Document Version:
Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

• A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
• The final author version and the galley proof are versions of the publication after peer review.
• The final published version features the final layout of the paper including the volume, issue and page numbers.
Link to publication

FOCUSED COMMUNICATION

The use of a real-time computer-aided detection system for visible lesions in the Barrett's esophagus during live endoscopic procedures: a pilot study (with video) 🎥

Kiki N. Fockens, MD, PhD,[1,*] Jelmer B. Jukema, MD,[1,*] Martijn R. Jong, MD,[1] Tim Boers, MS,[2] Joost A. van der Putten, PhD,[2] Carolus H. J. Kusters, MS,[2] Roos E. Pouw, MD, PhD,[1] Lucas C. Duits, MD, PhD,[1] Fons van der Sommen, PhD,[2] Peter H. de With, PhD,[2] A. Jeroen de Groof, MD, PhD,[1] Jacques J. Bergman, MD, PhD,[1] on behalf of the BONS-AI consortium†

Amsterdam, Eindhoven, the Netherlands

Background and Aims: This pilot study evaluated the performance of a recently developed computer-aided detection (CADe) system for Barrett's neoplasia during live endoscopic procedures.

Methods: Fifteen patients with a visible lesion and 15 without were included in this study. A CAD-assisted workflow was used that included a slow pullback video recording of the entire Barrett's segment with live CADe assistance, followed by CADe-assisted level-based video recordings every 2 cm of the Barrett's segment. Outcomes were per-patient and per-level diagnostic accuracy of the CAD-assisted workflow, in which the primary outcome was per-patient in vivo CADe sensitivity.

Results: In the per-patient analyses, the CADe system detected all visible lesions (sensitivity 100%). Per-patient CADe specificity was 53%. Per-level sensitivity and specificity of the CADe-assisted workflow were 100% and 73%, respectively.

Conclusions: In this pilot study, detection by the CADe system of all potentially neoplastic lesions in Barrett's esophagus was comparable to that of an expert endoscopist. Continued refinement of the system may improve specificity. External validation in larger multicenter studies is planned. (Clinical trial registration number: NCT05628441.) (Gastrointest Endosc 2024;100:527-31.)

Early Barrett's neoplasia often only exhibits minimal mucosal and vascular changes, which make its endoscopic detection challenging.[1,2] Because general endoscopists rarely encounter early neoplasia in Barrett's esophagus, they are often unfamiliar with these lesions.

The BONS-AI (Barrett's Oesophagus Imaging for Artificial Intelligence) consortium has committed to the development of a robust, "ready-for-use," real-time computer-aided detec-tion (CADe) system for the identification of Barrett's neoplasia to assist endoscopists in recognizing the early forms of this disease. The consortium consists of 15 international centers with a tertiary referral function for management of early Barrett's neoplasia as well as a leading technical university in the field of artificial intelligence. The CADe system has recently been developed and validated extensively in an ex vivo setting in 2 separate studies.[3,4]

