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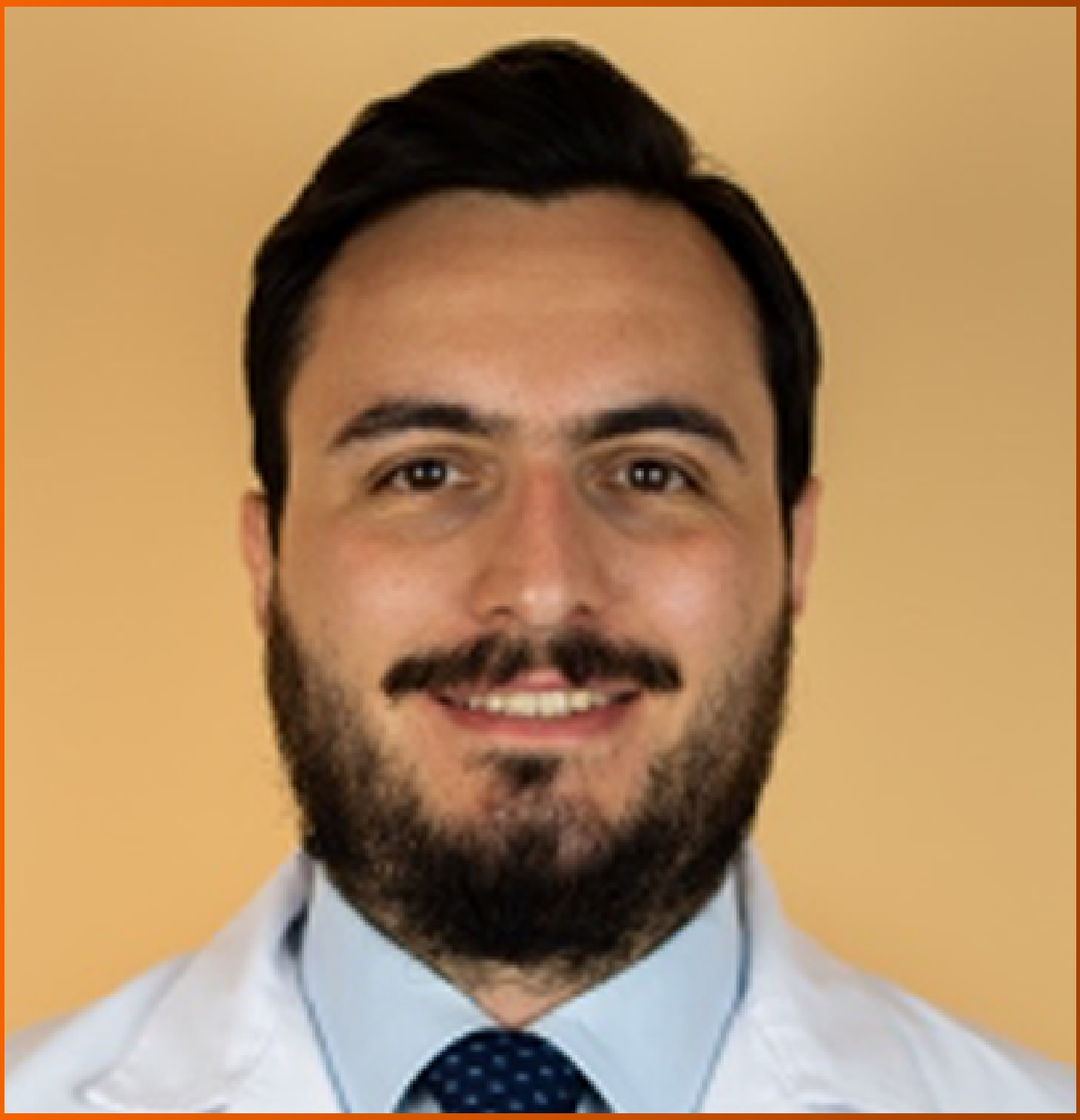

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AIGE

Artificial Intelligence in Gastrointestinal Endoscopy

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ABOUT COVER

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AIMS AND SCOPE

The primary aim of *Artificial Intelligence in Gastrointestinal Endoscopy* (*AIGE*, *Artif Intell Gastrointest Endosc*) is to provide scholars and readers from various fields of artificial intelligence in gastrointestinal endoscopy with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIGE mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastrointestinal endoscopy and covering a wide range of topics, including artificial intelligence in capsule endoscopy, colonoscopy, double-balloon enteroscopy, duodenoscopy, endoscopic retrograde cholangiopancreatography, endosonography, esophagoscopy, gastrointestinal endoscopy, gastroscopy, laparoscopy, natural orifice endoscopic surgery, proctoscopy, and sigmoidoscopy.

