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Feasibility Trial of the Newly Introduced Optical Enhancement Technology in Patients with Gastroesophageal Reflux Disease

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Endoscopy · Gastroesophageal reflux · Image enhancement

Abstract
Background: Optical Enhancement technology (OE) combines bandwidth-limited light and image enhancement processing technology to enhance subtle mucosal and vascular details. This is the first study assessing the new technology for the diagnosis of gastroesophageal reflux disease (GERD). ***Patients and Methods:*** Consecutive patients with GERD and controls were prospectively included. The distal esophagus was examined in all quadrants with high definition white-light endoscopy (HD-WLE) followed by OE and biopsies for histopathological analysis. Features observed only by OE were compared between controls and patients with GERD. ***Results:*** A total of 100 areas were evaluated. About 56% of patients had a diagnosis of GERD. The mean age of patients was 53 years (range 27–89 years), 60% were female. Compared to controls, patients with diagnosis of GERD showed significantly more often tortuosity ($p = 0.042$), dilation ($p = 0.0003$), and increased number ($p = 0.001$) of intrapapillary capillary loops (IPCLs). In addition, increased vascularity and mucosal breaks were significantly more often found in patients with GERD as compared to controls ($p < 0.05$). On multivariate analysis, increased number and dilation of IPCL were the best predictors of GERD. ***Conclusions:*** The newly introduced OE technology significantly improves the diagnosis of GERD compared to HD-WLE. The results should be confirmed in a multicenter trial.

Introduction

Gastroesophageal reflux disease (GERD) is one of the most common diseases of the esophagus, with an increasing incidence worldwide [1]. Its prevalence varies from 18

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to 27% in the USA and 8 to 26% in Europe [2]. GERD comprises of 3 entities, erosive reflux disease (ERD), non-erosive reflux disease (NERD), and Barrett's esophagus [3]. The latter has been established as a precancerous condition requiring extensive surveillance. Diagnosis of GERD is based on clinical, endoscopic, histologic, and functional parameters [4]. Of note, up to 70% of patients suffering from reflux-like symptoms (e.g., heartburn, regurgitation) do not show any endoscopic abnormalities [5] and are considered as NERD patients. Recent data have shown that advanced endoscopic imaging techniques, including Narrow Band Imaging (NBI; Olympus, Tokyo, Japan) and i-scan (Pentax Medical, Tokyo, Japan) allow for endoscopic visualization of distinct mucosal abnormalities in patients with NERD, thereby potentially allowing for a better diagnosis and therapy of those patients [6–9].

Most recently, the Optical Enhancement (OE; Pentax Medical, Tokyo, Japan) technology was introduced as a novel technique allowing exact visualization of the mucosal surface pattern morphology. OE combines optical and digital chromoendoscopy techniques allowing for both visualization of the mucosal surface pattern and mucosal vascular pattern morphology [10]. In particular, OE uses band-limited light emission at 415, 540, and 570 nm connecting the peaks of hemoglobin absorption spectrum as well as red light emission to increase the overall brightness of the image. Thus, OE enables the visualization of blood vessels and provides better illumination, especially in large lumen organs such as the stomach and the colon. This is the main difference of OE compared to other advanced imaging technologies that also narrow the red light such as NBI. Yet, no data are available on the potential of the novel OE technology for the diagnosis of GERD.

Therefore, the aim of the current study is to prospectively evaluate the diagnostic efficacy of the newly introduced OE technology as compared to high-definition white-light endoscopy (WLE) in patients suffering from GERD.

Materials and Methods

Endoscopic System and Principle

A video processor with OE technology (Pentax, Tokyo, Japan) was used in this study. For OE, the baseline transmittance between the peaks of the hemoglobin absorption spectrum is raised, resulting in an improved visualization of microvessels with a sufficient amount of light. The principle is based on optical filters achieving higher overall transmittance by connecting the peaks of the hemoglobin absorption spectrum (415, 540, and 570 nm), thereby creating a continuous wavelength spectrum.

