

Reliable Endoscopic Findings of Minimal Change Esophagitis for Diagnosis of Non-erosive Reflux Disease (NERD) Using High Definition Endoscopy with I-scan

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ABSTRACT

Background and Aims: Majority of patients with gastro-esophageal reflux disease (GERD) were non-erosive reflux disease (NERD). High definition (HD) endoscopy with I-scan could enhance visualization of mucosal and vascular pattern and might identify changes that were invisible at standard endoscopy. This study aimed to evaluate the endoscopic findings that may have diagnostic value for the prediction of NERD by using HD endoscopy with I-scan.

Methods: Patients with typical GERD symptoms and healthy control without GERD symptoms were included and 2 validated GERD questionnaires were completed. The endoscopist was blinded to the presence of reflux symptoms and distal esophagus was examined by using standard white light endoscopy followed by I-scan. Mucosal morphology at squamocolumnar junction (SCJ) observed by I-scan were compared between GERD patients and controls.

Results: Twenty-seven patients with reflux symptoms and 21 controls were included. Three patients with reflux symptoms had erosive reflux disease (ERD) and 24 had NERD. Gastric pit pattern adjacent to SCJ, triangular indentation, hyperemia (erythema), micro-erosion, scar and groove at SCJ (Trench sign) were clearly seen by HD endoscopy with I-scan. Comparing to controls, NERD had a significantly higher prevalence of Trench sign (ERD, 100%; NERD, 79.17%; controls, 23.81%) ($p < 0.001$), higher prevalence of gyrus gastric pit pattern (ERD, 100%; NERD, 87.50%; controls, 57.14%) ($p = 0.041$). The erythema at EGJ was also more common in NERD group ($p = 0.041$). The micro-erosions were found more often in NERD than control (29.17% vs. 4.76%) and scar was found only in NERD groups. The symptoms scores of all three groups were improved significantly after 2 weeks of PPI therapy.

Conclusions: Minimal change esophagitis (Trench sign, gyrus gastric pit pattern at SCJ and erythema) observed by HD endoscopy with I-scan could be used as reliable predictors to distinguished NERD patients from normal controls. Further studies are needed to validate these findings.

Key words : Gastro-esophageal reflux disease, GERD, NERD, high definition endoscopy, I-scan

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common condition worldwide; the prevalence of GERD are 2.5-7.1% in most population-based studies in Asia⁽¹⁾. However, more than 60% of patients with GERD show no or minimal changes on standard white light endoscopy and are classified as non-erosive reflux disease (NERD)⁽²⁾.

Since there are many new endoscopic techniques to detect minimal change esophagitis⁽³⁾ such as high resolution and high definition white light endoscopy, magnification endoscopy, chromoendoscopy, narrow-band imaging and confocal laser endomicroscopy, endoscopic findings for NERD patients can be divided into two groups: normal and minimal change esophagitis⁽⁴⁾.

Although various endoscopic findings of minimal change esophagitis for example erythema, whitish turbidity, edema, friability and increase vascularity of distal esophagus have been reported, there is no standard definition since most of them are too complex or has low inter-observer agreement⁽⁴⁾.

High definition (HD) endoscopy with I-scan is a new technology that could enhance visualization of mucosal and vascular pattern and might identify changes that were invisible at standard endoscopy. This study aimed to evaluate the endoscopic findings by using HD endoscopy with I-scan to identify findings that may have diagnostic value for the prediction of NERD yet are simple and have high inter-observer agreement.

METHODS

Study design and objective

The primary outcome of this prospective cohort study was to identify the endoscopic findings that have diagnostic value for the prediction of NERD (minimal change esophagitis) by using HD endoscopy with I-scan. The secondary outcome was to evaluate the response to proton pump inhibitor (PPI) in GERD patients with or without minimal change esophagitis.

