

Performance of artificial intelligence in the characterization of colorectal lesions

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Abstract

Background: Image-enhanced endoscopy (IEE) has been used in the differentiation between neoplastic and non-neoplastic colorectal lesions through microvasculature analysis. This study aimed to evaluate the computer-aided diagnosis (CADx) mode of the CAD EYE system for the optical diagnosis of colorectal lesions and compare it with the performance of an expert, in addition to evaluating the computer-aided detection (CADE) mode in terms of polyp detection rate (PDR) and adenoma detection rate (ADR).

Methods: A prospective study was conducted to evaluate the performance of CAD EYE using blue light imaging (BLI), dichotomizing lesions into hyperplastic and neoplastic, and of an expert based on the Japan Narrow-Band Imaging Expert Team (JNET) classification for the characterization of lesions. After white light imaging (WLI) diagnosis, magnification was used on all lesions, which were removed and examined histologically. Diagnostic criteria were evaluated, and PDR and ADR were calculated.

Results: A total of 110 lesions (80 (72.7%) dysplastic lesions and 30 (27.3%) nondysplastic lesions) were evaluated in 52 patients, with a mean lesion size of 4.3 mm. Artificial intelligence (AI) analysis showed 81.8% accuracy, 76.3% sensitivity, 96.7% specificity, 98.5% positive predictive value (PPV), and 60.4% negative predictive value (NPV). The kappa value was 0.61, and the area under the receiver operating characteristic curve (AUC) was 0.87. Expert analysis showed 93.6% accuracy, 92.5% sensitivity, 96.7% specificity, 98.7% PPV, and 82.9% NPV. The kappa value was 0.85, and the AUC was 0.95. Overall, PDR was 67.6% and ADR was 45.9%.

Conclusions: The CADx mode showed good accuracy in characterizing colorectal lesions, but the expert assessment was superior in almost all diagnostic criteria. PDR and ADR were high.

Keywords: Adenomas, artificial intelligence, colonic polyps, colonoscopy, computer-assisted diagnosis

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INTRODUCTION

Colonoscopy is well accepted as the most effective method for preventing colorectal cancer (CRC), as it

allows the detection and subsequent removal of precursor lesions (adenomas), thus reducing CRC incidence and mortality.^[1] The adenoma detection rate (ADR) is

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considered a major quality indicator, and its concept is based on the percentage of screening colonoscopies in which at least one adenoma was detected, which must be at least 25%.^[2] There is an inverse relationship between ADR and interval cancer: The higher the ADR, the fewer the cases of interval cancer.^[3] A significant adenoma miss rate has been observed, and the main reasons include failure to recognize the lesions, especially small, proximal, nonpolypoid lesions, and incomplete exposure of the colorectal mucosa, particularly due to suboptimal colonoscopic withdrawal technique.^[4]

Recent technologies with image-enhanced endoscopy (IEE) have allowed an increase in the visibility and detection of adenomas, as well as good-to-excellent results regarding the differential diagnosis between neoplastic and nonneoplastic lesions, which is operator-dependent.^[5-11] The most used classification for the characterization of lesions is the Japan Narrow-Band Imaging (NBI) Expert Team (JNET).^[12] However, it is not perfect, as it classifies both hyperplastic polyps and sessile serrated lesions (SSLs), precursors of CRC, as JNET type 1. Recently, multi-light technology has been developed with a light-emitting diode (LED) light source (BL-7000) and a video processor (VP-7000), known as the ELUXEO system (Fujifilm Co, Japan). This system has four LEDs that allow the use of IEE in blue light imaging (BLI), BLI bright (BLI-b), and linked color imaging (LCI) modes, in addition to white light imaging (WLI). A compact, more affordable processor has also been developed, consisting of three LEDs, with the features of WLI, BLI, and LCI, called ELUXEO Lite (EP-6000, Fujifilm Co, Japan). Both systems have an interface for artificial intelligence (AI).