Patients

A total of 25 patients were prospectively included in a time period of 12 months. In 14 patients, diagnosis of GERD [4] was made based on clinical information (Reflux Disease Questionnaire Score >3, [11]) or histopathological workout at the time of recruitment. About 11 patients without any GERD symptoms served as control patients. All patients gave their written consent and received esophagogastroduodenoscopy with the new OE technology. Patients with known esophageal disorders other than GERD were excluded from the study. The study was approved by the local ethics committee.

Endoscopic Procedure

All procedures in this study were performed using the i10 endoscope and the Optivista video processor with OE technology. Patients underwent conscious sedation and received cardiopulmonary monitoring during the examination. All patients were initially examined in all quadrants by high-definition WLE. The distal esophagus was consequently evaluated with OE. The following features were examined in all patients, as previously described [12–14]: (a) intraepithelial papillary capillary loop (IPCL) tortuosity, (b) IPCL dilation, (c) IPCL quantity, (d) vascularity, and (e) mucosal breaks.

Normal IPCLs were recognized endoscopically as hairpin-like structures with small diameter. Tortuosity was defined by the presence of corkscrewing or twisted nature of individual IPCLs. Dilatation of IPCLs was recognized by their increased size or caliber, whereas increment was recognized as an increase in the number of IPCLs in individual fields. Presence of micro erosions was detected as mucosal breaks not visible at standard endoscopy. Increased vascularity at the squamocolumnar junction were noted as being present or absent.

Statistical Analysis

Results are expressed as mean ± SD. The statistical analysis was conducted using SPSS program. *t*-Test and $\chi 2$ test were performed to assess OE compared with WLE on detected lesions. Data were analyzed using the Mann-Whitney U test to compare group means. A p value less than 0.05 was considered to represent a significant difference.

Results

Patient's Characteristics

The average age of patients at diagnosis was 53 years and ranged from 22 to 89 years. A total of 15 (60%) of the examined patients were female. The diagnosis of GERD was established in 14 (56%) patients. The control group consisted of 11 patients.

IPCL Characterization

About 57% patients with GERD showed tortuosity in IPCLs when examined with OE, whereas the same feature was seen in only 1 out of the 11 controls ($p = 0.042$). Dilation of the IPCLs was observed in 12 (86%) patients with

GERD. This feature was not seen in any of the patients in the control group ($n = 0$, $p = 0.003$).

Furthermore, GERD patients had significantly increased number of IPCLs at the esophagogastric junction in comparison to patients without reflux disease (12 vs. 1; $p = 0.001$). The main IPCL features in the study population are summarized in Table 1.

In Figures 1 and 2, endoscopic images of all 3 IPCLs' features (tortuosity, dilation, and vascularity) are depicted during WLE and OE.

Vascularity and Mucosal Breaks

Using the OE system, the vascularization of the area above the Z-line could be thoroughly examined. We found a significant proportion of patients with GERD with an increased vascularity of this specific region (79%, $n = 11$). The respective proportion of patients in the control group showed an increased number of blood vessels in the observed region in 27% of patients ($p = 0.03$). Moreover, 50% of patients with reflux symptoms showed mucosal breaks in the inspected areas. On the contrary, areas of slough or erythema could not be observed in any of the patients in the control group ($n = 0$, $p = 0.03$). The main findings related to vascularity and mucosal breaks in the study population are summarized in Table 1.

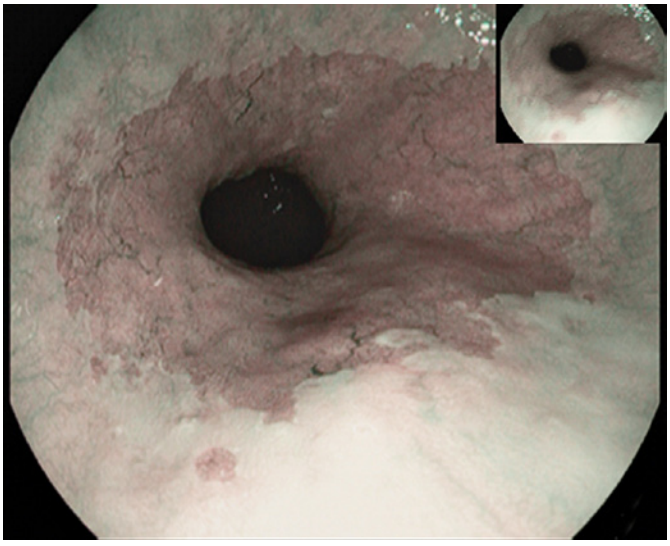

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Fig. 1. The Optical Enhancement technology utilizes optical filters in combination with digital post-processing for enhanced visualization of surface and vascular changes.