Patients selection

The patients with or without GERD symptoms presenting to gastrointestinal clinic of Maharaj Nakorn Chiangmai Hospital from November 2009 to November 2010 were invited to participate in this study. All patients completed 2 validated questionnaires (RDQ: reflux diagnostic questionnaire and HRQL: Health-re-

lated quality-of-life GERD questionnaire) after giving written informed consent. Patients were enrolled if they were 18 to 80 years of age and had ability to provide written informed consent.

Patients who have heartburn or regurgitation more than 2 times/week for at least 1 month were defined as having GERD and patient without any reflux symptoms served as controls. The exclusion criteria were 1) pregnancy, 2) cirrhosis or presence of gastroesophageal varices, 3) gastrointestinal hemorrhage, 4) angina pectoris, 5) allergy to PPI, 6) high risk or contraindication for endoscopy, and 7) chronic cough, laryngitis, and asthma.

METHODS

Patients who have prior taken PPI, H₂ receptor antagonist, domperidone, alginate-antacid must have a washout period of 4 weeks for PPI and 2 weeks for H₂ receptor antagonist, domperidone and alginate-antacid. During washout period, antacid 15 mL was allowed as a rescue medication.

The endoscopist was blinded to the presence of reflux symptoms and distal esophagus was examined using standard white light endoscopy followed by I-scan.

Four-quadrant photographs from the distal esophagus were obtained. Mucosal morphology at squamocolumnar junction (SCJ) observed by I-scan were compared between GERD patients and controls.

After the EGD was performed, all patients who have typical reflux symptoms were prescribed esomeprazole 20 mg twice daily for 2 weeks, then the same questionnaires were completed. The symptoms scores before and after treatment were compared.

Statistical analyses

The main analyses were conducted using Fisher's Exact test to compare the endoscopically visible changes on I-scan.

The improvement of the scores after treatment with PPI was analyzed by Wilcoxon Signed Ranks test. The difference of pre and post treatment scores between three groups of patients (ERD and NERD with or without minimal change esophagitis) was analyzed by Kruskal-Wallis test.

RESULTS

Twenty-seven patients with typical reflux symp-

toms (GERD) and 21 asymptomatic controls were included. Demographic characteristics were shown in Table 1. There were no statistically significant differences between the GERD and control groups.

In GERD group, mucosal breaks at EGJ were identified in 3 patients (ERD); all patients with ERD have mucosal break LA grade A. In control group, no mucosal break was detected. Accordingly, the patients were defined as ERD group, NERD group, and control group.

First, the GE junction was inspected with HD white light endoscopy then followed by inspection with preset I-scan mode (I-scan 1, 2 and 3). The gastric pit pattern adjacent to SCJ was classified into normal round pit pattern, tubular pit pattern and gyrus pit pattern. The squamocolumnar junction (SCJ) was examined for smoothness (smooth, shaggy or tattered), erythema, and triangular indentation of gastric mucosa, microerosion and groove at the junction that look like çtrenché. The adjacent mucosa was also observed for islets of squamous mucosa or islets of gastric mucosa and scar. The presence of hiatal hernia was also recorded (Table 1 and Figure 1-3).

