80441_Auto_Edited -check.docx

Artificial intelligence and inflammatory bowel disease: Where are we going?

Da Rio L *et al*. Artificial intelligence and IBD

Leonardo Da Rio, Marco Spadaccini, Tommaso Lorenzo Parigi, Roberto Gabbiadini, Arianna Dal Buono, Anita Busacca, Roberta Maselli, Alessandro Fugazza, Matteo Colombo, Silvia Carrara, Gianluca Franchellucci, Ludovico Alfarone, Antonio Facciorusso, Cesare Hassan, Alessandro Repici, Alessandro Armuzzi

Abstract

Inflammatory bowel diseases (IBD), namely ulcerative colitis (UC) and Crohn's disease (CD), are chronic and relapsing conditions that pose a growing burden on healthcare systems worldwide. Because of their complex and partly unknown etiology and pathogenesis, the management of UC and CD can prove challenging not only from a clinical point of view but also for resources optimization. Artificial intelligence (AI), an umbrella term that encompasses any cognitive function developed by machines for learning or problem solving, and its subsets machine learning and deep learning are becoming ever more essential tools with a plethora of applications in most medical specialities. In this regard gastroenterology is no exception, and due to the importance of endoscopy and imaging numerous clinical studies have been gradually highlighting the relevant role that AI has in IBD as well. The aim of this review is to summarize the most recent evidences on the use of AI in IBD in various contexts such as diagnosis, follow up, treatment, prognosis, cancer surveillance, data collection and analysis. Moreover, insights will be provided as for the potential further developments in this field and their effects on future clinical practice.

Key Words: Inflammatory bowel disease; Artificial intelligence; Machine learning; Crohn's disease; Ulcerative colitis; Computer-aided diagnosis

Da Rio L, Spadaccini M, Parigi TL, Gabbiadini R, Dal Buono A, Busacca A, Maselli R, Fugazza A, Colombo M, Carrara S, Franchellucci G, Alfarone L, Facciorusso A, Hassan C, Repici A, Armuzzi A. Artificial intelligence and inflammatory bowel disease: Where are we going? *World J Gastroenterol* 2022; In press

Core Tip: Management of patients with inflammatory bowel disease is complex and costly. Therefore, in this field, being able to improve clinical efficiency and optimize healthcare resources is a need of paramount importance. In this regard, artificial intelligence appears to be an extremely promising tool with a significantly wide range of potential applications that encompass diagnosis, treatment and follow up. This review aims to summarize the most recent and significant scientific findings regarding the application of artificial intelligence in inflammatory bowel diseases, providing a picture of the current state of the art and of future perspectives.

INTRODUCTION

Ulcerative Colitis (UC) and Crohn's disease (CD) are chronic and relapsing conditions that affect the gastrointestinal tract, labelled as inflammatory bowel diseases (IBD)[1,2]. In the last decades, IBD has emerged as a global disease with a conspicuous burden on public health and healthcare costs[3].

The diagnosis and management of IBD is complex and implies the interplay and synergy of various specialists, including clinical gastroenterologists, gastrointestinal endoscopists, radiologists, pathologists, surgeons and clinical nutritionists[4].

Along with histological assessment, endoscopy has a role of paramount importance in the diagnosis and the follow-up of IBD, while also being the mainstay for colorectal cancer (CRC) surveillance[5].

Due to the essential role of endoscopy and imaging in gastroenterology, and particularly in IBD, artificial intelligence (AI)-based image analysis can find numerous applications such as evaluation of endoscopic lesions, cancer detection, and assessment of disease activity (*e.g.*, prognosis and response to treatment)[6].

ARTIFICIAL INTELLIGENCE

AI is an umbrella term that encompasses any cognitive function developed by machines for learning or problem solving. A particular subset of AI is represented by machine learning (ML), a discipline that uses large datasets as an input in order to identify patterns of interaction among variables, furthermore allowing the possibility to apply these findings to new data[7].

A further subset and evolution of ML is deep learning (DL), that mimics the neuronal interaction in the human brain to develop artificial neural networks and subsequently convolution neural networks (CNN), that are then able to use the input data in autonomous fashion with the aim of assessing predictive factors of a specific outcome through the development of multiple levels of abstractions[8].