AI is a technology that mimics human cognitive function. More recently, deep learning AI has been developed and allows a more detailed real-time image analysis based on the artificial neural network, which has dramatically changed the field of visual computing. This change has the potential to improve physician performance by allowing those without expertise to produce better, highly accurate results and by enhancing the performance of fatigued endoscopists. Several computer-assisted diagnosis (CAD) systems have been used for the detection (CADE) and characterization (CADx) of lesions. The primary objective of this study was to evaluate the characterization of colorectal lesions by the CADx mode of the CAD EYE system compared with that by an endoscopist with expertise in IEE. As a secondary objective, we determined the polyp detection rate (PDR) and ADR of CADE.

PATIENTS AND METHODS

This prospective observational study was conducted in the Department of Endoscopy at Hospital Santa Casa de Caridade de Bagé, Southern Brazil, between July 6 and July 27, 2021, with 79 colonoscopies performed in this period. The study was approved by the research ethics committee of the institution and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from each study participant. Exclusion criteria were age <30 years, advanced CRC, inflammatory bowel disease, presence of adenomas diagnosed on a previous colonoscopy, or inadequate bowel preparation. All patients who did not meet the exclusion criteria were included in the study.

Lesions were evaluated according to their size, morphology, location, capillary pattern, and histology. Lesion size was measured with open biopsy forceps. Morphology was classified into polypoid and nonpolypoid lesions, in accordance with the Paris classification.^[13] The location was divided into the right colon segment (from the transverse colon to the cecum) and the left colon segment (from the rectum to the descending colon). The World Health Organization (WHO) classification for tumors was used for histopathological typing and grading.^[14] Lesions were divided into dysplastic (adenomas and intramucosal carcinomas) and nondysplastic (hyperplastic polyps and SSLs without dysplasia) as in the study by Sánchez-Montes *et al.*^[15] Adenomas ≥ 10 mm in diameter with a villous component and/or high-grade dysplasia were considered advanced adenomas. All colonoscopies were performed by the same endoscopist, with 14 years of experience in IEE. For colon cleansing, patients ingested 1 L of 10% mannitol solution on the day of the examination, preceded by a fiber-free, clear liquid diet for 1 day. Sedation was achieved with intravenous administration of midazolam and meperidine or fentanyl. Colonoscopy withdrawal time was >6 minutes in all examinations, under WLI and without zoom magnification, during the mucosal inspection. After detection, magnification was used on all diagnosed lesions combined with BLI IEE. Subsequently, the lesions were removed using biopsy forceps, snare polypectomy, or endoscopic mucosal resection and analyzed by a pathologist who was blinded to the endoscopic results.

Colonoscopy and CAD EYE system

All colonoscopies were performed with a high-definition (HD) device under magnification (EC-760ZP-VL, Fujifilm Co, Japan) and an integrated image processor and light source system (ELUXEO Lite), with a multi-light technology-based light source with three independent

high-intensity LEDs, thus producing high-quality images displayed in full HD resolution. Fujifilm Co developed its AI or CAD platform with a deep learning system, known as CAD EYE, which allows the detection (CADE) and characterization (CADx) of lesions based on the vascular pattern. To help prevent CRC by increasing the detection of adenomas, CAD EYE can be used in WLI or LCI mode and displays a visual identifier to mark the suspicious lesion, accompanied by a sound signal to draw attention to it. The characterization module functions in combination with the BLI technology, whose objective is to improve diagnostic accuracy and reach the level of experts. It classifies lesions into two types: neoplastic and hyperplastic. There is also display color characterization, with yellow signaling “neoplastic” and green signaling “hyperplastic.” CAD EYE can be activated simply with just one click of the scope switch, similar to the use of IEE, or even directly on the processor. In all examinations, AI was turned off during the insertion of the colonoscope and turned on only when the colonoscope was withdrawn from the cecum.