This video can be viewed directly from the *GIE* website or by using the QR code and your mobile device. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.
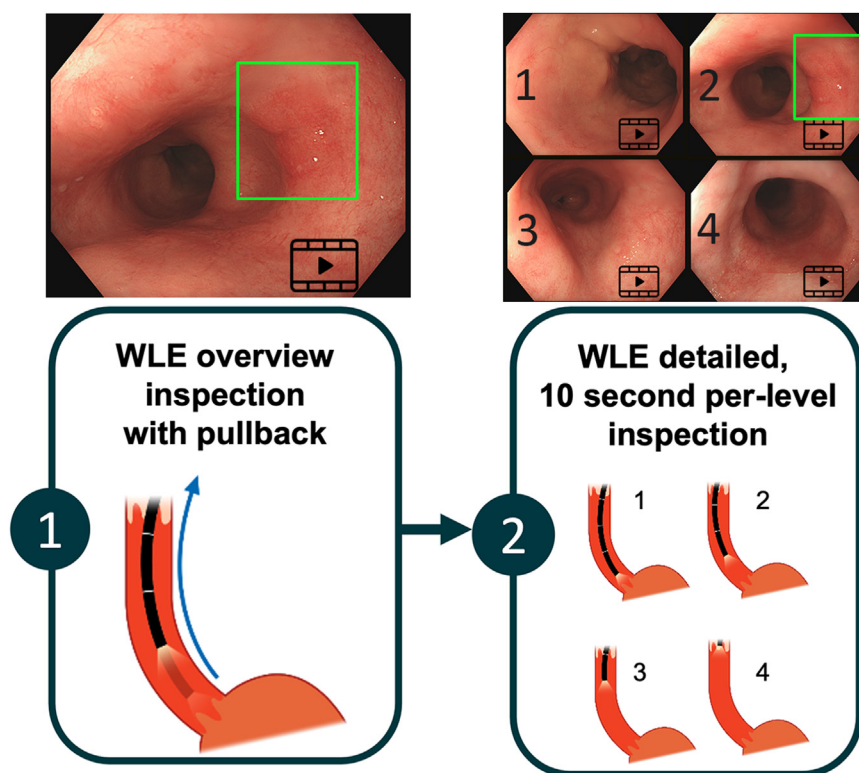
Figure 1. Visualization of endoscopy protocol. *WLE,* White-light imaging.

The current article presents a pilot study for a CADe system for use during Barrett's surveillance endoscopy.

METHODS

This prospective study was performed at the departments of Gastroenterology and Hepatology of both locations of the Amsterdam University Medical Centers (Academic Medical Center and VU University Medical Center). The Medical Research Involving Human Subjects Act did not apply to this study; official approval of this study was therefore waived by the Medical Ethics Review Committee of our center. The study was registered at ClinicalTrials.gov (NCT05628441).

The aim of this study was to evaluate the performance of our CADe system and to assess interaction of the CADe system with the endoscopists during live endoscopic procedures.

Development of the CADe system

The CADe system was recently developed by the BONS-AI consortium. It serves as a primary detection tool that alerts the endoscopist when visible abnormalities are present (Fig. 1). The rigorous data acquisition protocol and process of CADe development have been described elsewhere.[3,4]

Patient selection

A total of 30 patients were enrolled in the study; they were either patients with nondysplastic Barrett's esophagus under-going regular Barrett's surveillance or patients referred with high-grade dysplasia or esophageal adenocarcinoma. Patients were divided into a group with and a group without visible lesions. The ground truth was based on expert assessment during the endoscopic procedure. Histopathologic results were subsequently used for confirmation.

Endoscopic study procedure

The workflow for the evaluation of the Barrett's segment started with a slow pullback video. Furthermore, 10-second stationary "level videos" were taken every 2 cm in the Barrett's segment. This workflow is depicted in Figure 1.

Findings of the endoscopist and any detections of the CADe system were registered independently by a research fellow (K.N.F., M.R.J., J.B.J.). CADe detections where only registered when identified as such by the endoscopist. The endoscopist noted the presence of visible abnormalities and indicated if CADe detections matched any previously identified lesions or were false-positive detections. A more detailed description of the workflow, along with an explanatory video (Video 1, available online at www.giejournal.org), is presented in Appendix 1 (available online at www.giejournal.org).

Outcome measures

The performance of the CADe system was evaluated by using a per-patient and a per-level analysis in terms of sensitivity and specificity.

RESULTS

In total, 30 pullback videos and 106 level videos (30 patients) were generated and analyzed in real time by the CADe system. Of these 106 level videos, 32 level videos contained visible abnormalities, and 74 level videos did not contain visible abnormalities.