Among the numerous implementations of AI in medicine a promising field is that of automatic collection of complex and nuanced clinical data from electronic medical records (EMRs) through natural language processing (NLP), the subset of AI that studies the interpretation of the human language made by the computer[9,10].

Another fertile ground of application of artificial intelligence is the interpretation of radiologic imaging. A computer model based on computed tomography enterography allows for accurate characterization of intestinal fibrosis in CD, in some instances overperforming human radiologists[11].

In the context of gastrointestinal endoscopy, AI has found application in two main fields, namely in the detection of mucosal lesions, with computer-aided detection (CADe), and in the characterization of mucosal lesions, with computer-aided diagnosis, along with the evaluation of the quality of the endoscopic procedure itself, with computer aided monitoring[12-20].

Therefore, implementation of AI in IBD is a promising tool for improving the assessment of disease activity and reducing the interobserver variability in grading such activity[21]. In addition, similarly what already happening in the general population, CADe systems could eventually improve detection of IBD-associated dysplasia[22]. Finally, AI may also allow for application of precision medicine through the analysis of large databases, correlating differences in the biology of the patient with differences in susceptibility to develop IBD, the activity of disease and the response to specific therapies[23] (Figure 1). Such considerations are further supported by the growing number of clinical studies on the application of AI for IBD in recent years (Figure 2).

Table 1 summarizes the most impactful studies on AI in several fields of IBD that were identified after a literature review using PubMed (MEDLINE) from inception to November 6th 2022. The impact measure of the articles cited was assessed *via* the *Reference Citation Analysis* (RCA; Baishideng Publishing Group Inc.) tool.

AI IN ETIOLOGY, PATHOGENESIS AND DIAGNOSIS OF IBD

Although yet to be thoroughly understood, the etiology of IBD is known to depend upon the complex interplay of genetic, microbial and environmental factors and the immune system[24]. In this context, AI allows for more effective data analysis to evaluate the role of specific genes in the predisposition and development of IBD.

Genome-wide association studies (GWAS) have been employed in order to identify sequence variations related with specific conditions, with over 200 genes found to be potentially implicated in IBD etiology[25]. Such complex and large genomic data, however, are difficult to assess with standard analytical tools. In this context, studies have showed that ML and DL can effectively analyze GWAS data and overcome part of the inherent limitation of such methodology through algorithms of minimum Redundancy-Maximum Relevance and incremental feature selection[26-28].

Gut microbiota is thought to play a relevant role in the complex etiology and pathogenesis of IBD, partly concurring in providing a substrate that may range from protective to proinflammatory[29]. Moreover, in the context of dysbiosis, the taxonomic composition appears to vary between patients affected by IBD and unaffected subjects, but also between IBD subtypes, UC and CD. Promising studies in this field show that the application of ML algorithms on the analysis of gut microbiome data may assist the clinician in diagnosing IBD[30,31].

AI has been also employed in the attempt of supporting the conventional diagnosis of IBD. In this regard, isolated and combined endoscopic and histological parameters were used to develop ML models, that proved accurate in the classification of pediatric patients affected by IBD[32].

Additional models based on confocal laser endomicroscopy (CLE) were developed and, by quantitative analysis through cryptometry, proved able to provide a diagnosis of IBD with high sensitivity and specificity; moreover, such model managed further successfully differentiate between UC and CD[33].

AI APPLICATIONS FOR ENDOSCOPIC ASSESSMENT IN IBD

In order to rigorously define endoscopic disease activity through specific parameters and limit interobserver variability, a plethora of endoscopic scores have been developed in the field of IBD, the most relevant ones being the CD endoscopic index of severity and the simple endoscopic score for CD (SES-CD) for CD, and the Mayo endoscopic score (MES), the ulcerated colitis endoscopic index of severity (UCEIS) and the UC colonoscopic index (UCCIS) for UC[34-38].

Implementation of AI in this field therefore might be a further step towards reproducibility and homogeneity of endoscopic findings.

First successful attempts in identifying *via* AI the presence of mucosal remission or activity were made using dedicated CAD system based on CNN trained on large datasets of endoscopic still images in patients affected by UC[39,40].