The diagnostic performance of CADx was compared with that of the expert endoscopist. The performance of the expert for optical diagnosis was based on the JNET classification to make an accurate comparison with CADx, which was dichotomized into hyperplastic vs neoplastic lesions. Diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the receiver operating characteristic curve (AUC) were investigated. AUC values >0.91 were interpreted as excellent, 0.81–0.90 as good, and 0.71–0.80 as fair. The agreement was also evaluated using Fleiss’ kappa. Fleiss’ kappa values of 0.81–1.00 were interpreted as very good, 0.61–0.80 as good, 0.41–0.60 as moderate, 0.21–0.40 as fair, and <0.20 as poor.^[16]

Statistical analysis

Data were tabulated in an Excel spreadsheet and transferred to Stata, version 15.1, for statistical analysis. First, the results were summarized descriptively and presented as absolute (n) and relative frequencies (%). Numerical variables were expressed as mean and standard deviation (SD). Second, the distribution of the sample according to lesion type (neoplastic or hyperplastic) was analyzed using Fisher’s exact test, where a *P* value <0.05 was considered statistically significant. Third, reproducibility (accuracy and kappa coefficient) and diagnostic values (sensitivity, specificity, PPV, NPV, and AUC) were tested between the different diagnostic methods (pathology, AI, and expert). Finally, a subgroup analysis was performed for lesions ≤5 mm.

RESULTS

A total of 74 patients participated in the study. Of these, 52 had 110 colorectal lesions. Most participants were women (59.6%), with a mean age of 61.3 (SD, 12.7) years (range, 33–89 years). Five patients were excluded, one for each exclusion criterion. The mean lesion size was 4.3 (SD, 4.1) mm (range, 2–30 mm), with 93 lesions (84.5%) ≤5 mm in diameter. Morphologically, 50 lesions (45.5%) were classified as polypoid and 60 (54.5%) as nonpolypoid. Regarding location, 64 (58.2%) were in the left colon segment and 46 (41.8%) were in the right colon segment. Histopathologically, 80 lesions (72.7%) were classified as dysplastic, of which 75 (68.2%) were tubular adenomas, four (3.6%) were tubulovillous adenomas, and one (0.9%) was an intramucosal carcinoma, whereas 30 lesions (27.3%) were classified as nondysplastic, of which 27 (24.6%) were hyperplastic polyps and three (2.7%) were SSLs. There were six (5.5%) advanced adenomas. Among the 80 dysplastic lesions detected in 34 patients, there was predominance in women (58.8%) and in individuals aged ≥50 years (79.4%). Regarding shape, 42 (52.5%) were polypoid lesions and 38 (47.5%) were nonpolypoid lesions; 41 (51.2%) were located in the left colon segment, and 39 (48.8%) were in the right colon segment. The characteristics of the patients and lesions are shown in Table 1. Overall, PDR was 67.6% and ADR was 45.9%.

The analysis with AI showed 81.8% accuracy, 76.3% sensitivity, 96.7% specificity, 98.5% PPV, and 60.4% NPV.

Table 1: Description of the patient sample according to pathology (n=52 patients; 110 lesions)

Characteristic	n (%)		P*
	Nondysplastic lesions (n=30)	Dysplastic lesions (n=80)	
Sex			1.00
Female	11 (35.5)	20 (64.5)	
Male	7 (33.3)	14 (66.7)	
Age (years)			1.00
Up to 49	4 (36.4)	7 (63.6)	
50 or +	14 (34.2)	27 (65.8)	
Morphology			<0.01
Nonpolypoid	22 (36.7)	38 (63.3)	
Polypoid	5 (10.6)	42 (89.4)	
Size (mm)			1.00
≤5	26 (28.0)	67 (72.0)	
>5	4 (23.5)	13 (76.5)	
Location			0.02
Left colon segment	23 (35.9)	41 (64.1)	
Right colon segment	7 (15.2)	39 (84.8)	
Expert			<0.001
Hyperplastic	29 (82.9)	6 (17.1)	
Neoplastic	1 (1.3)	74 (98.7)	
Artificial intelligence			<0.001
Hyperplastic	29 (60.4)	19 (39.6)	
Neoplastic	1 (1.6)	61 (98.4)	

