8-2020

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Literature Review

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Short title: Goyal et al. Artificial intelligence and colorectal cancer

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Scope of Artificial Intelligence in Screening and Diagnosis of Colorectal Cancer

Abstract

Globally, colorectal cancer is the third most diagnosed malignancy. It causes significant mortality and morbidity, which can be reduced by early diagnosis with an effective screening test. Integrating artificial intelligence (AI) and computer-aided detection (CAD) with screening methods have shown promising results for colorectal cancer screening. AI could provide a "second look" for endoscopists to decrease the rate of missed polyps during a colonoscopy. It can also improve detection and characterization of polyps by integration with colonoscopy, various advanced endoscopic modalities like magnifying narrow-band imaging, endocytoscopy, confocal endomicroscopy, laser-induced fluorescence spectroscopy, and magnifying chromoendoscopy. In this review, we have discussed various AI and CAD applications in CRC screening, polyp detection, and characterization.

Keywords: Artificial Intelligence; Colorectal cancer; colon cancer; polyp; screening; colonoscopy; computer-aided diagnosis.
Introduction

Artificial Intelligence (AI) translates as having a computer program that mimics the learning and problem-solving capability of humans (1). The concept of AI dates back to as early as Aristotle’s (384–322 BC) study of logic; however, Alan Turing (1912–1954) built the first operational computer in 1940 known as Electromechanical Heath Robinson (2). AI in medicine has two main branches, virtual and physical. Machine Learning (ML) and Deep Learning (DL) represent the virtual branch of AI in medicine (3). The ML involves computer statistics and analytics to make predictive and descriptive models through the repetition of specific tasks. The ML comprises of unsupervised and supervised learning. As the name implies, unsupervised ML is to feed the data without prior knowledge, and the machine identifies the groups based on the similarities in data. In supervised ML, the machine is fed with input (individual descriptions) and output (an outcome of interest) data. The computer eventually outlines newer input/output pairs based on the information feeds (1). Bayesian inferences, decision trees, linear discriminants, support vector machines (SVM), logistic regression, and artificial neural networks (ANNs) are different models of ML (4).

For DL, the ML algorithms are used in layers of non-linear processing in two steps: a) Transformation- which refers to building a useful data model. b) Feature extraction- which refers to computational automation to focus on a targeted featured aspect of the data to increase the power of prediction (5). A DL-based model called a deep neural network (DNN) was developed because of increased demand for more accurate predictions. DNN is a complex neural architecture that automatically detects the input data's relevant features by using various consecutive filters (6). The physical branch is the second branch of AI in medicine, including medical devices and robots (3). Intensive research focused on the use of AI applications in the medical field is underway, which could provide unprecedented opportunities to improve the quality of healthcare (7).
Colorectal cancer (CRC) is the fourth most common cause of death due to cancer worldwide (8). Screening colonoscopy resulted in a 70% decrease in the CRC-related deaths by early detection and removal of preneoplastic and neoplastic lesions (9). One of the most crucial parameters of colonoscopy is the adenoma detection rate (ADR), which is a direct measure of the effectiveness of colonoscopy performed by an endoscopist (10). Post-colonoscopy CRC (PC-CRC) and CRC-related mortality are known to be inversely related to the adenomas detected during colonoscopy (10-13). In addition, there are also various other tools such as blood tests, stools tests, and imaging modalities that aid in the screening for CRC (14).

The role of AI in gastroenterology is increasing at a rapid pace, ranging from diagnosis and classification of dysplastic and neoplastic changes of the polyps to cystic fluid analysis, and accurate prediction models to determine the need for intervention with computer-aided detection and diagnosis (CAD) (7, 15). The incorporation of AI and its tools with known methods of screening and diagnosis of CRC can increase the diagnostic accuracy and potentially attenuate CRC-related mortality. Additionally, by real-time differentiation of neoplastic and benign tumors, AI can also decrease the unnecessary removal of non-neoplastic tumors, which can reduce the overall cost, procedure time, and associated complications. In this review, we aim to discuss current advancements in the role of AI for CRC screening in various modalities, including colonoscopic examination, blood and stool testing, and imaging. We will also elaborate on the role of AI in the colorectal polyp detection and their characterization.