A subsequent development was represented by the implementation of neural networks in order to assess disease activity not only on still images, but on the entirety of colonoscopy videos in real time. Also in this field, AI proved to be efficient in recognizing active disease, calculating scores, predicting the risk of clinical relapse and supporting clinicians in real time decision making for treatment[41-44].

Moreover, deep neural networks (DNN) trained on endoscopic images and histological reports of UC managed to identify patient in endoscopic remission and histological remission (HR) with such an accuracy that it may potentially obviate the need for biopsy collection and analysis to identify patients in remission[45].

With regards to prediction of *in vivo* histological activity, the first dedicated CAD system was recently developed for application in endocytoscopy, yielding a high accuracy when compared with the gold standard of pathologists' assessment[46].

Finally, in order to overcome the fact that conventional deep learning systems train CNN based on the subjective scoring of images done by clinicians, novel approaches have been developed based on algorithms that only analyze parameters such as pixel color data and vascular pattern recognition. Such objective computer-based and operator-independent tool provided a dedicated score that significantly correlated with both endoscopic and histological scoring systems[47].

Video capsule endoscopy (VCE) represents one of the main modality of investigating the small bowel in suspect or established CD[48]. The main scoring system used for disease activity quantification are the Lewis score and the capsule endoscopy Crohn's disease activity index, that take into account parameters such as extension, grading of inflammation and presence of strictures[49,50].

VCE video review, however, is time-consuming and requires high level attention during the observation of thousands of frames. In order to simplify this task, AI has been implemented with the objective of reducing the time needed for image assessment by selecting the most relevant frames or portions of the video.

Several CNN models have been developed in order to recognize pathologic findings such as erosions, ulcers and strictures, with very high accuracy[51-54].

Moreover, a study that assessed the review time for VCE showed how the employment of AI systems allowed clinicians to complete the task in a fraction of the time with no differences in overall accuracy[55].

In addition to recognition of disease activity, AI may find a relevant role also in the surveillance of colorectal neoplasia in patients with IBD, since a history of long-standing disease is a significant risk factor in developing CRC[5].

While AI is proving increasingly useful in the detection of colonic neoplasia in the general population with dedicated CADe systems, first attempts at developing specific application for surveillance in IBD are being made[13].

As of today, successful detection of dysplasia has been described in case reports regarding the application of ENDO brain, a CADe system, in endoscopy and endocytoscopy, respectively[56,57].

Along with CADe systems, AI may prove to be an effective and safe tool for real-time quality improvement of the examination as well (*i.e.*, withdrawal time, checking for blind spots), thereby potentially increaing the adenoma detection rate also in IBD patients[58].

AI IN IBD HISTOLOGY ASSESSMENT

HR is now considered an adjunct target of treatment in UC and arguably the most stringent way to assess remission[59]. Growing evidence shows that persistence of histologic disease activity, even in absence of macroscopic endoscopic inflammation, is associated with worse clinical outcome and risk of relapse[60]. More than 30 histological scores have been proposed to grade UC histological activity, but their application in clinical practice remains minimal, mainly due to the impracticality of the scores[61,62]. Even when the scores are applied, for example in clinical trials, the interobserver variability is very high, limiting comparison and reproducibility. Indeed, clinical trials increasingly resort to expensive central reading systems so that all biopsies are evaluated by few highly-qualified pathologists to reduce variability. Therefore, AI-based systems to automatically read UC biopsies would be of great help standardizing the assessment and reducing interobserver variability[63].

Trials in this field are ongoing, and initial results are promising. The first attempt to developed a CAD model to assess UC biopsies focused on eosinophils. The system had a good agreement compared to the manual count performed by human pathologists (interclass correlation coefficient = 0.81-0.92), but did not demonstrate an association between eosinophils counted and overall inflammatory activity[64]. More recently, Gui *et al*[65] proposed to simply UC activity assessment by taking into consideration the sole presence or absence of neutrophils, the hallmark of active inflammation. They proposed a simplified score, the PICaSSO histologic remission index (PHRI) that was then embedded into a CAD system that proved able to distinguish histological activity from remission in biopsies of UC with good accuracy. Further improvements to the same CAD have been recently presented showing that the neutrophil-only assessment by the CAD is largely consistent also with mainstay scores such as Robarts and Nancy histological indexes[66].