Per-patient analyses

Fifteen patients with a visible abnormality and 15 patients without a visible abnormality were included in this study. Supplementary Table 1 (available online at www.giejournal. org) presents the patient characteristics. In the pullback videos, the CADe system detected suspicious areas in 14 of the 15 patients with a visible abnormality. All these detected areas were subsequently confirmed in the corresponding level videos (Fig. 2). Furthermore, the single abnormality that was not detected in the pullback video was detected in the corresponding level video. Using the intended workflow, the CADe system thereby detected all visible abnormalities, resulting in a per-patient CADe sensitivity of 100%. In 13 of the 15 patients without a visible abnormality, a suspicious area was detected in the pullback video. In 7 of 13 patients, these false-positive detections persisted in corresponding level videos. There were no false-positive detections in the remaining level videos. This resulted in a per-patient specificity of 53%.

Per-level analyses

All level videos containing visible lesions were correctly identified by the CADe system (32 of 32; sensitivity, 100%). Of the 74 level videos without a visible abnormality, the CADe system correctly classified 54 videos as nondysplastic Barrett's esophagus, resulting in a per-level specificity of 73%.

DISCUSSION

This study describes the evaluation of a CADe system for visible lesions in the Barrett's esophagus in an in vivo pilot study. This CADe system has previously been developed and tested in an ex vivo setting by the international BONS-AI consortium and is envisioned to be used during Barrett's surveillance endoscopies.

The CADe system correctly identified all 15 visible lesions. Fourteen of these lesions were detected in the initial pullback video, and all were confirmed by the corresponding level videos. The remaining visible lesion was detected in the level video.

Many CADe systems in endoscopy are hampered by a high number of false-positive detections, which may lead to unnecessary biopsies and/or "alert fatigue" of the endoscopist.[5] Our CADe system also displayed false-positive detections, predominantly in the pullback videos. In 13 of 15 pullback videos, the CADe system displayed false-positive detections, which were reproduced in 7 corresponding level videos, resulting in a per-patient specificity of 53%.

It is important to note that in the pullback videos with a false-positive detection, only 1 to 3 areas were detected per patient. At worst, this would result in the acquisition of 1 to 3 additional biopsies in a minority of the patient population, whereas the length of the Barrett's segment (median length of 9 cm in this study) would dictate 16 random biopsies according to the Seattle protocol.[6] The rate of false-positive detections in this study may partially reflect the length of the Barrett's segment of our patient population.

In the level videos, the number of false-positive detections was lower (20 of 74 level videos without visible lesions; specificity, 73%). In the majority of level videos, there were no false-positive detections, which is a crucial finding for procedural operability of the CADe system.

This study has some unique features. First, the intended CADe workflow adheres to current guidelines for inspection of a Barrett's segment and is thereby easily adaptable in endoscopic workflows. Second, the CAD system operates in real time at 35 frames per second, using minimal computational resources. Its compact design enables easy integration into current endoscopy suites.

The current study also has limitations. First, this was a pilot study with a limited sample size, involving only 2 centers. Future research should expand to include more patients and additional centers. Second, the artificial 50:50 split of patients does not mimic the surveillance setting, in which neoplasia incidence is significantly lower. Finally, the CADe system was evaluated by expert endoscopists. The quality of endoscopic procedures will be more heterogeneous when performed by general endoscopists, although our standardized workflow consisting of a pullback video followed by a stationary level video may ensure more uniform image quality. This is an important limitation of nearly all CAD systems in endoscopy and is often referred to as the "domain gap"; most CAD systems have been developed in academic hospitals with extensive experience and state-of-the-art endoscopic equipment. The bulk of endoscopies are performed, however, at community hospitals, where the level of expertise and equipment is subject to considerable variation, leading to much more heterogeneous data than what were used for developing the CAD systems. This may lead to heavy degradation of artificial intelligence performance in daily practice.