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EDITORIAL

Artificial intelligence in Barrett's esophagus: A renaissance but not a reformation

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Abstract

Esophageal cancer remains as one of the top ten causes of cancer-related death in the United States. The primary risk factor for esophageal adenocarcinoma is the presence of Barrett's esophagus (BE). Currently, identification of early dysplasia in BE patients requires an experienced endoscopist performing a diagnostic endoscopy with random 4-quadrant biopsies taken every 1-2 cm using appropriate surveillance intervals. Currently, there is significant difficulty for endoscopists to distinguish different forms of dysplastic BE as well as early adenocarcinoma due to subtleties in mucosal texture and color. This obstacle makes taking multiple random biopsies necessary for appropriate surveillance and diagnosis. Recent advances in artificial intelligence (AI) can assist gastroenterologists in identifying areas of likely dysplasia within identified BE and perform targeted biopsies, thus decreasing procedure time, sedation time, and risk to the patient along with maximizing potential biopsy yield. Though using AI represents an exciting frontier in endoscopic medicine, recent studies are limited by selection bias, generalizability, and lack of robustness for universal use. Before AI can be reliably employed for BE in the future, these issues need to be fully addressed and tested in prospective, randomized trials. Only after that is achieved, will the benefit of AI in those with BE be fully realized.

Key Words: Barrett's esophagus; Artificial intelligence; Machine learning; Cognitive neural networks; Computer aided diagnosis; Endoscopy

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Core Tip: Screening and surveillance in patients with Barrett's esophagus (BE) remain problematic in regards to accuracy and adherence. This occurs in spite of recommendations and advances in endoscopic imaging. Artificial intelligence (AI) algorithms assist in endoscopic evaluation of BE by identifying potential targets for biopsy. This may occur by increasing endoscopic efficiency and diagnosing accuracy by decreasing procedure time. AI in BE has been developed by expert endoscopists and appear to perform similarly among them. At this point, the benefit of AI in BE may be for use by non-expert endoscopists and trainees to maximize BE endoscopic evaluation.

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INTRODUCTION

In 2020, the United States is estimated to record over 18000 new esophageal cancer cases and over 16000 deaths[1]. Furthermore, esophageal cancer remains in the top ten of cancers diagnosed and cause of cancer related death nationally. One common risk factor for esophageal adenocarcinoma (EAC) is the presence of Barrett's esophagus (BE). Currently, identification of early dysplasia requires an experienced endoscopist performing a diagnostic endoscopy consisting of random 4-quadrant biopsies to be taken every 1-2 cm within appropriate surveillance intervals based on absence or presence of dysplasia seen in the random biopsies[2-5]. Unfortunately, adherence to this recommendation remains inconsistent, particularly with low-grade dysplasia. Its subtle appearance and discontinuous nature can make it difficult to accurately biopsy areas for tissue pathology to confirm or rule out the diagnosis. In addition, there is significant difficulty for endoscopists to distinguish BE with low-grade dysplasiafrom high-grade dysplasia (HGD) or early adenocarcinoma. To combat this, high-definition white light, narrow band imaging (NBI), probe-based confocal endomicroscopy (pCLE), volumetric laser endomicroscopy (VLE) and optical computed tomography among others have all been tested and employed an in attempt to increase biopsy yield for accurate diagnosis[6-9]. However, early EAC is often flat and difficult to distinguish from the surrounding non-dysplastic Barrett's mucosa, even with these endoscopic advances. The rate-limiting step among of these technologies is that they are operator dependent, requiring hand-eye coordination to distinguish and biopsy suspicious areas, often-taking years to acquire the necessary skill set. Theoretically, artificial intelligence (AI) can assist in this by using methods of deep learning to identify and process - in real-time - endoscopic data that may not consciously appreciated by humans such as subtle changes in color and texture to aid in taking targeted biopsies rather than random biopsies.

There have been recent advances in the development and testing of AI and various machine learning (ML) algorithms to improve the ability to identify dysplastic and malignant mucosa. Previously, computer algorithms were trained to classify a patient's likelihood for EAC based on symptoms or compare patient biopsy cDNA microarrays to known EAC samples. These methods drew us closer to accurately diagnosing dysplasia and malignant mucosa, but their sensitivities/specificities could not match the parameters outlined in American Society for Gastrointestinal Endoscopy's Preservation and Incorporation of Valuable Endoscopic Innovations (PIVI) criteria for new technologies. PIVI criteria recommends that the sensitivity should be at least 0.90, specificity should be at least 0.80 and a negative predictive value of at least 0.98 for detecting HGD or BE[10]. AI makes use of several methods of ML. One commonly used method is the cognitive neural network (CNN). In CNN, each node (or "neuron") is connected to other nodes in a way that mimics real human neural networking. Several layers of neurons can exist to make a single decision to call a grouping of pixels on an image either normal tissue or dysplasia. Multiple recent studies have already experimented with the capabilities of such computer-aided diagnosis (CAD) (Table 1). The advantages that AI appears to confer per-endoscopy is a removal of the inter-observer or intra-observer variability in identification of non-