1. Screening of Colorectal Cancer

CRC causes significant mortality and morbidity. Early diagnosis by effective screening method has shown to decrease both mortality and morbidity related to CRC. There are multiple screening methods for CRC screening. It includes invasive tests like the colonoscopy and flexible sigmoidoscopy; stool tests like fecal immunochemical test (FIT), guaiac-based fecal occult blood test and multitarget stool DNA (MTS-DNA); radiologic tests like capsule endoscopy and computed tomographic colonography (CTC) and newer blood test, Epi procolon® (16, 17).
1.1 Colonoscopy

Colonoscopy is considered as the gold standard method of CRC screening due to high sensitivity, specificity, and ability to visualize directly and act (biopsy and resection of polyps) on cancerous and precancerous lesions. Multiple case-control studies and prospective studies have shown that colonoscopy screening resulted in a significant reduction in incidence and mortality due to CRC (18-21). However, the small size or flat polyps could be missed by naked eyes. A systematic review and meta-analysis showed 22% of the pooled miss rate for polyps of any size with colonoscopy (12). Another meta-analysis showed that 8.6% of CRC cases occur within three years of negative colonoscopy results (11). With the recent advancement of AI, CAD systems like real-time automatic detection systems have been studied to improve the ADR (22).

In an open-label, non-blinded, randomized study, 1058 patients were randomized to either routine colonoscopy (n=536) or computer-aided detection (CADe), colonoscopy with real-time automatic polyp detection (n=522) in order to determine the differences in polyp and adenoma detection rate in two groups. The CADe group had a 1.89-fold higher mean number of polyps detected than the routine colonoscopy group (95% CI 1.63 to 2.192, p<0.001). Similarly, the CADe group also found to have higher ADR (29.1% vs. 20.3%, p<0.001) compared to the routine colonoscopy group. More importantly, this difference was more pronounced for diminutive adenomatous (185 vs. 102; p<0.001) polyps. For large adenomas, the mean ADR for CADe and routine colonoscopy group was (77 vs. 58, p=0.075), not reaching statistical significance. However, this study was not double-blinded. Therefore, the results could have confounded by potential unrecognized factors. Further large multicenter double-blinded studies are needed (22).

1.2 Blood tests

Certain demographic and blood test data can be used to identify patients with high risk for CRC. Complete blood count (CBC) is one of the laboratory tests that can help identify patients who are at risk, especially due to the presence of microcytic iron deficiency anemia (23, 24). A retrospective case-control study revealed that patients with colon cancer tend to have anemia
and high RDW. High RDW was more pronounced in patients with right-sided colon cancer (25). High RDW was also found to be associated with an increased risk of mortality in CRC patients (26). In CRC patients, slow bleeding from cancer is thought to cause iron deficiency anemia and stools positive for the occult blood test, and it is observed more in elderly patients. AI can be useful in the risk assessment of the general population to determine the individuals at high risk for developing CRC based on their demographic data, CBC, and age. Although this is a relatively newer method for estimating the risk of CRC, studies done have shown promising results (23, 24).