*Fisher’s exact test

The level of agreement (kappa value) was 0.61, and the AUC was 0.87. Expert analysis showed 93.6% accuracy, 92.5% sensitivity, 96.7% specificity, 98.7% PPV, and 82.9% NPV. The kappa value was 0.85, and the AUC was 0.95. These evaluations with their respective 95% confidence intervals (CIs) are shown in Table 2. There was good agreement between AI and expert analyses (kappa = 0.75). In the subgroup analysis of lesions ≤ 5 mm, the expert had an accuracy of 92.5%, a sensitivity of 91.0%, a specificity of 96.2%, a PPV of 98.4%, an NPV of 80.6%, a kappa value of 0.82, and the AUC of 0.94, whereas the AI had an accuracy of 79.6%, a sensitivity of 73.1%, a specificity of 96.2%, a PPV of 98.0%, an NPV of 58.1%, a kappa value of 0.58, and the AUC of 0.85. The kappa value between expert and AI analyses was 0.74.

DISCUSSION

The elimination of colorectal adenoma has been recognized as a key strategy for the effective prevention of CRC by reducing the risk of developing this neoplasm. Colonoscopy is highly operator-dependent both for detecting lesions and for making optical diagnosis and subsequent management. Only reasonable results were reported by a study conducted in a non-academic setting, with 77% sensitivity, 78.8% specificity, and 77.9% accuracy in differentiating between neoplastic and non-neoplastic lesions with IEE.^[17] Our previous study using IEE with the BLI mode for the same purpose showed a sensitivity of 95.7%, a specificity of 95.2%, and an accuracy of 95.5%.^[10] Similar to the study by Sánchez-Montes *et al.*,^[15] dysplastic lesions (72.7%) predominated in our series, including diminutive lesions (72.0%).

The primary goal of AI in colonoscopy is to improve the performance of non-expert endoscopists by helping them achieve results comparable to those obtained by experts. Tischendorf *et al.*^[18] showed significantly better results for the expert group regarding specificity (85.7% vs 61.2%, $P = 0.0005$) and accuracy (91.9% vs 86.2%, $P = 0.023$)

compared with a computer-based algorithm (CBA), with equal sensitivity (93.8%). According to the authors, a possible explanation for this difference is that human observers may unconsciously consider additional features other than vascular patterns. In the study by Gross *et al.*,^[19] the expert group had better results in all diagnostic criteria than the non-expert group. When comparing CBA vs non-experts, the results were significantly better for the CBA group regarding sensitivity (95% vs 86%), NPV (92.4% vs 81.1%), and accuracy (93.1% vs 86.8%) ($p < 0.001$). Experts and CBA achieved a comparable performance. In the study by Renner *et al.*,^[20] CADx had an accuracy of 78.0%, a sensitivity of 92.3%, a specificity of 62.5%, a PPV of 72.7%, and an NPV of 88.2%. The same analysis for two experts showed 77.0% and 84.0% accuracy, 73.1% and 92.3% sensitivity, 75.0% and 81.3% specificity, 80.0% and 80.9% PPV, and 73.6% and 90.0% NPV. The kappa values between CADx and the two experts were 0.43 and 0.49. The CADx performance for diminutive rectosigmoid polyps had an accuracy of 82.9% (same as that of the experts), a sensitivity of 100%, a specificity of 77.8%, a PPV of 57.1%, and a NPV of 100%. In the present study, the accuracy obtained by the expert was 93.6%, sensitivity was 92.5%, specificity was 96.7%, a PPV was 98.7%, and NPV was 82.9%, whereas for AI, the results were 81.8%, 76.3%, 96.7%, 98.5%, and 60.4%, respectively, with the expert being significantly superior to the AI ($p < 0.01$) in terms of accuracy, sensitivity, and NPV. The AUC value was 0.95 (excellent) for the expert and 0.87 (good) for AI. The agreement between expert and AI was good (kappa = 0.75). For lesions ≤ 5 mm, all diagnostic criteria assessed by the expert were $>90\%$, except for an NPV of 80.6%, whereas for AI, accuracy was 79.6%, sensitivity was 73.1%, specificity was 96.2%, PPV was 98.0%, and NPV was 58.1%. The agreement between expert and AI remained good (kappa = 0.74).