In conclusion, in this study, we tested a CADe system for visible lesions in the Barrett's esophagus during real-time procedures in 30 patients. The CAD-assisted workflow described here closely mimics current endoscopic inspection standards. The CADe system identified all neoplastic lesions correctly with an acceptable number of false-positive detections.
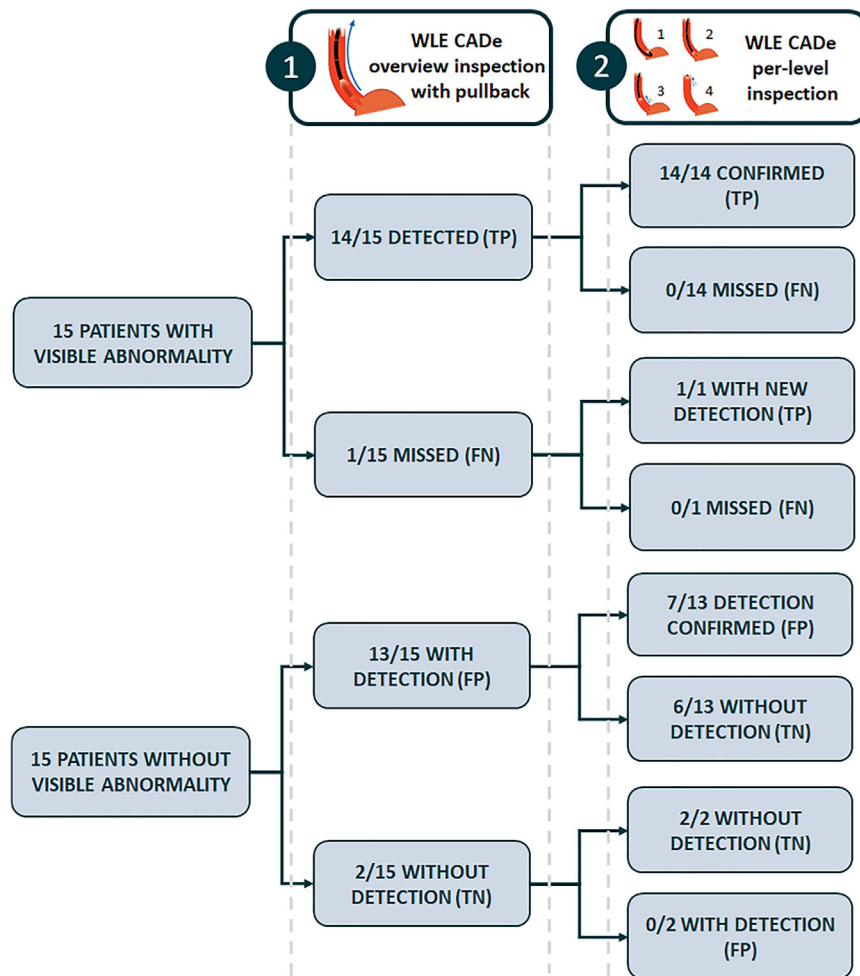
DISCLOSURE

Figure 2. Flowchart of per-patient results for patients included with and without a visible abnormality. *WLE*, White-light endoscopy; *CADe*, computer-aided detection; *TP*, true positive; *FN*, false negative.

REFERENCES

1. Beveridge CA, Mittal C, Muthusamy VR, et al. Identification of visible lesions during surveillance endoscopy for Barrett's esophagus: a video-based survey study. Gastrointest Endosc 2023;97:241-7.e242.

2. Bergman J, de Groof AJ, Pech O, et al. An interactive web-based educational tool improves detection and delineation of Barrett's esophagus-related neoplasia. Gastroenterology 2019;156:1299-308.e1293.

3. Fockens KN, Jukema JB, Boers T, et al. Towards a robust and compact deep learning system for primary detection of early Barrett's neoplasia: initial image-based results of training on a multi-center retrospectively collected data set. United European Gastroenterol J 2023;11:324-36.

4. Fockens K, Jong M, Jukema J, et al. A deep learning system for detection of early Barrett's neoplasia: a model development and validation study. Lancet Digital Health 2023;5:e905-16.

5. de Groof AJ. Artificial intelligence in endoscopy: transition from academic development to integration into daily endoscopic practice. Endoscopy 2022;54:785-6.

6. Sampliner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett's esophagus. The Practice Parameters Committeeof the American College of Gastroenterology. Am J Gastroenterol 1998;93:1028-32.

Endoscopedia

Endoscopedia has a new look! Check out the redesign of the official blog of *GIE*, *VideoGIE,* and *iGIE*. Use the QR code to connect to the latest updates or visit us at **www.endoscopedia.com**.

