The Clinical Significance of Endoscopic Findings of Minimal Change Esophagitis and its Diagnostic Value in Egyptian NERD Patients

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List of Contents

Title	Page

List of Contents (Cont.)

Title	Page

List of Tables

List of Figures

List of Figures (Cont.)

List of Abbreviations

Abbreviations	
GERD	Gastro esophageal reflux disease
ASGE	American society of gastroenterology
PPI	Proton pump inhibitor
NERD	Non erosive reflux disease
EMS	Esophageal manometric studies
HRAs	Histamine receptor antagonist
DRQol	Disease related quality of life
IEE	Image enhanced endoscopy
NBI	Narrow band imaging
HRME	High resolution magnification endoscopy
LES	Lower esophageal sphincter
D.B.IEE	Dye based image enhanced endoscopy
E.B.IEE	Equipment based image enhanced endoscopy
LA classification	Los Angles calassification
IPCL	Intra papillary capillary loop
SCJ	Squamo-columnar junction
FICE	Fujinon intelligent color enhancement mode
SEM	Surface enhancement mode
PM	Pattern mode
VM	Vascular mode
HDC	High definition chromoendoscopy
NCCP	Non cardiac chest pain
MII	Multi channel intral luminal impedence

INTRODUCTION

Gastroesophageal reflux disease (GERD) is defined as the reflux of gastric contents into the esophagus, leading to esophagitis, reflux symptoms sufficient to impair the quality of life, and increased risk of long-term complications ***(Barlow et al., 2005).***

This definition emphasizes that gastroesophageal reflux becomes a disease when it either causes macroscopic damage to the esophagus or affects the quality of life ***(Kim et al., 2011).***

GERD can be divided into erosive (ERD) and non erosive (NERD) reflux disease, and the presence or severity of erosive esophagitis at endoscopy has been defined using mucosal breaks based on the Los Angeles classification ***(Caviglia et al., 2007).***

Therefore, NERD has been regarded as reflux symptoms with the absence of mucosal breaks in the esophagus at endoscopy ***(Caviglia et al., 2005).*** However, in the Asian literature, NERD has been divided into normal and minimal changes based on endoscopic finding ***(Kim et al., 2011)***, which differs from the general concept of NERD as endoscopy-negative reflux disease. Although the endoscopic findings of minimal changes are not clearly defined, some studies have reported a high rate of minimal-change lesions in NERD patients ***(Kiesslicha et al., 2004).***

This implies the possible over estimation of minimal-change lesions in NERD patients, irrespective of their clinical significance. Therefore, this study will evaluate the clinical significance of minimal change esophagitis by investigating whether the endoscopic findings of minimal changes have diagnostic value for NERD in a prospective study.

AIM OF THE WORK

To evaluate the clinical significance of minimal change esophagitis at endoscopy and examine whether such changes have diagnostic value in non erosive reflux disease (NERD) or not.

CHAPTER I: INTRODUCTION TO GERD

GERD is a spectrum disease, i.e., a disease composed by many patient subgroups, ranging from symptomatic disease without mucosal lesions (NERD) to the complications of erosive esophagitis, such as esophageal stricture, ulceration or Barrett's esophagus ***(Pace and Porro, 2006).***

Montreal consensus defined GERD as "a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications." Symptoms are "troublesome" if they adversely affect an individual's wellbeing ***(Pace and Porro, 2006).***

A distinguishing feature of the Montreal definition is that it does not use the term "nonerosive reflux disease" but rather subdivides esophageal syndromes into symptomatic syndromes and syndromes with esophageal injury. Hence, functional heartburn does not fit the Montreal definition of GERD, whereas it is included under the umbrella of nonerosive reflux disease. The distinction between GERD and episodic heartburn in the Montreal definition is in the word "troublesome" ***(Pace and Porro, 2006).***

In the absence of esophageal injury, heartburn symptoms of insufficient frequency or severity to be perceived as troublesome by the patient (after assurance of their benign nature) do not meet the Montreal definition of symptomatic esophageal GERD syndrome ***(Marrer et al., 2008).***

As far as the epidemiological features are concerned, the prevalence of at least monthly GERD symptoms ranges between 26% to 44% whereas the prevalence of endoscopic esophagitis at open access endoscopy or in symptomatic patients seem to be very high, up to 20%, with an incidence rate in the general population about hundred time lower. The principal complication, e.g., Barrett's esophagus, has a prevalence of 15-20% of the GERD population, with a rate of adenocarcinoma development of about 0.5% per patient year of follow up. Mortality for uncomplicated GERD is negligible ***(Marrer et al., 2008).***

Different esophageal and extra-esophageal symptoms (even in the absence of detectable lesions), and macroscopic lesions such as erosive or ulcerative esophagitis or so-called atypical manifestations (laryngitis, pharyngitis, dental erosions, and many others). From this brief introduction is already clear that GER disease (GERD) is a broad disease, with a large clinical spectrum of signs and symptoms, interesting not only the esophageal area but many other regions of the body, including the mouth, lungs, ear, nose and throat, and which can be accompanied or not by esophageal lesions ***(Pace and Porro, 2006)***.

Almost all the transitions are possible amongst groups, even if the progression from one stage to the other has been described mainly based upon retrospective data.

The natural history of the disease is poorly investigated; available data would suggest that symptoms of GERD tend to persist and to worsen with time, independently from the presence and severity of mucosal lesions or the severity of esophageal acid exposure at presentation ***(Fass et al., 2009).***

It is therefore evident that the epidemiology of GERD is difficult to assess because this disease encompasses at least three broad groups of patients ***(Pace and Porro, 2006)***:

- Those with typical symptoms, such as heartburn and regurgitation but without reflux esophagits, so called non erosive reflux disease (NERD) patients.
- Patients with reflux esophagitis, and with or without complication, such as stricture, specialized intestinal metaplasia.
- Patients with atypical manifestations

Postulated theories of GERD mechanism:

The mechanisms by which patients with GERD develop symptoms remain incompletely understood. It is postulated that sensitization of esophageal chemoreceptors either directly by exposure to acid reflux or indirectly through release of inflammatory mediators is responsible for symptom generation in GERD ***(Fass et al., 2009).*** Also, morphological changes result in an increase in para cellular permeability, allowing acid to reach sensory nerve endings located within the intercellular spaces.

However, this altered permeability does not explain symptoms in GERD, specifically in NERD and in functional heartburn as most acid reflux events (95%) that occur in these patients are never perceived and symptoms occur even in the absence of acid reflux, suggesting the importance of other factors in modulating esophageal acid perception ***(Fass et al., 2009).***

Reducing acid exposure in patients with GERD appears to normalize the sensitivity to acid ***(Marrero et al., 2009)*** However, the emergence of symptoms in patients with a normal esophageal mucosa and thus without obvious inflammation remains perplexing, particularly among patients with functional heartburn where little or no reflux actually occurs.