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ABOUT COVER

Editorial board member of *Artificial Intelligence in Gastroenterology*, Palittiya Sintusek is an Assistant Professor at Chulalongkorn University (CU), Thailand. She received her BSc in 2004, residency and fellowship training at King Chulalongkorn Memorial Hospital, CU in 2012. She received her MSc from University College London (UCL) and was awarded Bill Marshall fellowship at Great Ormond Street Hospital in 2015, a clinical attachment at King's College Hospital and a research fellowship at Dubowitz neuromuscular disease, UCL in 2016. She became lecturer in gastroenterology, Department of Pediatrics, CU since 2017. Her research interests are focus on neurogastroenterology, Wilson disease and viral hepatitis. Assistant Professor Palittiya Sintusek has co-led the implementation of clinical practice guideline for functional constipation in children in Thailand and participates in multicenter study of ESPGHAN working group on esophageal atresia.

AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Gastroenterology* (*AIG*, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

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EDITORIAL

Digital histology in celiac disease: A practice changer

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Abstract

Artificial intelligence (AI) has grown tremendously in the last decades and is undoubtedly the future era in medicine. Concerning digestive diseases, applications of AI include clinical gastroenterology, gastrointestinal endoscopy and imaging, and not least pathological diagnosis. Several gastrointestinal pathologies require histological confirmation for a positive diagnosis. Among them, celiac disease (CD) diagnosis has been in the spotlight over time, but controversy is still ongoing with regard to the so-called celiac-type histology. Despite efforts to improve histological diagnosis in CD, there are still several issues and pitfalls associated with duodenal histology reading. Several papers have assessed the accuracy of AI techniques in detecting CD on duodenal biopsy images and have shown high diagnostic performance over standard histology reading. We discuss the role of computer-assisted histology in improving the assessment of mucosal architectural injury and inflammation in CD patients, both for diagnosis and follow-up.

Key words: Celiac disease; Histology; Artificial intelligence; Computer; Digital; Diagnosis

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Core tip: Histology in celiac disease (CD) diagnosis is hampered by several pitfalls, from low adherence to biopsy sampling recommendations and reporting of results to significant inter-observer variability. A quantitative, computer-assisted histological assessment of mucosal biopsies could overcome many of the current limitations of conventional histology. We herein discuss the current evidence on artificial intelligence-based histology in CD diagnosis and its role in improving histological measurements in CD.

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DIGITAL HISTOLOGY IN CELIAC DISEASE – A PRACTICE CHANGER

Artificial intelligence (AI) has grown tremendously in the last decades and is undoubtedly the future era in medicine. From optimizing diagnosis to guiding therapy, AI can be a real practice changer in several medical specialties. Concerning digestive diseases, applications of AI include clinical gastroenterology, gastrointestinal (GI) endoscopy and imaging and pathological diagnosis. It is well known that several GI pathologies require histological confirmation for a positive diagnosis. Among them, celiac disease (CD) is a well-recognized systemic autoimmune disorder triggered by gluten ingestion in genetically susceptible individuals, whose diagnosis in adults is based on testing for specific antibodies and histological examination of the small bowel mucosa. CD diagnosis has been in the spotlight over time with several guideline updates, but controversy is still ongoing with regard to the so-called celiac-type histology[1,2]. While significant improvement has been made concerning mucosal sampling techniques, site sampling, number and processing of biopsies and standardization of histopathology reports, there are still many issues and pitfalls associated with duodenal histology reading[3,4]. The issues of bulb biopsies, sampling-associated artifacts, orientation and readability of biopsy samples, inter-observer variability and low adherence to currently available histology reporting systems have all been a matter of debate in recent literature and have set the need for optimizing histological diagnosis in CD[5,6].

With growing medical data and the need to optimize care in a setting of limited human resources, AI has emerged as a breakthrough solution for improving diagnosis, treatment selection and even guiding prognosis in various medical fields. Several AI techniques have been used, such as machine learning, decision trees, support vector machines and artificial neural networks[7]. In gastroenterology, several applications have been validated both for the GI tract and hepato-biliary-pancreatic pathology[8-10].

CD has been a good candidate for AI applications, owing to its clear-cut diagnosis and the validation of endoscopic markers of villous atrophy[11]. At first, most of the interest with AI in CD was oriented on computer-aided detection of villous atrophy[12], but recently there has been a switch in focus on digital histology in CD. Several papers have assessed the accuracy of AI techniques in detecting CD on duodenal biopsy images and have shown high diagnostic performance over the standard histology reading. Using a machine learning–based histopathological analysis model, Syed *et al*[13] showed a 93.4% case-detection accuracy on 3118 images from duodenal biopsies of patients with environmental enteropathy, CD and controls. A deep learning approach on automated detection of CD was described by Wei *et al*[14] in 212 biopsies (1230 slides), which identified CD, normal mucosa and non-specific duodenitis with 95.3%, 91.0%, and 89.2% accuracy, respectively. A novel, quantitative histology algorithm proposed by Das *et al*[15] has been developed on digitized images of duodenal biopsies from a derivation cohort of 261 subjects (137 controls, 124 CD) and then validated on 225 subjects (105 controls, 120 CD), discriminating CD from controls with 90.3% sensitivity and 93.5% specificity; this Q-histology classification system was proven superior to all existing histological classification systems (Marsh, Marsh-Oberhuber, Corazza-Villanacci, Ensari) with regard to intra- and interobserver agreement. Moreover, in a real-world setting, even these qualitative scoring systems are rarely used in pathology reports, which are often just descriptive[5,16].

Computer-assisted histological assessment of duodenal biopsy slides overcomes many of the issues associated with conventional histology. In contrast with the currently available, subjective, qualitative evaluation of slides, digital histology provides a quantitative assessment of duodenal mucosal biopsies and could be of great use in equivocal cases, in measuring changes on follow-up biopsies and in multicentric clinical trials. Besides providing quantifiable measurements, an automated histology image analysis could reduce the burden of pathology departments by prescreening histology slides and saving only those that are preliminarily classified as diseased mucosa to be reviewed by the pathologists[14]. Not least, computer-assisted quantitative histology could provide arguments for cases of mild enteropathy that could otherwise be mislabeled as normal or for cases of refractory CD.

A large European multicentric study with central pathology reading has shown an alarmingly high discordance rate of 7.1% in labelling a case as either CD (Marsh 2/3)

or non-CD (Marsh 0/1)[17]. Considering the implications of either missing a diagnosis of CD or misdiagnosing a normal individual as CD, there is a promising role for computer-assisted histology in CD. AI-techniques can provide objective and accurate histological measurements in CD diagnosis and help avoid all the confounding factors associated with currently used conventional histology. Also, AI-based histology could be used as an alternative to expert pathologists in clinical trials, where small changes of the mucosa may occur with different interventions, and precise measurements are warranted[16].

At a glance, AI-based diagnosis might seem the perfect practice changer in CD management. However, there are some pitfalls with CD diagnostic based on AI techniques. On one hand, there is the issue of correctly labelling a histology image as appropriate for reading; previous studies have shown that bad orientation of samples can require re-cuttings for proper reading and correct diagnosis, and this is currently eyed by the pathologist[18]. Moreover, there is the wide-spectrum of non-celiac villous atrophy, which can pose diagnostic challenges[19].

At present, we are simplifying the continuum of mucosal injury in CD patients with a categorical score, in one of the Marsh-Oberhuber classes. Using computer-assisted histology, we can significantly improve the assessment of mucosal architectural injury and inflammation in CD patients, both for diagnosis and follow-up.

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