It has been demonstrated that an accurate optical diagnosis depends on the endoscopist's skills and experience in IEE, being therefore examiner-dependent. In real-time optical biopsy with NBI, only 25% of gastroenterologists assessed polyps with $>90\%$ accuracy.^[21] Kominami *et al.*,^[22] using AI, showed an accuracy of 94.9%, a sensitivity of 95.9%, a specificity of 93.3%, a PPV of 95.9%, and an NPV of 93.3%, with an agreement with the endoscopic diagnosis of 97.5% (kappa = 0.95). Jin *et al.*^[23] demonstrated that the optical diagnosis performances of novices, expert endoscopists, and IEE-trained expert endoscopists were 73.8%, 83.8%, and 87.6%, respectively, and their diagnostic accuracy improved with CADx (85.6%, 89.0%, and 90.2%, respectively). Without CADx, the novice group had significantly lower accuracy than both experts ($p = 0.049$)

Table 2: Comparison of diagnostic performance between artificial intelligence and experts

Indicator	Artificial intelligence	Expert
Accuracy	81.8% (95% CI 78.8–84.8)	93.6% (95% CI 92.4–94.8)
Kappa	0.61 (0.47–0.76)	0.85 (0.74–0.96)
Sensitivity	76.3% (95% CI 65.4–85.1)	92.5% (95% CI 84.4–97.2)
Specificity	96.7% (95% CI 82.8–99.9)	96.7% (95% CI 82.8–99.9)
PPV	98.4% (95% CI 91.3–100.0)	98.7% (95% CI 92.8–100.0)
NPV	60.4% (95% CI 45.3–74.2)	82.9% (95% CI 66.4–93.4)
AUC	0.87 (0.81–0.92)	0.95 (0.90–0.99)

PPV: Positive predictive value, NPV: Negative predictive value, AUC: Area under the ROC curve. When comparing the two performances, the accuracy, kappa, sensitivity, NPV, and AUC values of the expert were superior to those of artificial intelligence ($P < 0.01$)

and trained experts ($p = 0.001$), whereas with CADx, the accuracy of novices almost reached the level of performance of experts ($p = 0.102$). In the study by Chen *et al.*,^[24] CADx showed a sensitivity of 96.3%, a specificity of 78.1%, an accuracy of 90.1%, a PPV of 89.6%, and an NPV of 91.5%. For experts, the same criteria ranged from 97.3% to 97.9%, 65.6% to 77.1%, 87.0% to 90.5%, 84.8% to 89.3%, and 93.7% to 94.0%, respectively, whereas for novices, they ranged from 81.9% to 97.3%, 65.6% to 88.5%, 80.3% to 88.0%, 84.2% to 93.5%, and 68.5% to 93.1%, respectively. The agreement between AI and the two experts was 87.7% and 88.3%. In a previous study, our interobserver agreement using IEE with flexible spectral imaging color enhancement (FICE) was good ($\kappa = 0.80$).^[25]