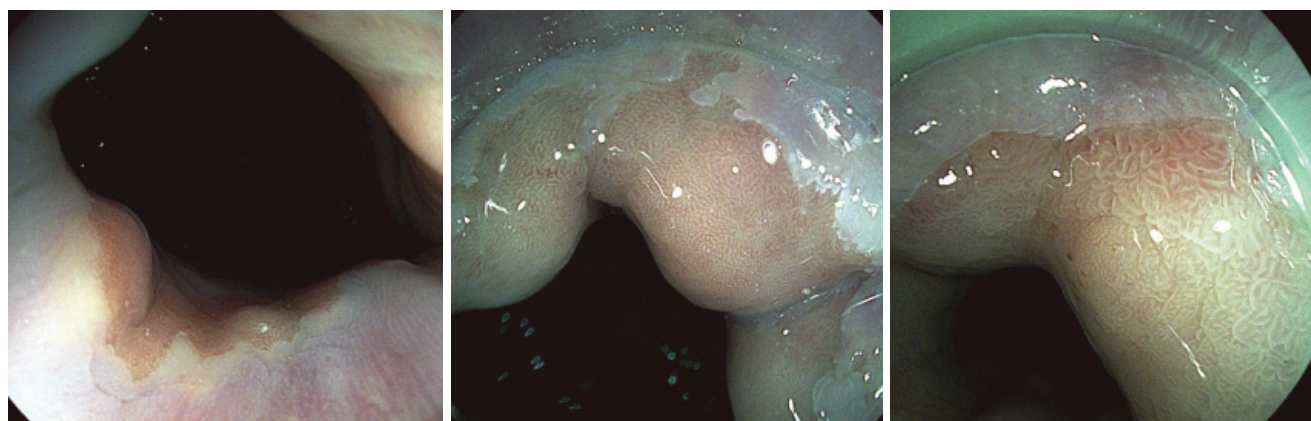
In comparison to controls group, the endoscopic findings that had a significantly higher prevalence in NERD group were Trench sign (ERD, 100%; NERD, 79.17%; controls, 23.81%) ($p < 0.001$), gyrus gastric pit pattern (ERD, 100 %; NERD, 87.50 %; controls, 57.14 %) ($p = 0.041$) and erythema at EGJ (ERD, 100 %; NERD, 87.50 %; controls, 57.14 %) ($p = 0.041$). The endoscopic findings that were found more often in NERD group but do not reach statistically significant difference were micro-erosions (29.17% vs. 4.76%) ($p = 0.051$), scar (ERD, 33.3%; NERD, 4.2%; controls, 0%) and hiatal hernia (ERD, 66.7%; NERD, 8.3%; controls, 0%) (Table 2).

The Trench sign had better diagnostic value than gyrus gastric pit pattern and erythema at EGJ since it had higher area under ROC curve (AUROC): 0.756 for Trench sign and 0.652 for gyrus gastric pit pattern and erythema at EGJ. The sensitivity and specificity of trench sign for diagnosis of 75% and 76.2% accordingly (Figure 4).

In patients who had typical reflux symptoms and had received 2 week of esomeprazole treatment, the symptoms scores assessed by RDQ and HRQLGERD

Table 1. Baseline characteristics.

	Reflux symptoms N = 27	Control N = 21	<i>p</i> -value
Age (mean ± SD)	48 ± 11	53 ± 12	0.23
Female (%)	22 (81.50%)	11 (52.40%)	0.07
BMI (mean ± SD)	22.63 ± 4.84	23.35 ± 2.83	0.55
Smoking (%)	3 (11.10%)	2 (9.50%)	1.00
Alcohol drinking (%)	1 (3.70%)	3 (14.30%)	0.31



Normal round

Tubular

Gyrus

Figure 1. Gastric pit patterns.

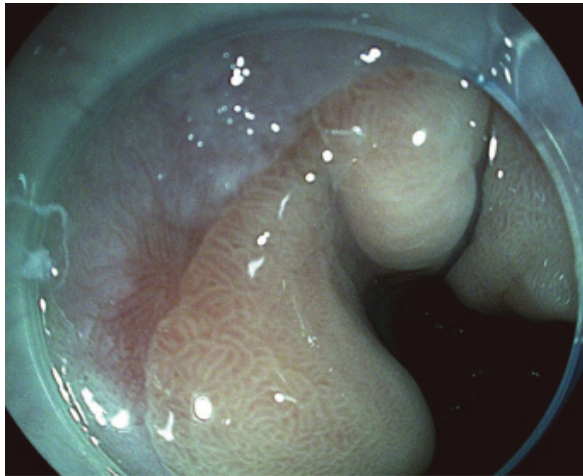


Figure 2. Hyperemia at EGJ.

were reduced significantly ($p < 0.001$). Mean RDQ frequency were reduced from 12.70 to 5.96, mean RDQ severity were reduced from 11.33 to 5.78, mean HRQLGERD score were reduced from 14.00 to 7.63. However, there was no difference in the mean difference among patients in ERD, NERD with minimal change (Trench sign) and NERD without minimal change groups (Table 3).