A binational study used the electronic medical records data from two unrelated patient populations (Israel and UK) to develop an ML-based prediction model (MeScore) for identifying individuals at high risk of CRC based on their CBC, age, and sex. Israeli cohort data set was randomly divided into derivation dataset (80%) and validation (20%) dataset. Whereas the UK case-control data set was used to create an external validation set. The predictive model was created using the Israeli derivation dataset and then applied to both Israeli and UK validation dataset of CRC patients who had CBC done three to six months before the diagnosis. The area under the receiver operating characteristics curve (AUC) (measuring the overall performance of the model) for detecting CRC was 0.82 ± 0.01, and 0.81 for the Israeli and UK validation set, respectively. Similarly, specificity at 50% sensitivity was 88 ± 2% and 94 ± 1% respectively for the Israeli and UK validation sets for CRC cases 3-6 months before diagnosis. While comparing this model to age alone, AUC, Odds ratio, and specificity were 0.81 vs. 0.72, 32 vs. 2, and 90% vs. 79%, respectively, showing outperformance of the predictive model. Similar results were obtained for the sex alone predictive value. Moreover, the number of detected new cases of CRC increased by 115% when gFOBT and predictive models were combined in the Israeli data set. This study showed that this model, MeScore, could detect high-risk patients in a primary care setting (24).

Kinar et al. conducted a study to analyze the performance of an ML-based algorithm (MeScore) in predicting CRC in average CRC risk individuals, based on their CBC (27). A total of 112,584 subjects (aged between 50 to 75 years) with non-CRC from the Maccabi Health Service (MHS)
dataset were recruited who underwent CBC in the last six months. Using the MeScore system, all these individuals were assigned a score from 1 to 100 based on the CBC report information. The model also incorporated demographic information such as age and sex of subjects as well. Average MeScore was found to be 59.3 and 46.8 in males and females, respectively. Using MeScore cutoff of the top three percentile (score >97.02) and top one percentile (score >99.38), the odds ratio for CRC diagnosis was found to be 10.9 (95% CI 7.3 to 16.2) and 21.8 (95% CI 13.8 to 34.2) respectively. False-positive tests based on three percentile cutoffs were seen due to the use of anticoagulant, gastrointestinal illness, and another cancer diagnosis. This study showed that ML algorithm tools like MeScore could be used to identify high-risk patients who should undergo screening colonoscopy(27).

Machine learning tool, ColonFlag performance for early detection of CRC was evaluated based on the gender, age, and CBC from the US-community based insured population using Kaiser Permanente Northwest Region (KPNW) tumor registry. A total of 17,095 patients were included in the study, with 900 CRC patients and 16,195 CRC-free control patients. Data about patient demographics and CBC was obtained from the dataset. The AUC for detecting CRC was found to be 0.80 ± 0.01, with 0.81 for women and 0.79 for men. As the time interval since the last CBC increased, the odds ratios for CRC detection decreased. Odd ratios at 99% specificity for detecting CRC in patients aged 40-89 years were 34.7 and 20.4 for 0-180 days and 181-365 days after CBC, respectively. This study showed that early stage (0-II) CRC could be identified 180-360 days prior to CRC diagnosis by ColonFlag (23).

1.3 CT colonography (CTC)

CTC is a non-invasive imaging test for CRC (28, 29). CAD can improve CTC diagnostic capability to differentiate between different lesions and improve detection capability. Song et al. conducted a study where they used the Haralick texture analysis method along with CTC to differentiate between various lesions based on texture features. The virtual pathological model was formed based on the Haralick texture analysis method to investigate the usefulness of high order derivatives like gradient and curvature. Texture features were validated on 148 lesions of 8mm
to 30mm sized polyps using a support vector machine classifier. AUC of classification in differentiating neoplastic from non-neoplastic lesions improved from 0.74 (using the image intensity alone) to 0.85 (by combining the high-order texture features) (29).

A study on the 24 patients who underwent colonoscopy and CTC on the same day and had non-polypoidal T1 tumors with the endoscopic classification of 0-IIa (n=11) and IIa +IIc (n=13). CAD software (ColonCAD API 4.0, Medicsight plc) was integrated with a CTC radiologic workstation. Data were collected at three sphericity settings, operating points for CAD, and analyzed using Fischer’s exact test. With CAD, tumor detection sensitivity increased as sphericity decreased (83.3%, 70.8%, and 54.1% at sphericity of 0, 0.75, and 1). Whereas, false positives CAD per patient decreased with increasing sphericity. Small benign polyps led to false positive detection (over 20% at sphericity setting of 0), although the majority were due to normal colon anatomy. The results of this study indicated that CAD could be useful for the detection of morphologically flat non-polypoidal cancer (28).