Other studies on CAD systems for assessment of UC are ongoing and preliminary results are promising[67,68] (Table 2).

Further applications of CNN in computational pathology have been studied in order to empower the pathologist's accuracy and efficiency, with models trained on whole slide images that were able to effectively support the pathologists by excluding non-diagnostic slides, while retaining optimal sensitivity[69].

AI IN PROGNOSIS AND PREDICTION OF RESPONSE TO TREATMENT

Being able to predict the course of disease with regards to severity and progression is of the utmost importance in IBD patients in order to implement specific management strategies accordingly[70].

Studies have showed that by employing NLP and ML algorithms trained on several clinical data from EMRs (*i.e.*, demographics, laboratory tests, endoscopy reports) it was possible to predict disease severity and surrogate markers of disease flare such as outpatient steroid use or hospitalization[9,71,72].

Furthermore, initial studies on the use of ML to predict the prognosis of patients affected by UC have showed that the endoscopic mucosal healing predicted by a DNN model was associated with prognostic features (reduced risks of hospitalization and colectomy) with statistical significance[73].

Lack of response to biological therapies (around 1 out of 3 patients with anti-TNF-alpha therapy) or progressive decline in response over time is an issue of paramount importance in IBD, with a significant economic toll on healthcare costs[74]. For this reason, the possibility to anticipate the likelihood of a patient responding to a specific biological drug prior to its start represents a cost-effective approach to treatment individualization.

ML has been implemented also to deal with the complexity of such topic with encouraging results.

Through the use of ML on clinical data from trials, researches managed to develop random forests to predict the response to biologics such as infliximab, vedolizumab and ustekinumab, both in CD and in UC with encouraging results[75-78].

The integration and analysis of patients' molecular and clinical features *via* ML algorithms therefore appears to be a promising field with great potential in terms of patient management and optimization of healthcare costs[79].

AI IN PRECLINICAL SETTINGS AND DRUG DISCOVERY

Design and discovery of new drugs are complex processes hampered by high cost and time consumption. Furthermore, especially in recent years, the process of drug discovery has to deal with the increasing wealth and complexity of data from various "omics" (*i.e.*, genomics, proteomics)[80].

AI, however, is proving to be a crucial tool in the development of novel drug candidates modernizing this field as well. Among the various implementation of ML and DL in the drug discovery process we can list peptide synthesis, virtual screening (structure-based and ligand-based), prediction of toxicity, drug monitoring and release, quantitative structure-activity relationship and drug repositioning[81].

In the field of IBD AI has already been employed in drug discovery with encouraging initial results. Computational approaches have been used to identify metabolite-target interactions using the dataset of the IBD cohort from the Human Microbiome Project 2, followed by ML analyses aimed at ranking metabolites according to importance in IBD and identifying possible human targets through virtual ligand-based screening. 983 high quality connections between metabolites from the gut microbiota and human proteins possibly relevant to IBD were identified, thus providing multiple novel drug targets for potential immune therapies[82].

Another relevant application of DL was the construction of a scaffold-based molecular design workflow aimed at developing drug candidates targeted towards the discoidin domain receptor 1. Through a deep generative model, molecular docking and virtual profiling, a high-quality scaffold-based molecular library was established, subsequently leading to the synthesis of a molecular compound that effectively inhibited the expression of proinflammatory cytokines, showing extraordinary kinase selectivity and significant therapeutic protection in *ex vivo* and *in vivo* animal models respectively[83].