DISCUSSION

The minimal changes of distal esophagus in GERD patients had been shown to correlate with abnormal acid exposure⁽⁵⁾. This study demonstrated that

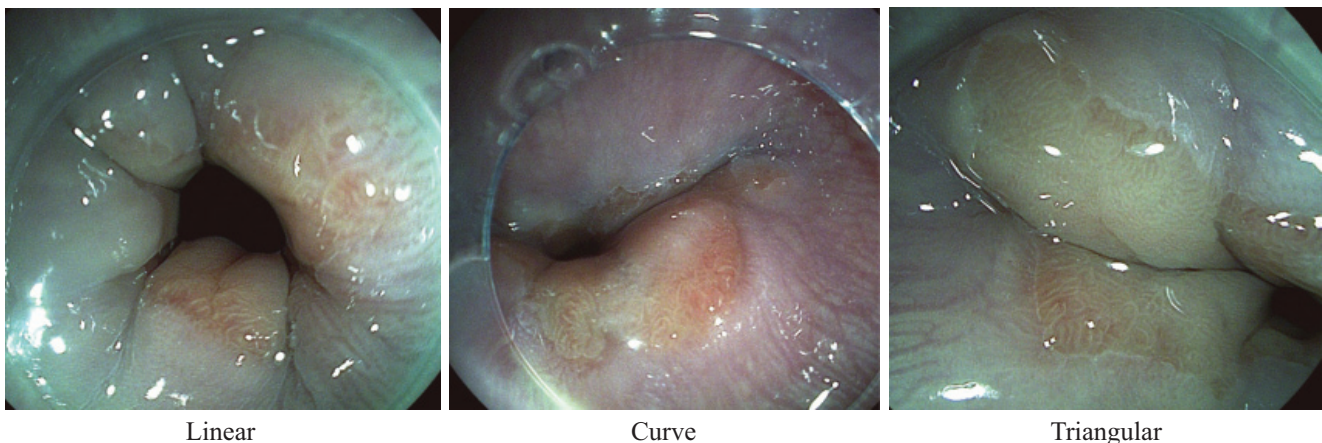


Figure 3. Trench with hyperemia.

Table 2. Endoscopically visible changes on I-scan.

	ERD N = 3	NERD N = 24	Control N = 21	p-value
Gastric pit pattern (%)				
N-pit	0 (0)	8 (33.3)	10 (47.6)	0.374
T-pit	3 (100)	21 (87.5)	20 (95.2)	0.611
G-pit	3 (100)	21 (87.5)	12 (57.1)	0.041
Triangular Indentation	0 (0)	8 (33.3)	11 (52.4)	0.237
Smooth Z line	2 (66.7)	6 (25)	3 (14.3)	0.469
Shaggy Z line	1 (33.3)	9 (37.5)	13 (61.9)	0.139
Tattered Z line	0 (0)	9 (37.5)	5 (23.8)	0.356
Islets of squamous mucosa	0 (0)	7 (29.2)	5 (23.8)	0.746
Islets of columnar mucosa	0 (0)	2 (8.3)	5 (23.8)	0.225
Trench sign	3 (100)	19 (79.2)	5 (23.8)	<0.001
Micro-erosion	1 (33.3)	7 (29.2)	1 (4.8)	0.051
Scar	1 (33.3)	1 (4.2)	0 (0)	1.000
Erythema	3 (100)	21 (87.5)	12 (57.1)	0.041
Hiatal hernia	2 (66.7)	2 (8.3)	0 (0)	0.491