1.4 Colon capsule endoscopy

Colon capsule endoscopy (CCE) is a minimally invasive procedure that can be used as a CRC screening method in patients with incomplete colonoscopy and contraindication for sedation use. It requires more laxatives than colonoscopy and CTC as laxatives help expulsion of the capsule from the GI tract along with cleansing. Capsule endoscopy requires manual reading and interpretation of images for polyp detection, increasing the risk of error. AI techniques can automate the interpretation of results (30, 31). Balnes-Vidal et al. conducted a study to develop a DL-based CNN algorithm for automatic polyp detection and also to develop an algorithm to match CCE and colonoscopy detected polyps based on their size, location, and morphology. A total of 255 people with FIT positive from the Danish national screening were included in this study. All these patients underwent first CCE and then colonoscopy and histopathology of removed polyps. Out of 255, 131 patients had at least one polyp detected in both CCE and colonoscopy. A total of 168 polyps were matched in both CCE and colonoscopy groups by the polyp matching algorithm. Autonomous polyp detection algorithm showed accuracy, sensitivity, and
specifiçity of 96.4%, 97.1%, and 93.33%, respectively, for polyp detection compared to manual polyp detection (30).

2. Polyp Detection

Although colonoscopy is considered a gold standard test to detect CRC, it is not 100% sensitivity. This is especially true for adenoma <5 mm. For adenoma 6mm or larger, the sensitivity of colonoscopy ranges from 75-93% (32). This sensitivity also depends on various factors, including bowel preparation, mucosal surface visibility, and operator dependent. Repeat surveillance colonoscopy is recommended in patients depending upon the number, histopathologic characteristics, and size of polyps (33). A retrospective observation population-based analysis using National Health Service (NHS) data from 2001 to 2010 showed that PC-CRC rates ranging from 2.5 to 7.7% depending upon the method used and exclusion criteria applied (11). Another population-based study conducted on data of colonoscopy and histopathological reports from the Netherlands cancer registry (2001-2010) showed that 86% of PC-CRC were related to inadequate examination and missed or incomplete removed lesions (34). Most of the missed PCCRC were on the right-sided, proximal, flat, and small size (11, 34). Therefore, there is a need for various methods/techniques to improve polyp detection to prevent PC-CRC, and AI could be utilized to achieve this (8, 33).

Karkanis et al. used color wavelet features (CWF) technique to detect tumors from colonoscopic video frame sequences. Sixty patients with small polyps were included in this study, and results showed high sensitivity and specificity (99.3±0.3% and 93.6±0.8%) on classified image regions to detect colorectal polyps with use of CWF features. However, this study was done using static images instead of real-time colonoscopy videos (35). Endoscopic imaging material classification can be done by either a pit-pattern scheme or coarse classification. There are six different classes based on pit-pattern and two different classes (benign and malignant) based on coarse classification. Hafner and colleagues described the use of an automated classification system for endoscopic images to detect tumors. A total of 484 zoomed-colonoscopic images were classified based on two/six different classes using discriminative frequency components. The classification accuracy for six and two classes found to be 86.8% and 96.9%, respectively (36).
Most small colorectal polyps are hyperplastic with little to no risk of turning to CRC, so an accurate diagnosis of these polyps is needed to prevent unnecessary resections and complications associated with it. In a single-center study from Japan, a unique convolutional neural network (CNN) system based on CAD utilizing AI was developed to study endoscopic images extracted from colonoscopy videos (37). A total of 1200 images from colonoscopies were included, and additional video images from 10 cases were applied as a test. The accuracy of the 10-fold cross-validation test was found to be 0.751, meaning the decision by CNN was correct in 7 of 10 cases (37). Urban et al. did a study which tested the ability of computer-assisted image analysis using CNN to detect polyps (38). In this study, the CNN model was trained using a sample of 8641 images with 4088 unique polyps from more than 2000 screening colonoscopies. The training and testing of the CNN model were performed by different methods like cross-validation, training on the dataset, and testing on another or testing against expert reviewers as reference. CNN identified polyps with an accuracy of 96.4% and an AUC of 0.991 in cross-validation experiments. When tested on an independent dataset, AUC was found to be 0.74, with an accuracy of 96.4%. These results showed that the CNN model could decrease missed adenomas and thus improve ADR, but static images were used in this study. Therefore, further multicenter studies using live video needed to evaluate the utility of CNN in colonoscopy (38). There is high potential in the application of CNN for the detection of adenomas and screening of colorectal cancer.