CONCLUSION

Based on the numerous advances in the field of IBD in recent years, it is foreseeable that AI will gain an ever-greater role in the standard patient care, ranging from evaluation of the risk of developing IBD, to assistance in the assessment of mucosal activity or detection of dysplasia, to support in histopathological reporting, prediction of disease course and treatment efficacy (Table 1). At the same time the integration of AI in daily practice will lead to changes in clinical practice itself, getting us closer to the concept of precision medicine and its subsequent improvement in the quality of care and optimization of healthcare costs (Figure 3). As for research, AI is proving to be a irreplaceable aid in the collection and analysis of large data, while also limiting subjectiveness and interobserver variability, simplifying standardization and providing a feasible alternative to the need of independent central reading in clinical trials. The implementation of AI in everyday practice is expected to improve diagnostic accuracy and reproducibility by allowing for a better standardization of lesion features and classification and by increasing the detection rate of small and subtle mucosal abnormalities or lesions. Moreover, evidences show how AI may have a role also in advanced endoscopic techniques, such as CLE or molecular imaging. Through these advanced application AI will support the clinician by detecting microscopic and even molecular details otherwise invisible, thereby paving the way to the potential incorporation of ultrastructural and molecular endpoints in IBD endoscopy. Nonetheless, with regard to future applications of AI, there are several issues that will need solving, such as how to provide more transparency of the AI algorithms, how to assess and choose among different models with similar purposes and how to effectively allocate resources in the plethora of models that will be available, to only list a few[84]. To the best of our knowledge, this is the first review on the role and the future perspective of AI in IBD that takes into account the first clinical applications in a real world setting that are now available from the most recent clinical studies. Nevertheless, the chief limitation is represented by the limited amount of evidence that support our review, which is inevitably due to the scarcity of data currently available for the topic itself from the literature. Undoubtedly further studies are direly needed to build a more robust and comprehensive foundation for future analyses. In brief, while the human component is unlikely to be substituted altogether in future clinical practice and while a few questions still await an answer, AI is an extremely promising means of improvement in patient care and resource optimization.

Figure Legends

Figure 1 Application of artificial intelligence in inflammatory bowel diseases for precision medicine. AI: Artificial intelligence.

Figure 2 Clinical studies on the application of artificial intelligence in inflammatory bowel diseases in the last 25 years (as of November 6th 2022).

Figure 3 Fields of application of artificial intelligence in inflammatory bowel diseases. IBD: Inflammatory bowel disese.

Table 1 Main studies of artificial intelligence application in the various fields of inflammatory bowel diseses

Ref.	Field	Study features	Main finding
Isakov *et al*[26], 2017	IBD genetics	ML model to assess 16390 genes in IBD and healthy patients	Identification of 347 IBD-risk genes (67 newly identified)
Cheng *et al*[27], 2019	IBD genetics	Software analysis to assess the genetics of 32713 IBD patients	Identification of several genes potentially implyed in UC; identification of 11 common gene onthology terms for UC
Yuan *et al*[28], 2017	IBD genetics	Software analysis to assess 12754 genes in IBD and healthy patients	Identification of 41 genes closely associated with IBD
Mihajlović *et al*[30], 2021	IBD and microbiota	ML classification algorithm to identify IBD from 1638 fecal samples	Confirmation of strong connection between IBD and specific fecal microbial species
Manandhar *et al*[31], 2021	IBD and microbiota	ML model analysis of fecal microbiota from 729 IBD patients and 700 healthy controls	Identification of 117 bacterial taxa with a potential role in diagnostic screening of IBD
Mossotto *et al*[32], 2017	IBD diagnosis	ML model to assess 287 pediatric patients with IBD	Accuracy of 83.3% of the combined endoscopy-histology ML model in the classification of pediatric IBD patients
Quénéhervé *et al*[33], 2019	IBD diagnosis	AI analysis of CLE images from 50 IBD	AI analysis with 100% sensitivity and specificity

		patients and 9 healthy controls	for IBD diagnosis, 92% sensitivity and 91% specificity of IBD differential diagnosis
Ananthakrishnan *et al*[9], 2013	IBD diagnosis and data collection	NLP model trained and validated on 700 UC partients and 700 CD patients to improve case definition and identification from EMRs	NLP model provides better accuracy (AUC 0.94-0.95) than models using only the International Classification of Diseases 9th revision for IBD case definition and identification
Stidham *et al*[39], 2019	IBD endoscopy	DL model for UC severity trained on 16514 endoscopic images	Similar performance of the DL model and experienced human reviewers in grading UC endoscopic severity
Ozawa *et al*[40], 2019	IBD endoscopy	CNN-based CAD system for UC severity trained on 26304 endoscopic images	CAD system with AUCs of 0.86 and 0.98 in identification of Mayo score 0 and 0-1 respectively
Maeda *et al*[41], 2021	IBD endoscopy	Endoscopic AI model used in real time on 135 UC patients in clinica remission	Endoscopic applications of real time AI prediscts clinical relapse of UC with statistical significance
Gottlieb *et al*[42], 2021	IBD endoscopy	DL algorithm to assess UC severity on 795 full-length endoscopy videos	DL algorithm showed significant inter-rater agreement to human central readers for

