



Original research article

## The added value of magnifying endoscopy in diagnosing patients with certain gastroesophageal reflux disease



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## ABSTRACT

**Purpose:** In most cases gastroesophageal reflux disease proceeds without macroscopic erosions in the esophagus. We aimed to clarify if abnormalities detectable in magnifying endoscopy may offer additional diagnostic criteria for gastroesophageal reflux disease and to what histopathologic structures do they correspond.

**Patients/methods:** Esophageal mucosa above and below Z-line was evaluated under x115 magnification in 67 gastroesophageal reflux disease patients (11 with erosive reflux disease, 28 with Barrett's esophagus, 28 with nonerosive reflux disease) and in 12 patients without gastroesophageal reflux disease (negative control group). Features characteristic of gastroesophageal reflux disease were specified by comparing erosive reflux disease and Barrett's esophagus patients with negative control group. Afterwards the presence of identified features were evaluated in nonerosive reflux disease group. Interobserver agreement in the recognition of the proposed criteria was rated. Biopsies collected from the mucosa above Z-line were evaluated histologically after hematoxylin and eosin staining.

**Results:** Endoscopic lesions characteristic of gastroesophageal reflux disease were: microerosions, abnormal intrapapillary capillary loops, obscured palisade vessels, white points, big triangular indentations of Z-line and villous mucosa below Z-line. The presence of two or more of the above features indicated gastroesophageal reflux disease with 97% sensitivity and 75% specificity. Substantial interobserver agreement was achieved in evaluation of obscured palisade vessels, abnormal intrapapillary capillary loops and white points. Endoscopic lesions were correlated to histology. Lesions identified with magnifying endoscopy were helpful in discerning between negative control group and nonerosive reflux disease patients.

**Conclusions:** Magnifying endoscopy reveals abnormalities that can be used as additional endoscopic diagnostic criteria of gastroesophageal reflux disease.

### 1. Introduction

Gastroesophageal reflux disease (GERD) is an increasing problem with approximately 20% of Western countries population suffering nowadays from its symptoms [1]. GERD is the most frequent diagnosis in gastroenterological outpatient clinics and causes a great burden to health resources [2]. GERD is also among the strongest known risk factors for esophageal adenocarcinoma which incidence has risen 6 fold during the last 40 years [3]. Diagnosis of GERD can be made based on typical symptoms and positive response to anti-secretory treatment [4]. Indications for further testing include treatment failure, diagnostic uncertainty and treating or preventing complications. Ambulatory

reflux monitoring like 24-hour pH-metry or pH-impedance can provide confirmatory evidence of GERD [5]. However, in many countries pH monitoring is less available than endoscopy, especially outside the reference and academic centers. GERD continues to be a common indication for upper gastrointestinal endoscopy reaching 24% of all procedures in the United States [2]. Based on the result of endoscopy, GERD can be divided into three types: Barrett's esophagus (BE), erosive reflux disease (ERD) and nonerosive reflux disease (NERD). BE and ERD have typical appearance in standard endoscopy but in case of NERD, which constitutes up to 65% of all patients, no lesions are visible [6]. Therefore, conventional endoscopy has low sensitivity as a diagnostic tool for GERD. Methods improving ability of endoscopy to detect GERD

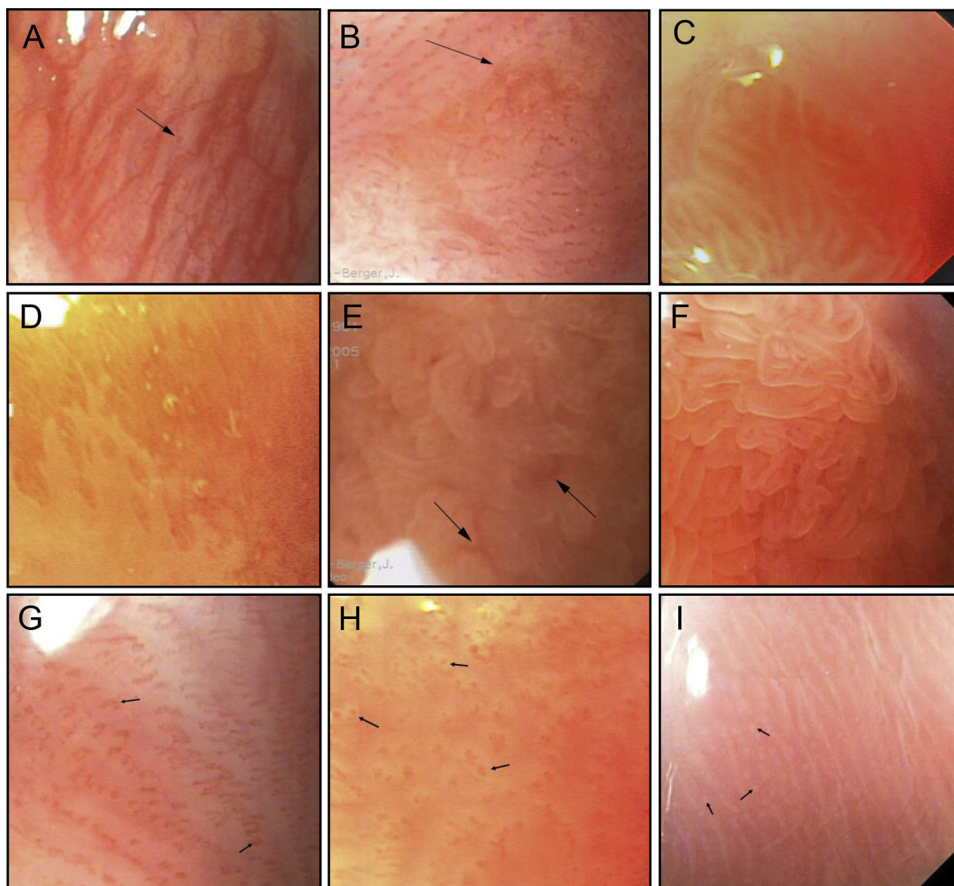
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**Fig. 1.** (a) Normal squamous mucosa. Palisade vessels transparent, few intrapapillary capillary loops visible as dots (arrow). (b) Microerosion (arrow). (c) Big triangular indentation of Z-line. (d) Serrated Z-line. (e) Blood vessels transparent through columnar mucosa (arrows). (f) Villiform columnar mucosa below Z-line. (g) Abnormal intrapapillary capillary loops within squamous mucosa - increased in number, elongated, dilated (arrows). Palisade vessels obscured. (h) White points visible as whitish halation encircling intrapapillary capillary loops (arrows). Palisade vessels obscured. (i) White points visible as pinpoint spots in the absence of apparent intrapapillary capillary loops (arrows). Palisade vessels obscured.