Nevertheless, Fernandez-Esparrach et al. used routine colonoscopy videos to assess the capability of Window Median Depth of Valley accumulation (WM-DOVA) energy maps system, which defines polyp boundaries as valleys of image intensity to overcome the challenge of static images (33). Twenty-four videos containing 31 different polyps were taken from routine colonoscopies. With the WM-DOVA model, all polyps were detected correctly in at least one frame, but sensitivity was only 70% using 3.75 as a threshold value for energy map maximum, which is likely due to a small study sample. This method was found to be more useful for detecting small and flat polyps, which are easy to miss (33). In a pilot study, retrospective data were collected from a sample of 73 colonoscopy videos, including 155 colorectal polyps to develop an AI-assisted CAD polyp detection system. Both frame-based and polyp-based analyses were
performed. Sensitivity, specificity, and accuracy found to be 90.0%, 63.3%, and 76.5% respectively for frame-based analysis, where for polyp-based analysis, sensitivity was found to be 94% (39).

To further study the efficacy of polyp detection in real-time, a DL algorithm was developed with data from 5545 colonoscopy images of 1,290 patients (40). Image analysis validation was done on 27,113 colonoscopy images obtained from 1,138 patients with at least one detected polyp (Dataset A) and also on a public database of 612 images from 128 colonoscopy videos with confirmed polyps (Dataset B). Whereas video analysis validation was done on videos of 38 colonoscopies with 110 confirmed polyps (Dataset C) and also on full-length unalerted colonoscopy videos from 54 patients (Dataset D). For Dataset A, per-image sensitivity, specificity and AUC was 94.38% (95% confidence interval (CI): 93.80%, 94.96%), 95.92% (95%CI: 95.66%, 96.18%) and 0.984 respectively and for dataset B, per-image sensitivity was 88.24%, (95%CI: 85.76%, 90.72%). For Dataset C, per-image sensitivity found to be 91.64% (95%CI: 91.42%, 91.86%), and per-polyp sensitivity 100%, and for dataset C, per-image specificity was 95.40% (95%CI: 95.36%, 95.44%). The use of a multi-threaded processing system in the algorithm can process 25 frames per second, and the latency was of 76.80 ± 5.60 milliseconds in real-time video analysis. This CAD system is shown to have high performance both in image and video colonoscopy and can be used as quality measures and also as a second look for endoscopists (40).

3. Polyp Characterization

Another critical aspect in the diagnosis of colorectal polyp is an accurate polyp characterization. Most of the current literature differentiates polyp into a neoplastic or non-neoplastic polyp. Multiple advanced modalities like magnifying narrow-band imaging (NBI), endocytoscopy, confocal endomicroscopy, laser-induced fluorescence spectroscopy, and magnifying chromoendoscopy are being utilized in the polyp characterization.
3.1 Magnifying Narrow band imaging (NBI)

NBI is an image-enhanced form of endoscopy that narrows the bandwidth of spectral transmittance using optic filters for sequential green and blue illumination. This technique helps to examine microvascular patterns, which is associated with histological features and depth of submucosal invasion. NBI magnification can be useful for polyp characterization (41, 42).

