lesions (RRR 5.07; 95% CI 3.44 - 7.46; $p < 0.001001$) and 6 - 9 mm lesions (RRR 2,75; 95% CI 1.64 - 4.60; $p < 0.001$), while no advantage seemed to be present for the detection of ≥ 10 mm lesions (RRR 1.25; 95% CI 0.71-2-21; $p = 0.435$). Notably, in our study, CAD-EYE system improved polyps' detection independently from colon location and from lesion morphology (Table 4). Finally, considering lesions' histology, CADE is associated to a higher detection of non-advanced adenomas (RRR 2.97; 95% CI 2.02 - 4.38; $p < 0.001$) and serrated lesions (RRR 14.02; 95% CI 5.37 - 36.62; $p < 0.001$), while no significant improvement was found for advanced adenomas (RRR 1.35; 0.34 - 5.34; $p = 0.667$) and adenocarcinomas (RRR 1.3; 95% CI 0.52 - 3.23; 0.574).

Per Patient analysis	CADe (n = 250)	Control (n = 450)	Total number (n = 700)	RRR [95%CI]	p-value*
Size Lesions					
≤ 5 mm	242 (77%)	150 (55.56%)	392 (67,07%)	5.07 (3.44 - 7.46)	<0.001
6-9 mm	42 (13,1%)	47 (17,41%)	89 (15,09)	2.75 (1,64 - 4.60)	<0.001
> 10 mm	29 (9,27%)	73 (27,04)	102 (17,5)	1,25 (0,71 - 2.21)	0.435
Location					
Proximal colon	135 (43,13)	123 (45,56)	258 (44,25%)	3.83 (2.60 - 5.61)	<0.001
Distal colon	178 (56,87%)	147 (54,44)	325 (55,75%)	3.46 (2.28 - 5.26)	<0.001
Morphology					
Polypoid	264 (84.34%)	228 (84.44%)	492	3.62 (2.52 - 5.21)	<0.001
Non-polypoid	45 (14.38%)	30 (11.11%)	75	5.51 (2.74 - 11.07)	<0.001
Histology					
Non-advanced adenomas	197 (62.94)	209 (77.41)	406 (69.64)	2.97 (2.02 - 4.38)	<0.001
Advanced adenomas	6 (1.92)	12 (4.44)	18 (3.09)	1.35 (0.34 - 5.34)	0.667
Sessile serrated lesions	40 (12.78)	9 (3.33)	49 (8.40)	14.02 (5.37 - 36.62)	<0.001
Adenocarcinoma	4 (1.28)	12 (4.44)	16 (2.74)	1.3 (0.52 - 3.23)	0.574
Non-neoplastic lesions	66 (21.09)	28 (10.37)	94 (16.12)	7.43 (4.13 - 13.37)	<0.001

Table 4: Association of CAD-EYE with detection of lesions, according to several lesion characteristics.

*: The reference category for all comparisons is "no lesions" See text for details in the statistical analysis.

Discussion

The use of real-time CADe during colonoscopy increases polyps and adenomas detection rate [9,13-15]. A recent meta-analysis showed a 29.6% ADR with AI versus 19.3% without AI [16]. Another systematic review has shown a pooled ADR significantly higher (36.6% vs 25.2%) when colonoscopies were performed with incorporation of artificial intelligence [11]. Our study seems to confirm these results showing a 75,6% and 49,98% relative increase in PDR and ADR in the CADe group. Also, polyps detected per colonoscopy are improved by the use of AI, resulting in an increase of about 50% in the CADe group. Improving PDR and ADR is mandatory to reduce the adenoma miss rate, known to be around 26% for adenomas and 9% for advanced adenomas [8], and, consequently, the resection of missed lesions would lower interval cancer incidence [8,17]. Our data support the hypothesis that the use of artificial intelligence could help the same operator to improve his ability to recognize more lesions when these are detected and highlighted by the CADe. In our study in the CADe group were