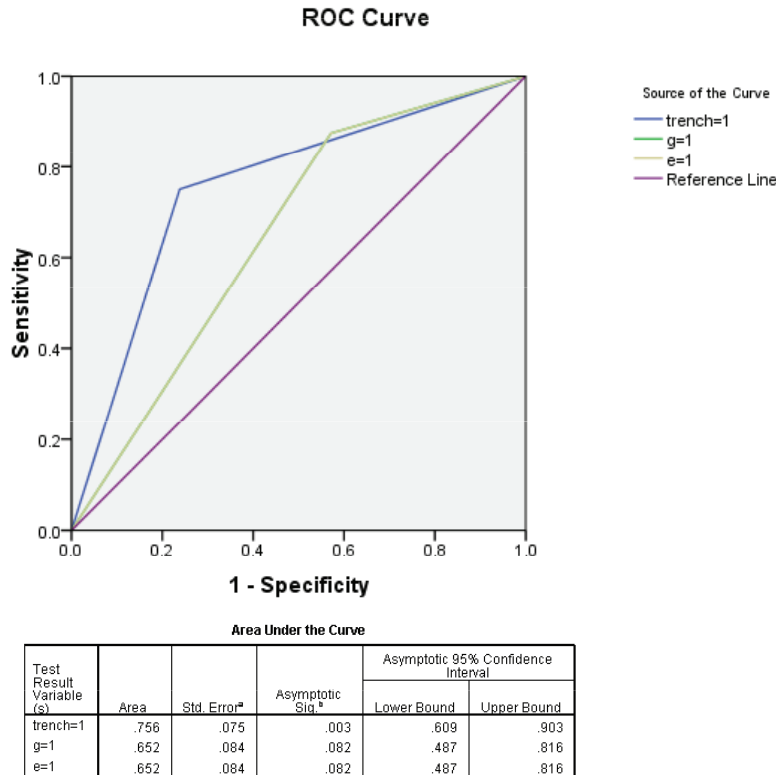


Figure 4. The sensitivity and specificity of Trench sign.

Table 3. Mean symptoms scores difference.

	Mean difference	p value
RDQ frequency difference		
ERD	10.33	0.53
Trench	15.08	
No trench	12.10	
RDQ severity difference		
ERD	14.50	0.82
Trench	14.45	
No trench	12.00	
HRQLGERD difference		
ERD	11.83	0.68
Trench	14.87	
No trench	12.00	

the endoscopic findings of mucosal injuries that associated with NERD were presence of “Trench” sign, gastric pit pattern and erythema at EGJ.

The presence of gastric pit pattern and erythema at EGJ had been reported as the findings in NERD patients in other studies⁽⁶⁻⁹⁾ but this was the first time that the trench sign was reported. In addition, in this study trench sign had a better diagnostic value than the other two.

The sensitivity and specificity of trench sign was moderately high (around 75%); however, the actual accuracy may be higher because patients with hyper-sensitive esophagus and functional heartburn may have symptoms without any signs of mucosal injury.

The frequency of these three findings was highest in ERD group and lowest in control group. This seemed to correlate with the spectrum of mucosal injuries from acid exposure among these groups.

In this study, patients with GERD symptoms respond to PPI very well and there was no significant difference of symptoms scores among patients with mucosal injuries (ERD and NERD with Trench sign) and patients without mucosal injury. The reason may be the small sample size in groups of ERD and NERD without Trench sign.

When compared with other minimal changes that were reported previously⁽⁶⁻⁹⁾, the presence of Trench sign was easy to use and had a reasonable accuracy. Accordingly, this finding may be more practical in clinical practice.

The limitation of this study were that the 24-hours pH monitoring study was not performed to correlate the degree of acid exposure with the endoscopic findings and the post-treatment endoscopy was not per-

formed to confirm resolution of the findings after symptoms disappeared.

In conclusion, our study demonstrated the new simple endoscopic finding that correlate with GERD symptoms. This finding is not only helpful for diagnosis of NERD but may also identify patients who had more acid exposure. However, there are still need for further validation and evidence of clinical significance.

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