In a prospective study, the computer-based method was developed for classification for colorectal polyps (43). A total of 214 patients with 434 polyps of size 10 mm or less were included in the study, and all these patients underwent zoom NBI colonoscopy. Diagnostic performance of two experts (who routinely used magnification colonoscopy with NBI for >4 yrs.), two non-experts (performing colonoscopy for at least one year but never used NBI) and computer-based algorithm compared for polyp classification as neoplastic or non-neoplastic. Results for polyp classification were comparable for expert and computer-based methods with sensitivity, specificity, and accuracy of 93.4% vs. 95.0%, 91.8% vs. 90.3%, and 92.7% vs. 93.1%, respectively. Whereas the non-expert group was inferior with a sensitivity of 86.0%, a specificity of 87.8% and accuracy was 86.8% (43). In another retrospective study, a computer-aided system was developed to predict the classification of colorectal lesions based on NBI magnifying colonoscopy images. A total of 371 NBI magnifying images of colorectal lesions from patients who underwent colonoscopy between January 2005 to July 2010 were included, and the performance of the computer-aided system was compared to two experienced endoscopists and histologic diagnosis. The computer-aided system showed diagnostic accuracy, sensitivity, and specificity of 97.8%, 97.8%, and 97.9%, respectively. Interestingly, the diagnostic agreement between computer-aided classifier systems and two experts was 98.7%, with no significant difference (42).

The optical diagnosis of colorectal polyps differs between endoscopists, so a computer-assisted optical biopsy (COAB) system was developed using machine learning to differentiate between neoplastic and non-neoplastic polyps. A total of 275 polyps were detected during colonoscopy and imaged using the unmagnified high-definition white light and narrowband image mode (44). Two experts also reviewed a total of 788 images available (602 were for training machine learning algorithms and 186 for COAB testing), and all images in optical polyp characterization. The CAOB
approach accuracy, sensitivity, and the negative predictive value were 78.0%, 92.3%, and 88.2%, respectively. However, the accuracy obtained by two expert endoscopists was 84.0% (p= 0.307) and 77.0% (p=1.000) and thus did not differ significantly from COAB predictions (44).

Bryne et al. developed a deep convolutional neural network (DCCN) for real-time assessment of untouched endoscopic video images to differentiate between adenomatous and hyperplastic diminutive colorectal polyps (45). Only NBI video frames were used in this study. Out of 125 polyp videos evaluated by the AI model to differentiate between adenomatous and hyperplastic polyp, it did not build confidence to predict histology in 19 polyp videos. In the remaining 106 videos with high confidence for prediction, AI model accuracy, sensitivity and specificity for identification of adenoma was 94% (95% CI: 86% to 97%), 98% (95% CI: 92% to 100%), 83% (95% CI: 67% to 93%) respectively. This model showed high accuracy in differentiating adenomatous and hyperplastic polyps. Although this model showed promising results, these results need to be validated in true live colonoscopies (45). Another study conducted where a CAD with deep neural network (DNN-CAD) was developed and tested to classify the diminutive colorectal polyp NBI images (46). From Taiwan’s tertiary hospital database, 1476 images of neoplastic polyp images and 681 hyperplastic polyp images with size less than 5 mm were obtained. Histology information of all these polyps was used as a reference. Information from a test set of 96 hyperplastic and 199 neoplastic polyps' images were used to compare the diagnostic ability of DNN-CAD with the novice (n=4) and expert endoscopists (n=2). DNN-CAD showed sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 96.3%, 78.1%, 89.6%, and 91.5%, respectively, of identifying hyperplastic and neoplastic polyps in a test set. The average time to classify polyps by DNN-CAD was 0.45 ± 0.07 seconds while that for experts was 1.54 ± 1.30 seconds, and non-experts were 1.77 ± 1.37 seconds (p<0.001). The intra-observer agreement (kappa score) was 1 in DNN-CAD classified polyps; however, amongst the novice and expert endoscopists, the intraobserver and interobserver agreement were lower (46).