Table 1. Distribution of endoscopic features using optical enhancement

Characteristic	GERD, *n* (%)	Control, *n* (%)	*p* value
IPCL tortuocity	8 (57.1)	1 (0.09)	0.042
IPCL dilation	12 (85.7)	0 (0)	0.0003
IPCL increased	12 (85.7)	1 (0.09)	0.001
Increased vascularity	11 (78.6)	3 (27.3)	0.03
Visible mucosal breaks	7 (50)	0 (0)	0.03

IPCL, intrapapillary capillary loop.

Discussion

This is the first study showing the potential of the most recently introduced OE technology for the diagnosis of GERD. The OE technology significantly improved the diagnosis of GERD compared to high-definition WLE, thereby potentially allowing for a better diagnosis and therapy of patients.

GERD is associated with a large social-economic burden [15]. Furthermore, Barrett's esophagus is a serious complication of GERD since it is considered a precursor for esophageal adenocarcinoma. Thus, the need for an accurate and early diagnosis of GERD is of major importance [16]. However, the establishment of GERD diagnosis remains in most cases time consuming and challenging due to the absence of endoscopic findings. Even though 24-h esophageal pH monitoring is considered the gold standard for the confirmation of NERD, false-negative or false-positive results are common [17]. In a recent retrospective study 44% of patients with esophageal dysmotility, 57% of patients with eosinophilic esophagitis, and 73% of patients with gastroparesis showed pathologic acid reflux according to pH measures [18]. Furthermore, the benefit of histological examination for the diagnosis of NERD remains controversial, such that current guidelines do not recommend biopsies from normal esophageal mucosa for this purpose [19]. In this context, current studies focus on the utility of new imaged enhanced endoscopy techniques to improve the low sensitivity of conventional endoscopy for the diagnosis of GERD [20].

In the present study, the clinical utility of the OE system in a group of patients with GERD and controls was assessed. We showed a significant increase in quantity, dilation, and tortuosity of IPCLs in patients with GERD. Our results suggest a distortion of the micro-vascularization at the squamocolumnar junction, which cannot be detected using conventional WLE and is not present in

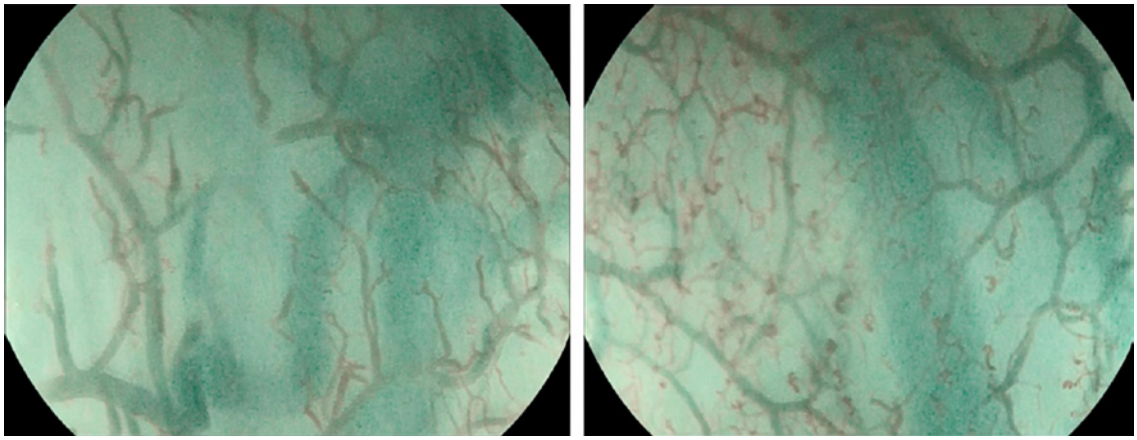

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Fig. 2. Optical Enhancement combined with optical magnification imaging reveals subtle details in patients with GERD. Dilation and an increased number of intrapapillary capillary loops were more often identified in GERD patients compared to controls.