APPENDIX 1

Additional information on computer-aided detection–assisted endoscopic workflow

All endoscopic procedures were performed by 3 Barrett's expert endoscopists (J.J.B., R.E.P., L.C.D.) using EZ1500 endoscopes and X1 processors (Olympus, Tokyo, Japan). Procedures were performed between May 2022 and October 2022. During the study procedure, the endoscopists cleaned the Barrett's segment and then documented the extent of the Barrett's segment according to the Prague classification.[1] Subsequently, the Barrett's segment was carefully inspected for the presence of visible abnormalities, after which patients were allocated to group 1 or group 2. After this initial assessment, the endoscopist was provided with real-time feedback from the computer-aided detection (CADe) system, thus mimicking the envisioned clinical application of the CADe system.

The CADe assisted workflow is visualized in Figure 1 and consisted of the following routine: first, the endoscopist recorded a standardized pullback video of the Barrett's segment, starting at the gastroesophageal junction, slowly pulling back the endoscope until the most proximal extent of the Barrett's segment. Findings of the endoscopist and any detections of the CADe system were registered independently by a research fellow (K.N.F., M.R.J., J.B.J.). CADe detections where only registered when identified as such by the endoscopist. The endoscopist noted the presence of visible abnormalities and indicated if CADe detections matched any previously identified lesions, or if they were false-positive detections. After the pullback video, the endoscope was positioned ±2 cm above the gastroesophageal junction, and a 10-second video was recorded. These recordings were obtained in overview, without focus on any visible abnormalities, if present. These recordings (so called "level videos") were obtained every 2 cm in the Barrett's segment, until the most proximal extent. Per level, the findings of the endoscopist and the detections of the CADe system were again registered. Supplementary Figure 1 presents examples of included cases.

Statistical analysis

Statistical analysis was performed by using R Studio Version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria). For descriptive statistics, variables with skewed distribution are presented as median (interquartile range). Performance metrics are displayed using sensitivity and specificity findings.

Additional information on histopathologic support for visual ground truth

All visible abnormalities were either removed by endoscopic resection (EMR or endoscopic submucosal dissection) or targeted biopsy samples were obtained. All CADe detections were sampled by targeted biopsies. If no visible lesions were detected by both the endoscopist and CADe, random biopsy samples were obtained according to the Seattle protocol.[2]

While the criterion standard for presence or absence of visible abnormalities during the study procedure was the assessment of the endoscopist, histopathology results were also analyzed. In 13 of 15 visible lesions, histopathology results showed high-grade dysplasia or esophageal adenocarcinoma. In 2 patients with visible lesions, histopathology showed no dysplasia (Supplementary Figs. 2 and 3). These lesions were indicated as clearly abnormal, however, and thereby potentially neoplastic by the expert endoscopist, and they should therefore be recognized as such by a primary CADe system. This is in line with current guidelines, which dictate targeted histologic sampling or endoscopic resection of all visible abnormalities.[3,4] In 4 of 15 cases in the group with no visible abnormalities, histopathology results revealed low-grade dysplasia at 1 to 3 levels. Because the endoscopist did not detect any visible abnormalities, these cases are considered as true-negative predictions, even though histopathology results indicated low-grade dysplasia.
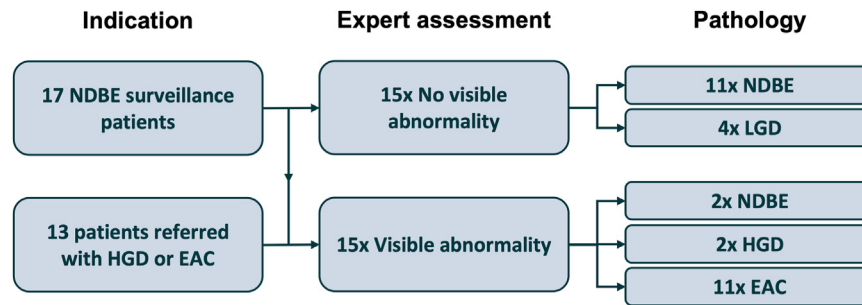
SUPPLEMENTARY REFERENCES