Table 1 Computer-aided diagnosis of Barrett's esophagus

Ref.	Year	Study design	Lesions	Imaging modality	Image qualification	Teaching dataset	Validation method	Outcomes	Compared to expert/current standard
van der Sommen *et al*[11]	2016	Retrospective	HGD, early EAC	WLI	High quality, clear visible/absence of lesions	100 images	LOO	Per-image SPEC/SENS: 83%/83%; Per-patient SPEC/SENS: 86%/87%	Inferior
de Groof *et al*[12]	2019	Retrospective	Non-dysplastic and dysplastic BE	WLI	1280 × 1024 pixels – HD	60 images	LOO	Accuracy: 0.92; SENS: 0.95; SPEC: 0.85	NA
Swager *et al*[13]	2017	Retrospective	HGD, early EAC	VLE	High quality image database	60 images	LOO	AUC: 0.95, 0.89, 0.91	Superior
Ebigbo *et al*[15]	2020	Prospective	Early EAC	WLI	1350 × 1080 pixels and 1600 × 1200 pixels – HD	129 images	LOO	Accuracy: 0.899; SENS: 0.837; SPEC: 1.00	NA

AUC: Area under the curve; BE: Barrett's esophagus; EAC: Esophageal adenocarcinoma; HD: High definition; HGD: High-grade dysplasia; LOO: LEAVE-one-out; NA: Not available; SENS: Sensitivity; SPEC: Specificity; VLE: Volumetric laser endomicroscopy; WLI: White light imaging.

normal lesions, combined with rapid, objective analysis of all visual inputs in such a way that is consistent and not subject to fatigue. CAD can allow endoscopists to take targeted, high-yield biopsies in real-time. Compared to taking random biopsies per the Seattle protocol or using enhanced imaging, CAD may increase efficiency and accuracy for making a diagnosis by limiting the chance of missing neoplastic mucosa. Moreover, CAD may decrease risk by decreasing sedation time secondary to decreased procedure length.

Recent studies would indicate that CAD can be successful in the detection of neoplastic lesions in BE. Von Der Sommen *et al*[11] developed a ML algorithm that used CAD to analyze texture and color in static images to detect early neoplastic lesions in BE. The sensitivity and specificity were between 0.90 to 1.00 and 0.65 to 0.91 respectively. In a study by Groof *et al*[12], six experts identified likely neoplastic tissue in the same image and used these expert-delineated images to train the computer algorithm to identify neoplastic BE and non-dysplastic BE in test cases. The resulting sensitivity and specificity of the computer algorithm was 0.95 and 0.85 respectively. Swager *et al*[13] used CAD on *ex vivo* VLE images to retrospectively detect non-dysplastic BE and HGD or early adenocarcinoma. They were able to achieve a sensitivity of 0.90 and specificity of 0.93 while using VLE as the reference images rather than high-definition white light endoscopy.

Though the data is promising, nearly all research has focused on training an algorithm on a set of retrospectively gathered images. Because of this, these studies are unfortunately subject to selection bias since the images are often curated for high definition and typically from a single endoscopy center. Therefore, the algorithms are usually overtrained on a relatively small sample set and not generalizable to other images of poorer quality or a population with different incidence and/or prevalence of BE. A sparing number of prospective or real-time studies currently exist and these are performed on a rather small number of samples. Furthermore, standardization of AI systems is proving difficult, given that the details of the algorithm are in a "black box" and inaccessible to critique and direct modifications. The struggles that have been encountered in using AI for identification of Barrett's mucosa have been encountered in identifying early esophageal cancers. Though promising, the thresholds to detect early esophageal cancer are below PIVI criteria which may be secondary to limited images and lack of ability to identify images in real time. Hashimoto *et al*[14] may have found a way to overcome previous difficulties by being able to create a faster algorithm which allowed for a real time video overlay using a large database of images. Using this technique, Hashimoto *et al*[14] were able to identify early esophageal neoplasms with high accuracy.

The process of standardization of ML algorithms poses a difficult challenge. The algorithm may be different for white light endoscopy compared to NBI, VLE or pCLE. It is possible that subtle differences such as the brand of endoscope, wavelength of

light or white balance could impact specificity or sensitivity of a tested algorithm. There is no guarantee that a single algorithm would work both in populations of high prevalence of BE and populations of low prevalence. Ideally, several algorithms should be tested prospectively and compared to the current gold standard of random biopsy in large, multicenter randomized clinical trials. Some of these studies are currently ongoing. User databases such as ImageNet or GastroNet contain samples of labeled images for use for training and testing of algorithms, but there is need for databases of patients with varying prevalence of risk factors for BE to determine if a single algorithm is robust enough to accurately diagnose BE nationwide.

To date, the ML platforms used have been developed by expert endoscopists. A recent study published by Ebigbo *et al*[15] used real-time AI to identify cancer in BE and found that the AI system performed in a similar fashion to the expert endoscopist. Such programs can also help train non-experts and gastroenterology fellows alike by giving real-time feedback, thus propagating more expert endoscopists in a shortened timeframe. Of course, endoscopists who are not BE experts can also benefit as well.

CONCLUSION

AI represents a renaissance in endoscopy, but not a reformation. The benefit may lie in the improvement in recognition of dysplastic and malignant tissue among non-expert endoscopists or gastroenterology fellows, since expert endoscopists have similar performance to AI. Generalizability, robustness of a single or few algorithms that can apply to either different imaging modalities or diverse populations, and the ability to easily modify an algorithm are current obstacles that need to be addressed before we can reliably use AI in endoscopic management of BE.

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