			prediction of UC severity
Yao *et al*[43], 2021	IBD endoscopy	Endoscopic AI model (CNN) to assess UC grading used on 169 endoscopy videos and compared to dual central reader review	AI model approximates the scoring of experienced reviewers for grading of UC endoscopic activity
Byrne *et al*[44], 2021	IBD endoscopy	DL model (CNN) to detect and assess UC activity leveraged on > 375000 frames	DL model resulted well aligned with scoring guidelines and experts' performance
Takenaka *et al*[45], 2020	IBD endoscopy	DL algorithm trained on endoscopic images and bipsy results and tested on 875 UC patients	DL model identified with an accuracy > 90% patients in endoscopic and histologic remission
Maeda *et al*[46], 2019	IBD endoscopy (endocytoscopy)	CAD system to predict persistent histologic flogosis from endocytoscopy validated on 100 UC patient	CAD system provided a diagnostic accuracy of 91% with perfect reproducibility for identification of persistent histologic inflammation
Bossuyt *et al*[47], 2020	IBD endoscopy	AI algorithm based on pixel color data and pattern recognition from endoscopic images	AI algorithm ("red density") provides an objective computer-based assessment of UC disease activity with good

		tested on 55 patients	correlation with endoscopic and histological scoring systems
Aoki *et al*[51], 2019	IBD endoscopy (VCE)	AI system (CNN) tested on 10440 small-bowel images for detection of erosions and ulcers in CD	AI system showed an accuracy of 90.8% for detection of erosions and ulcers
Klang *et al*[52], 2020	IBD endoscopy (VCE)	DL algorithm applied on 17640 VCE images for ulcers detection in CD	DL algorithm provided an accuracy ranging from 95.4 to 96.7% with an AUC of 0.99 for ulcers detection
Klang *et al*[53], 2021	IBD endoscopy (VCE)	DL model applied on 27892 VCE images for identification of intestinal strictures in CD	DL model showed an accuracy of 93.5% in stricture identification and excellent differentiation between strictures and other lesions
Ferreira *et al*[54], 2022	IBD endoscopy (VCE)	DL model trained and validated on 8085 VCE images for detection of erosions and ulcers in CD	DL model provided an accuracy of 92.4% and a precision of 97.1% for lesion detection
Aoki *et al*[55], 2020	Video capsule endoscopy	Comparison between standard endoscopist reading and reading after AI	The mean VCE video reading time resulted significantly shorter after AI model (CNN) screening

		model screening of 20 full-length VCE videos	compared to standard reading
Maeda *et al*[56], 2021	IBD endoscopy (surveillance)	Case report of dysplasia detection by AI system in a patient with long standing UC	AI system (EndoBRAIN) identified 2 colonic lesions that harboured low-grade displasia upon histoogical examination
Fukunaga *et al*[57], 2021	IBD endoscopy (surveillance)	Case report of dysplasia detection by AI system in a patient with long standing UC	AI system (EndoBRAIN) identified a rectal lesions that harboured high-grade displasia upon histoogical examination
Reddy *et al*[72], 2019	IBD prognosis	ML model employed on 82 CD patients' EMRs to predict disease course	ML model can predict inflammation severity with high accuracy (AUC 92.8%) from EMRs data
Takenaka *et al*[73], 2022	IBD prognosis	ML model validated on endoscopic images and biopsy results from 875 UC patients to predict disease course	Histologic remission detected by the ML model correlates with a significant reduction in clinical relapse, stenoid use, hospitalization and colectomy
Li *et al*[75], 2021	Response to treatment	ML model empolyed on 174 CD patients to predict response to infliximab	ML model based on clinical and serological parameters showed an accuracy of 0.85 for prediction of response to infliximab