3.2 Magnifying chromoendoscopy

Magnifying chromoendoscopy is a technique to enhance visualization of pit patterns of polyp's surface to differentiate between benign and neoplastic polyps. Magnification endoscopes have
an individual lens attached, increasing the magnifying factor from 80 to up to 150, and improving accuracy in detecting lesions during colonoscopy. In magnifying chromoendoscopy, dye spray like indigo carmine or methylene blue/crystal violet used along with magnifying endoscopy to recognize the pit patterns on the polyp surface (47-49). Pit pattern can be very helpful in the diagnosis of submucosal CRC (47). CAD can be used with magnifying chromoendoscopy to automate and diagnose the malignant potential of the colorectal polyps with high sensitivity (48, 49). There can be interobserver variation even in between experienced endoscopists to completely characterize the pit pattern correctly.

Takemura and colleagues created and analyzed an automated computer-based system, named as HuPAS version 1.3 that could outline pits identified on digital magnifying endoscopic images (48). A total of 134 regular pit pattern images were included in the study to compare the ability of an automated computer-based system and endoscopist to characterize colorectal polyps. The automated computer-based system showed an accuracy of 98.5% (132/134) in identifying the colorectal lesion's pit patterns. Their computer-based system was in 100% agreement with endoscopic diagnosis by endoscopist for type I and II pit patterns, and for type III and IV, it was able to diagnose in 96.6% and 96.7% cases respectively (48).

3.3 Endocytoscopy
Endocytoscopy (EC) allows ultra-magnification of the real-time images to 380 to 480 folds. In EC, a contact light microscopy system is added to the distal tip of the colonoscope, which enables on-site evaluation of nuclei and cytological structure for pathologic diagnosis of lesions in real-time. It is shown to be 94.1% accurate in differentiating neoplastic lesions compared to 96% with biopsy (47, 50). EC requires expert endoscopists to interpret results, and it is very operator-dependent. Therefore, developing a CAD system for EC will allow interpretation by non-expert endoscopists also.

CAD-EC was developed and tested in a pilot study of 152 patients with small colorectal polyps (≤ 10mm) (50). CAD-EC system was compared with two experts and two trainee endoscopists in
predicting neoplastic changes in the colorectal lesions. For CAD-EC and EC evaluation by expert, accuracy and sensitivity were found to be 89.2% (95% CI, 83.7%-93.4%) vs. 92.3% (95% CI, 89.0%-94.9%) and 92% (95% CI, 86.1%-95.9%) vs 92.7% (95% CI, 89.0%-95.5%), respectively. Trainee endoscopists had much lower accuracy of 80.4% and sensitivity of 81.8% when compared to CAD-EC. The results of this study showed that CAD-EC has a sensitivity and accuracy comparable to expert endoscopists, and could also provide an instant diagnosis as it takes 0.3 seconds per lesion (50).

In another retrospective study, CAD-EC was developed and evaluated to differentiate between invasive CRC and adenomatous lesions (51). The image database was generated based on a consecutive series of EC images from 242 patients. From the dataset, 5543 images were used to construct the CAD-EC algorithm and 200 images to test the system. CAD-EC showed a sensitivity of 89.4%, specificity of 98.9%, the accuracy of 94.1%, PPV of 98.8%, and NPV of 90.1% in differentiating invasive cancer from adenoma. Although this study showed a promising result, it was conducted on a database of EC images, so further multicenter clinical trials on real-time colonoscopy videos are needed (51).

3.4 Confocal endomicroscopy/confocal laser endomicroscopy

Confocal endomicroscopy/confocal laser endomicroscopy is available in the biomedical field since 1961 (52). It allows magnification up to 1000-fold in real-time images and thus allows real-time in vivo histological images of gastrointestinal mucosa (52). Probe-based confocal laser endomicroscopy (pCLE) usually performed by endoscopist experts in this technique and required much training. A computer-based system can provide objective support for pCLE diagnosis. Andre and et al. developed and studied the diagnosis ability of computer-based automated pCLE classification and compared it with expert endoscopists who made the diagnosis based on pCLE videos alone to differentiate between neoplastic and non-neoplastic polyps (53). A total of 135 images of colon polyp from 76 patients were included, and histopathological diagnosis was used as standard criteria. Results revealed sensitivity, specificity, and accuracy of 92.5% vs. 91.4%, 83.3% vs. 84.7%, and 89.6% vs. 89.6%, respectively, for computer-based automated pCLE
classification and expert performance in differentiating neoplastic and non-neoplastic lesions and these differences were not statistically significant (53).