1. Sharma P, Dent J, Armstrong D, et al. The development and validation of an endoscopic grading system for Barrett's esophagus: the Prague C & M criteria. Gastroenterology 2006;131:1392-9.
2. Sampliner RE. Practice guidelines on the diagnosis, surveillance, and therapy of Barrett's esophagus. The Practice Parameters Committee of the Amrican College of Gastroenteroloy. Am J Gastroenterol 1998;93:1028-32.
3. Wani S, Qumseya B, Sultan S, et al. Endoscopic eradication therapy for patients with Barrett's esophagus-associated dysplasia and intramucosal cancer. Gastrointest Endosc 2018;87:907-31.e909.
4. Weusten BLAM, Bisschops R, Dinis-Ribeiro M, et al. Diagnosis and management of Barrett esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy 2023;55:1124-46.
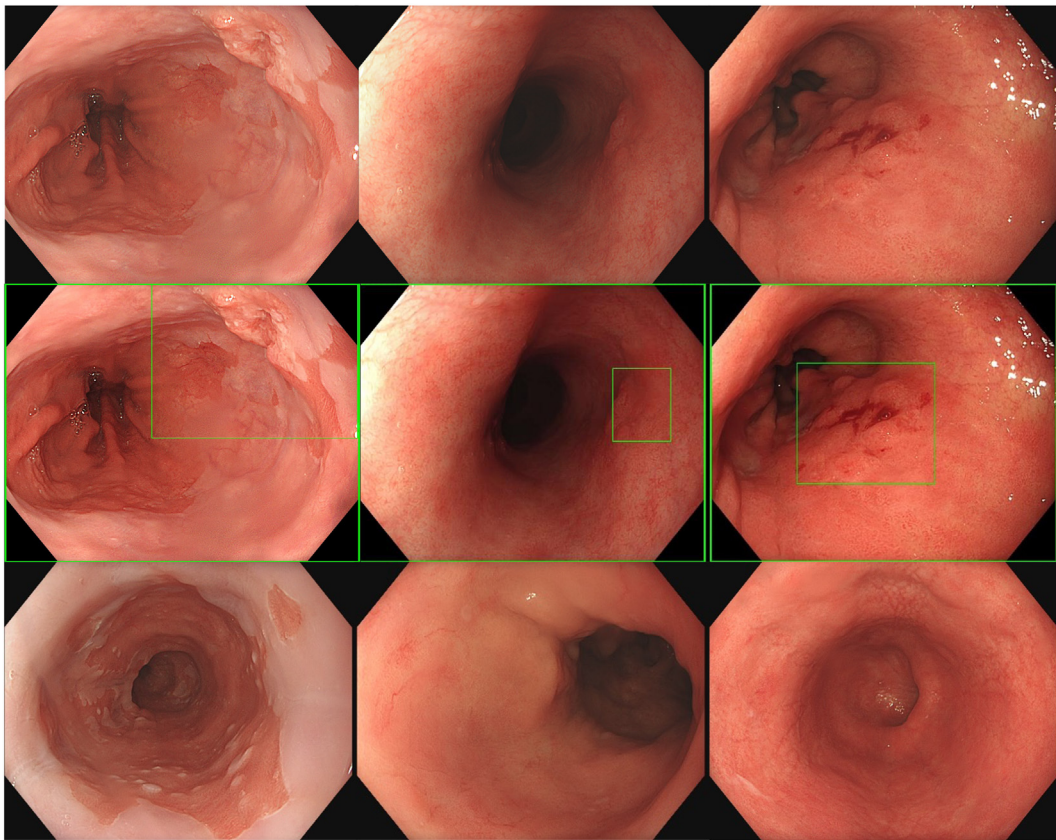
Supplementary Figure 1. Examples of included cases. Upper row: neoplastic cases; middle row: corresponding computer-aided detection predictions; lower row: nondysplastic cases.
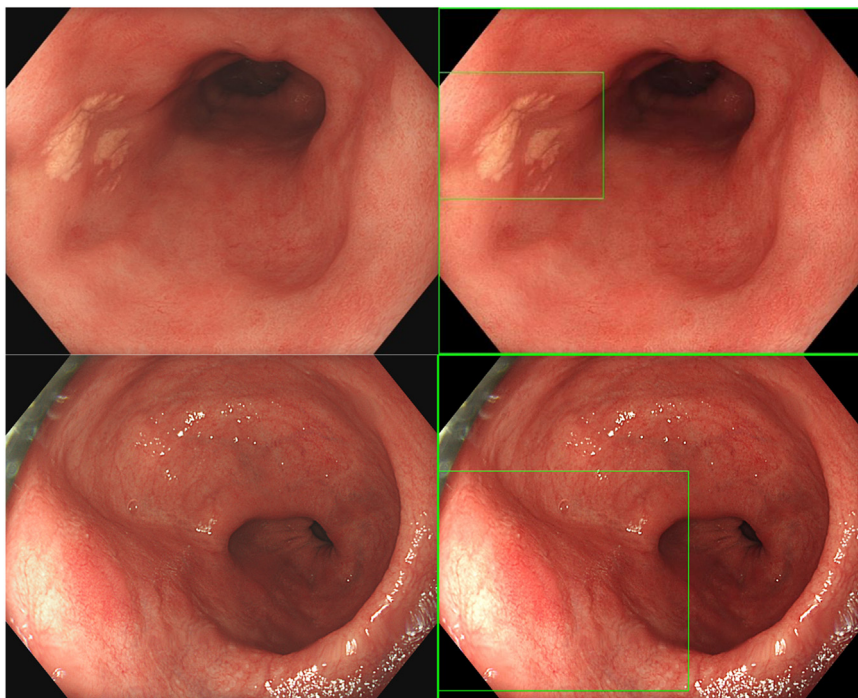
Supplementary Figure 2. Two cases with visible abnormalities but nondysplastic Barrett's esophagus in histopathology results.