patients without reflux symptoms. Similar results have been reported by Sharma et al. [12] who examined 50 patients with GERD and 30 controls with NBI. They observed an increased number, tortuosity, and dilatation of IPCLs in GERD patients (66, 80, and 80% respectively). Nevertheless, 14, 37, and 17% of controls showed in NBI similar microvascular alterations, whereas in our study these were almost absent in the control group. Increment and dilatation of IPCLs as characteristic features of GERD have also been reported in other trials using magnifying endoscopy and NBI [8, 13, 21]. In a recent trial of 20 patients with GERD and 60 controls, the same endoscopic findings were reported using either i-scan or NBI [22]. Lv et al. [13] detected, however, no significant difference in the presence of prolonged, dilated, or tortuous IPCLs, whereas Banerjee showed that IPCLs' dilatation resolves under treatment with proton pump inhibitors, suggesting their role as possible predictors for NERD and response to treatment [8].

In the second part of our study, we investigated the utility of OE in identifying structural changes on the mucosa of patients with GERD. We detected significant higher vascularization and mucosal breaks in GERD patients than in subjects without GERD. Previously, high-resolution endoscopy and chromoendoscopy had been used in GERD patients to evaluate findings not visualized by WLE [23, 24]. It has been reported [23] that subtle endoscopic findings such as vascular injection or vascular spots above the Z-line, villous mucosal surface, and islands of squamous cell epithelium below the Z-line are criteria of a minimal change esophagitis in patients with GERD.

Similar minimal changes in the squamocolumnar junction of the esophagus have been reported in other studies comparing the utility of i-scan, FICE with that of WLE [6, 7, 25–28]. In all these trials, image-enhanced endoscopy increased the diagnostic yield of reflux esophagitis by detecting, in accordance with our results, mucosal and vascular alterations at the distal esophagus adjacent to the Z-line. However, in a study by Kim et al. [29] in 1,445 patients, the prevalence of minimal change esophagitis was not significantly different between patients with GERD and patients without GERD suggesting reconsideration of their clinical significance.

To the best of our knowledge, this is the first prospective trial evaluating the diagnostic utility of OE in patients with benign esophageal diseases such as GERD. Kodashima et al. [30] has shown that OE can improve the detection and characterization of esophageal squamous cell cancer. The OE technology uses wavelengths that correspond to the peaks of the hemoglobin absorption spectrum as the main wavelength of the illumination light. Due to its high illumination intensity, it provides additional information for the microvascular patterns also in organs with a large lumen.

This study has certain limitations. First, it was a single-center study which was conducted at a tertiary referral institution. Also, it was an unblinded pilot trial; therefore, an operator bias cannot be excluded. In addition, no 24-h pH monitoring was performed in the patient cohort considered. Therefore, there might be a cross contamination that supposedly reflects the few controls which showed increased vascularity, tortuosity, and an increase in IPCLs. Nevertheless, esophageal pH monitoring has

limitations of its own, which include inadequate sensitivity, especially in the milder forms of GERD. At last, although a prospective inclusion was performed, no sample size calculation was done due to the novelty of the OE technology. The number of patients who participated in our study was based on the clinical presentation of patients in our endoscopy department during a period of approximately 1 year. Further studies can now use the results of the present study to conduct an adequate statistical workout.

Recent advances in endoscopic imaging have been made in an effort to improve the detection of esophageal diseases. However, whether such advances have improved the detection of esophageal pathologies compared to conventional high-definition WLE is still under debate. We have shown for the first time that OE has a significant additional effect in distinguishing the minimal vascular and structural changes in GERD compared with WLE. However, further multicenter trials are necessary to evaluate the diagnostic utility of OE in patients suffering from GERD, as well to compare its diagnostic accuracy with that of other advanced imaging techniques.

Disclosure Statement

The authors have no conflicts of interest to declare.

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