3.5 Laser-induced fluorescence spectroscopy (LIFS)

Laser-induced fluorescence spectroscopy (LIFS) is a technique that provides real-time automatic differentiation of colorectal polyps as benign or neoplastic. It is an optical fiber device, WavSTAT, that is installed into biopsy forceps. It emits laser waves that are absorbed by targeted tissue and then release light to give optical biopsy results of whether the targeted lesion is neoplastic or non-neoplastic (54, 55). Diagnostic accuracy of WavSTAT was compared to WavSTAT along with high-resolution endoscopy in 87 patients with 207 colorectal polyps (size less than 10mm). The diagnostic accuracy of WavSTAT alone (74.4%) and WavSTAT with high-resolution endoscopy (79.2%) and it did not meet the criteria for the American Society for Gastrointestinal Endoscopy (ASGE) performance threshold for assessment of small colorectal lesions (54). Rath et al. studied a new version of the LIFS system called WavSTAT4, which could predict a colorectal neoplasm in vivo within 1 sec. In a prospective observational study, histology of 137 small polyps (≤ 5mm size) from 27 patients who underwent screening or surveillance colonoscopy was predicted with LIFS using WavSTAT4 and compared to traditional histopathological results. The sensitivity, specificity, NPV and accuracy of LIFS using WavSTAT4 was found to 81.8% (95%CI 59%–94%), 85.2% (95 %CI 77.1%–90.9 %), 96.1% (95 %CI 89.7%–98.8 %) and 84.7%, respectively. This study shows that the LIFS with WavSTAT4 can predict colorectal lesion histology, and these results were more pronounced in small polyps in the distal colorectal area (55).

3.6 Autofluorescence endoscopy

Endogenous fluorophores in the colorectal tissue emit natural tissue fluorescence upon excitation by light. The autofluorescence imaging (AFI) system analyzes the fluorescence and provides green/red (G/R) image (9). AFI colonoscopy produces real-time pseudo-color images with neoplastic lesion appears green and non-neoplastic lesion appears red/magenta (56, 57). Aihara and colleagues developed a color analysis software that enables analysis of colorectal lesion with AFI and studied the diagnostic ability of this software in a prospective study of 32
patients with 102 colorectal lesions. Lesions were labeled as neoplastic (<1.01) and non-neoplastic (≥1.01) based on the G/R ratio. Results showed that the mean G/R ratio was 0.86 for neoplastic lesions, 1.12 for non-neoplastic lesions, and 1.36 for normal mucosa. This study showed that colorectal lesions could be differentiated into neoplastic and non-neoplastic based on AFE and decrease unnecessary interventions (56).

**Conclusion**

AI has expanded exponentially over the last few years in the gastroenterology field, especially in gastrointestinal cancer screening and diagnosis. Implementation of AI and CAD technology with colonoscopy and various endoscopic modalities is showing promising results for screening and diagnosis of CRC. In colorectal polyps detection and classification, AI and CAD can provide clinicians assistance and a second look in establishing the diagnosis. Multiple studies showed that computer-aided software could provide real-time optic biopsies comparable to expert endoscopist performance. Nevertheless, most of the data is available based on small studies at tertiary care centers. Further large multicenter clinical trials are needed to establish the diagnostic accuracy of AI technology in the real world.

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Final approval: All authors

**Funding:** This article received no external funding

**Acknowledgments:** None

**Conflict of Interest:** All authors declare no conflict of interest.
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