Supplementary Figure 3. Flowchart illustrates the process from referral indication until pathology result. *NDBE*, Nondysplastic Barrett's esophagus; *HGD*, high-grade dysplasia; *EAC*, esophageal adenocarcinoma.

SUPPLEMENTARY TABLE 1. Characteristics of included patients and number of patients per location and endoscopist

Characteristic	Combined (N = 30)	Patients with visible lesion (n = 15)	Patients without visible lesion (n = 15)
Demographic			
Median age, y	67	68	67
Sex, male	25 (83)	13 (87)	12 (80)
Barrett's imaging			
Circumferential BE, cm	7 (3-9)	6 (2-10)	9 (7-10)
Maximum extent BE, cm	9 (6-10)	8 (6-11)	9 (7-10)
Primary Paris type			
0-Ip/s	–	3 (20)	–
0-IIa	–	9 (60)	–
0-IIb	–	3 (20)	–
0-IIc	–	0 (0)	–
Pathology: worst overall histology			
Intestinal metaplasia/no dysplasia	13 (43)	2 (13)	11 (73)
Low-grade dysplasia	4 (13)	0 (0)	4 (27)
High-grade dysplasia	2 (7)	2 (13)	0 (0)
Esophageal adenocarcinoma	11 (37)	11 (73)	0 (0)
Endoscopic center			
VUmc hospital	25 (83)	14 (93)	11 (73)
AMC hospital	5 (17)	1 (7)	4 (27)
Endoscopist			
Endoscopist no. 1	13 (43)	7 (47)	6 (40)
Endoscopist no. 2	10 (33)	5 (33)	5 (33)
Endoscopist no. 3	7 (23)	3 (20)	4 (27)

Values are n (%) or median (interquartile range) unless otherwise indicated.
BE, Barrett's esophagus; *VUmc*, VU University Medical Center; *AMC*, Academic Medical Center.