Waljee *et al*[76], 2018	Response to treatment	AI model employed on 472 CD patients to predict response to vedolizumab	AI model based on clinical and serological parameters was able to identify patients that would achieve a corticosteroid-free biologic remission at week 52 of vedolizumab
Waljee *et al*[77], 2018	Response to treatment	ML algorithm employed on 491 UC patients to predict response to vedolizumab	ML algorithm based on clinical and serological parameters was able to identify patients that would achieve a corticosteroid-free biologic remission at week 52 of vedolizumab
Doherty *et al*[78], 2018	Response to treatment	AI model to assess response to treatment with ustekinumab in 306 patients with CD	AI model can detect patients in remission based on clinical data and fecal microbioma at week 6 and 22 of ustekinumab

AI: Artificial intelligence; AUC: Area under the curve; CAD: Computer-aided detection; CD: Crohn's disease; CLE: Confocal laser endomicroscopy; CNN: Convolution neural networks; DL: Deep learning; UC: Ulcerative colitis; CD: Crohn's disease; EMR: Electronic medical record; IBD: Inflammatory bowel disese; ML: Machine learning; NLP: Natural language processing; VCE: Video capsule endoscopy.

Table 2 Artificial intelligence application for histological assessment of ulcerative colitis

Ref.	Study design	Population	Outcome	Results
Vande Casteele *et al*[64], 2022	Cohort study	Colonic biopsies from 88 UC patients with histologically active disease	To assess a DL machine in quantifying eosinophils in colonic biopsies and validate against pathologists' count	The AI system highly agreed with manual eosinophil count by pathologists (ICC 0.81-0.92)
Peyrin-Biroulet *et al*[67], 2022	Cohort study	200 histological images of UC biopsies	To evaluate an AI algorithm in assessing histological disease activity according to the Nancy index	The CNN model had an excellent agreement with pathologists in the assessment of the Nancy index (ICC 0.84)
Villanacci *et al*[66], 2022	Cohort study	614 biopsies from 307 UC patients	To test a CNN-based CAD system for evaluating HR based on PHRI, Robarts and Nancy indexes	The CAD system accurately assessed HR (sensitivity 89%, specificity 85% for PHRI) and similar performance for Nancy and Robarts

AI: Artificial intelligence; CAD: Computer-aided detection; CNN: Convolution neural networks; DL: Deep learning; HR: Histological remission; ICC: Interclass correlation coefficient; PHRI: PICaSSO histologic remission index; UC: Ulcerative colitis.

80441_Auto_Edited -check.docx

ORIGINALITY REPORT

6%

SIMILARITY INDEX

PRIMARY SOURCES

1	www.science.gov Internet	80 words — 2%
2	encyclopedia.pub Internet	37 words — 1%
3	academic.oup.com Internet	23 words — < 1%
4	David Chen, Clifton Fulmer, Ilyssa O Gordon, Sana Syed et al. "Application of Artificial Intelligence to Clinical Practice in Inflammatory Bowel Disease – What the Clinician Needs to Know", Journal of Crohn's and Colitis, 2022 Crossref	21 words — < 1%
5	dokumen.pub Internet	20 words — < 1%
6	watermark.silverchair.com Internet	19 words — < 1%
7	Duchesne, Charlène, Patrick Faure, François Kohler, Marie-Pierre Pingannaud, Guillaume Bonnaud, Franck Devulder, Laurent Abramowitz, Christian Boustière, and Laurent Peyrin-Biroulet. "Management of inflammatory bowel disease in France: A nationwide survey among private gastroenterologists", Digestive and Liver Disease, 2014.	17 words — < 1%

Crossref

8	Jouke J.H. van der Laan, Anne M. van der Waaij, Ruben Y. Gabriëls, Eleonora A.M. Festen, Gerard Dijkstra, Wouter B. Nagengast. "Endoscopic imaging in inflammatory bowel disease: current developments and emerging strategies", Expert Review of Gastroenterology & Hepatology, 2020 Crossref	16 words — < 1%
9	jitc.bmj.com Internet	14 words — < 1%
10	journals.lww.com Internet	10 words — < 1%
11	Ryan W. Stidham, Kento Takenaka. "Artificial Intelligence for Disease Assessment in Inflammatory Bowel Disease: How Will it Change Our Practice?", Gastroenterology, 2022 Crossref	9 words — < 1%
12	doaj.org Internet	8 words — < 1%

EXCLUDE QUOTES	OFF	EXCLUDE SOURCES	OFF
EXCLUDE BIBLIOGRAPHY	OFF	EXCLUDE MATCHES	OFF