Recently, CAD EYE analysis using BLI for CADx demonstrated a sensitivity of 96.3%, a specificity of 88.7%, and an accuracy of 94.9%.^[26] Yoshida *et al.*^[27] reported a sensitivity of 93.3%, a specificity of 90.9%, and an accuracy of 92% for experts. There was a significant difference in CADx accuracy between CAD EYE (with magnified BLI) and the trainee group (87.8% vs 79.0%, $P = 0.04$). In a multicenter study, CADx from CAD EYE was significantly superior in terms of diagnostic accuracy to experts (95.0% vs 81.7%, $P = 0.03$) and novices (95.0% vs 66.7%, $P < 0.001$), as well as in terms of sensitivity (95.6% vs 61.1%, $P = 0.03$; 95.6% vs 55.4%, $P < 0.001$, respectively). NPV was 87.5% for CADx.^[28] In a previous study, when we analyzed only rectosigmoid lesions ≤ 5 mm with IEE (BLI), all diagnostic criteria had values $>90\%$, including NPV (94.8%).^[10] In the study by Weigt *et al.*,^[29] CADx with BLI showed an accuracy of 83.6%, a sensitivity of 85.0%, and a specificity of 79.4%. Evaluating the same criteria, experts showed 79.3% accuracy, 79.0% sensitivity, and 80.4% specificity, whereas non-experts + CADx showed 80.1%, 86.0%, and 62.7%, respectively. Therefore, the accuracy was similar in the three groups. However, the non-expert + CADx group had significantly lower specificity ($p < 0.05$) than that of the other groups and significantly higher sensitivity ($p < 0.05$) than that of experts. According to the authors, a possible explanation for the higher sensitivity of non-experts than experts is that the former allowed themselves to be influenced by the interpretation of the AI.

A meta-analysis of five randomized controlled trials involving 4354 patients showed significantly better ADR results for the CADe group than for the control group (36.6% vs 25.2%) ($p < 0.01$).^[30] There was no difference between the groups in advanced ADR. In the present series, we detected six advanced adenomas,

accounting for 5.5% of the lesions. Another meta-analysis of 10 randomized controlled trials identified a significant increase in ADR ($p < 0.001$) and PDR ($p < 0.001$) in favor of AI.^[31] In the study by Repici *et al.*,^[32] despite the high ADR observed in the control group (40.4%), ADR was higher (54.8%) in the CADe group. Several studies have reported increased ADRs in CADe groups, but some of them have shown low ADRs in the control group. This difference may be explained by the different levels of expertise of the endoscopists participating in the studies. We evaluated lesion detection using AI alone and found a high ADR of 45.9% and a PDR of 67.6%, involving not only individuals undergoing screening colonoscopy but also symptomatic patients under follow-up.

Limitations of this study include the fact that it was conducted in a single endoscopy center and by the same endoscopist experienced in IEE. Also, the study involved a small sample of lesions. Another limitation was the difficulty of AI in differentiating SSLs from hyperplastic polyps, as both lesions have a similar vascular pattern, being classified as JNET type 1 and, therefore, within the same group of non-dysplastic lesions. As a final limitation, our study was not a randomized trial to compare PDR and ADR between AI and endoscopist.

In certain cases, by interpreting the predictive diagnosis given by the AI in a different manner, the endoscopist changes the position of the colonoscope in the lesion, thus making the CADx change its interpretation. This shows that there is still some degree of operator dependence to achieve better results. The possibility of less experienced endoscopists being passively influenced in their diagnoses and decisions by erroneous AI predictions should be acknowledged. Also, there is the possibility of developing a new generation of technology-dependent endoscopists, with reduced caution, interest, and ability to improve the recognition and characterization of lesions. It should be noted that the endoscopist will be liable for any misdiagnosis; therefore, only a well-trained physician will be able to accept or reject the interpretation provided by AI.

In conclusion, AI yields good accuracy in the optical diagnosis of colorectal lesions, but its performance is inferior to that of an expert. It showed high ADR and PDR. For the inclusion of AI in clinical practice, in addition to improving the performance of endoscopists who lack expertise, it is necessary to ensure that AI will provide a safe basis for treatment choice.

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Conflicts of interest

There are no conflicts of interest.

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