detected more lesions, mostly diminutive and 6 - 9 mm lesions. These results underline that CADe- colonoscopy could be very useful in the identification of smaller lesions, that are usually more difficult to detect, as already shown in other studies [9,16]. In our study, the use of CADe leads to an increase of both polypoid and nonpolypoid lesions. To note, the total number of nonpolypoid lesions in the two groups is relatively small (45/313 in the CADe group vs 30/270 in the control group). It is probably due to the fact that many of the diagnosed lesions are diminutive and small (< 10 mm) for which it has been demonstrated a fair interobserver agreement with Paris classification [18]. Unexpectedly, we identified fewer advanced adenomas and adenocarcinomas in the CADe group in comparison to the control group. There are some possible different explanations for this result. Firstly, CADe group data were collected during Covid-19 pandemic, during which our colon cancer screening program has been temporarily suspended such as most national and regional ones of which only some were significantly curtailed [19]. From our data in the CADe group patients who underwent a screening colonoscopy were about 26% fewer than in the control group. Our data reasonably reflect the disruption in colon cancer screening programs that occurred during the Sars-Cov-2 pandemic. A recent Italian National Screening Observatory (ONS) report has shown how our national screening program has slowed down, causing a complete suspension of both first (fecal immunochemical test) and second (colonoscopies) levels in some areas [20]. Notably, the ONS estimated that 1168 CRC and 6700 advanced adenomas had not been diagnosed, compared to what expected under normal circumstances [20]. Secondly, complete data (endoscopic and histological) were available only for the smaller lesions removed simultaneously during the colonoscopy because the major lesions removal was usually postponed to a dedicated operative session whose data weren't available at the time of data collection. The third possible reason is that after the detection of a suspected adenocarcinoma or an AA, some operators may have stopped the evaluation with AI. This bias is explainable by the retrospective nature of our study, for which no a priori protocol has been defined with uniform and standardized indication for operators regarding the application of CADe and data collection. After all, probably it is reasonable to not find a significant difference in detection of AA with the use of AI, as show in a recent systematic review [16], but more studies are needed to clarify these results.

Regarding hyperplastic polyps and sessile serrated lesions (SSL), we obtained a significant increase of their detection in the study group. SSL are early precursor lesions in the serrated neoplasia pathway, accounting for 10–15% of sporadic CRC [2,21]. This carcinogenic model is characterized by the progression from normal cells to hyperplastic polyps, to serrated adenomas and, finally, to cancer. Therefore, SSL are considered to be one of the major contributors to “interval cancers”, especially for proximal CRC [22]. Cause by their slightly elevated morphology, serrated lesions are difficult to identify and the use of AI seems to be helpful to improve our detection skills.

It is also real that we obtained a significant improvement in the diminutive and small lesions detection, that are mostly nonadvanced lesions, which shouldn't rapidly, maybe never, evolve in malignant advanced neoplasia. However, their removal could impact on the long-term CRC incidence, but there is no supporting evidence that it could give an advantage in the interval cancer rate reduction. Further studies are needed.

Some limitations of our study must be mentioned. First, due to its retrospective nature, our study was hindered by inevitable difficulties in data collection. Second, it was not randomized; however, all consecutive patients in the period underwent CAD-EYE, with no differences in patient selection compared to the first period. Besides, the protocol for CADe use was not standardized across all operators, and this might have underestimated the detection rate in the CAD-EYE group.

Our study might lack limited external validity for its cross sectional single center nature but our results are very similar to those of other recent randomized multicentric studies and systematic review and meta-analysis [9,16,11].

Finally, a psychological bias should be considered, since the use of AI, might have brought the operator to pay more attention during the exam (Hawthorne effect).

Conclusion

Our study represents, to our knowledge, the first real-life AI-colonoscopy experience in a high-volume Endoscopy Center due to the recent introduction of advanced technology equipment - CAD-EYE system. This study showed a 75,6% and 49,98% relative increase in PDR and ADR in the CAde group (absolute increase of 27,38% and 15,33% respectively). Real-time AI-aided colonoscopy applied in the routine endoscopic activity could significantly improve diagnostic ability especially for diminutive lesions detection. Our encouraging results deserve confirmation in multicenter, prospective studies.

Statement of Author Contributions

All authors significantly participated in the drafting of the manuscript or critical revision of the manuscript for important intellectual content and provided approval of the final submitted version. Individual contributions are as follow: CA and SA designed and coordinated the study, interpreted data and wrote the manuscript. LS designed did statistical analyses and reviewed the manuscript. GGG supervised the installation of the CAD-EYE system. All the other authors performed endoscopic examinations, locally collected data, and reviewed the paper for final approval. CA supervised SA reviewed the paper and made final critical revision for important intellectual contents.

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