are awaited.

One of advanced techniques developed for better evaluation of gastrointestinal tract is magnifying endoscopy (ME). The system of lenses inside the endoscope allow for optical magnification of the image and therefore detailed evaluation of mucosal surface and blood vessels. Because the degree of magnification is operator dependent, it is possible to obtain both standard and magnified images during the same endoscopic procedure.

Normal squamous mucosa of distal esophagus is transparent for longitudinal palisade vessels located in submucosa. At a magnification of x90, apart from the palisade vessels, regularly arranged, sparse, small pin-point like intrapapillary capillary loops (IPCLs) of lamina propria mucosae are visible [7] (Fig. 1a). The border between squamous and columnar epithelium, so-called Z-line is even, located at the upper end of gastric folds. Distally to the Z-line no vessels are seen and the surface of mucosa has regular dot-like pit pattern [8,9].

Research on novel endoscopic methods described a variety of minimal changes in NERD patients such as minute apical mucosal breaks, triangular indentations or serrated Z-line, obscured palisade vessels, enlarged IPCLs, villiform mucosa and transparent vessels below the Z-line [9,10,11] Most of the previously published studies on so-called minimal change esophagitis are of preliminary character and reproducibility of their findings still requires confirmation. Defining easy to detect features of GERD may increase the importance of endoscopy in NERD evaluation and reduce the demand for pH-metry.

Histological changes in GERD include elongation of the mucosal papillae, basal cell hyperplasia, inflammatory cells infiltration and dilated intercellular spaces [12,13]. Such lesions are also detected in NERD and acid-suppressing therapy reverses them [14]. However some studies point out low sensitivity and specificity of those findings [15].

The aim of our study was to evaluate which minimal lesions visible in ME in patients with features of GERD detected with conventional

endoscopy are most characteristic and may serve as additional diagnostic criteria. We studied interobserver agreement for the presence of these minimal lesions. For better understanding of endoscopic morphological abnormalities, we searched for their histologic equivalents. Finally, we assessed the presence of identified minimal lesions in patients with NERD.

## 2. Patients and methods

### 2.1. Patients

We enrolled prospectively patients diagnosed with GERD on the basis of typical symptoms and positive response to proton pump inhibitor (PPI) treatment. Before inclusion, the patients with symptoms suggestive of GERD had two visits in our ambulatory clinic. During the first visit patients not treated with PPI were evaluated according to a questionnaire developed by Carlsson et al. [16] with a cut-off point for diagnosis of GERD at score 4 and were prescribed double standard dose of PPI (20 mg of omeprazole or 40 mg of pantoprazole twice a day) for 2 weeks. During the second visit patients with positive response to the prescribed treatment were diagnosed with GERD, qualified to the study (moment of inclusion) and referred for gastroscopy. The time between inclusion and endoscopy was up to 3 months. During that time patients were allowed to take PPI on demand but had to stop this treatment a week before endoscopy. We also included patients with previously diagnosed BE who were referred for upper gastrointestinal endoscopy as a periodic endoscopic screening for neoplasia. These patients were on chronic treatment with standard dose of PPI once daily or twice daily depending on subjective symptoms with 1-week off PPI before endoscopy. One week off PPI served as unification of the examined group with the negative control group, which did not take PPI at all and unification of the examined group itself, because particular GERD

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