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Abstract

ANATOMICAL, CLINICAL, PATHOLOGICAL AND ENDOSCOPIC CORRELATIONS IN EROSIVE ESOPHAGITIS, ESOPHAGEAL PRENEOPLASTIC LESSIONS AND ESOPHAGEAL ADENOCARCINOMA

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Introduction:

Gastroesophageal reflux disease (GERD) is a frequent disease with a prevalence of 10-20% in western countries and with an increasing incidence in the rest of the world. In addition to economic and medical resources involved in this chronic condition, it is accompanied by impaired quality of life and predispose the patients to develop Barrett's esophagus and esophageal adenocarcinoma. The choice of this topic was motivated by the increasing incidence of reflux pathology in our day to day work and, on the other hand, by the fact that the majority of epidemiological data are coming from economically well-developed countrys, where the prevalence of GERD and Barrett's esophagus is high whereas the prevalence of *H. pylori* infection in population is low.

The prevalence of erosive esophagitis and Barrett's esophagus is not known in central and eastern european countries, an area with high prevalence of H. pylori infection.

Many questions about the epidemiology and risk factors for erosive esophagitis or Barrett's esophagus remained unanswered. Therefore, this study aimed to determine the prevalence of erosive esophagitis, Barrett's esophagus and esophageal adenocarcinoma and stratification of risk factors involved in their development.

This PhD thesis comprises three studies: one retrospective and two prospective observational studies on series of consecutive patients who underwent upper gastrointestinal endoscopy (EDS) in the Laboratory of Digestive Endoscopy at Emergency County Hospital of Targu Mureș.

Study 1: Epidemiological aspects of the preneoplastic and neoplastic lesions of the esophagus

In the first study we aimed preneoplastic and neoplastic esophageal lesions epidemiology with emphasis on esophageal adenocarcinoma. We conducted a retrospective study in patients with endoscopically and histologically confirmed diagnosis of esophageal cancer or Barrett's esophagus from January 1, 2006 December 31, 2010.

Results: The data of our study showed an increased incidence of both esophageal adenocarcinoma and Barrett esophagus. in the studied period of time, but epidermoid carcinoma remains the prevalent histology in our area. Epidermoid carcinoma/adenocarcinoma ratio decreased from 3.33/1 in 2006 to 1.33/1 in 2010. Regarding gender distribution, we observed a high predominance of males with a male/female ratio of 7.45/1. The median age at diagnosis in esophageal cancer was 61.69 ± .9.57 years, and was higher for esophageal adenocarcinoma, 65.75 ± 9.60 years. Young age (<50 years) was statistically significantly correlated with the development of epidermoid carcinoma ($p < 0.05$), while advanced ages (> 70 years) were significantly associated with the development of esophageal adenocarcinoma. (Odds Ratio: 3.714, 95% CI: 1.328 to

10.387). Lessions in the lower third of the esophagus was statistically significantly associated with esophageal adenocarcinoma ($p < 0.0001$) (Odds Ratio: 33.44, 95% CI: 7.241 to 154.51). Barrett's esophagus also shows an increasing incidence, the application of new diagnostic methods (chromoendoscopy with methylene blue) raising its rate of histological confirmation.

Conclusions: Esophageal adenocarcinoma incidence has increased, but the most common histological form in our area remains epidermoid carcinoma.

Study 2: Correlations between infection with H. pylori, hiatal hernia and Barrett's esophagus

The purpose of the second study was to determine the correlation between the presence of Helicobacter pylori infection and gastric histopathological changes induced by infection and E. Barrett development in an area with a high incidence of H. pylori infection and correlation with other risk factors involved in its development. We conducted a prospective observational study on a series of consecutive patients who underwent upper gastrointestinal endoscopy between 01.01.2008-31.12.2010. We included newly diagnosed patients with Barrett's esophagus, histologically confirmed.

Our data showed a low prevalence of E. Barrett with histologically confirmation, 6.9 patients/1000 persons examined, the most commonly encountered beeing short Barrett's esophagus. The presence of hiatal hernia was significantly correlated with Barrett's esophagus in the study, while H. pylori infection was less common among patients with Barrett's esophagus compared with the control group, without being able to demonstrate a protective effect of this infections.

Study 3: Clinical and endoscopic correlations in erosive esophagitis

The third study aimed to determine the prevalence of erosive esophagitis and stratification of risk factors involved in their development.

Methods: We performed a prospective observational study between 01.01.2010-31.12.2010 which included newly diagnosed patients with erosive esophagitis. Classification of oesophagitis lesions was classified in 4 degrees, according to Los Angeles classification in A, B, C, D. Patients were stratified into two groups: mild esophagitis (grade A and B) or severe esophagitis (grade C and D).

Results: Our data showed that erosive esophagitis is a frequent disease (357 patients), the most common forms of esophagitis beeing grade A and B: 240 (67.22%), patients with esophagitis grade A (LA) 58 (16.24%), patients with grade B esophagitis (LA) 31 (8.68%), patients with grade C esophagitis and 28 (7.84%) patients with esophagitis grade D.

Of the risk factors involved in the development of esophagitis, association of hiatal hernia to severe esophagitis was highly statistically significant $p = 0.0005$ (Odds Ratio: 2.874: 95% CI: 1.589 to 5.198). Also analyzing the correlation between the size of the hernia and esophagitis severity, large hiatal hernias association with severe esophagitis was highly statistically significant $p < 0.0001$ (Odds Ratio: 4.794: 95% CI: 2.406 to 9.551). H. pylori infection was present in similar proportions in patients with mild esophagitis: 30.20% (90 patients), respectively 30.50% (18 patients) in the group with severe esophagitis, with no statistical difference between the two groups.

Studying the correlation between increased BMI (over 25) and severe reflux esophagitis development we achieved a statistically significant association $p < 0.05$ (Odds

Ratio: 1.783: 95% CI: 1.016 to 3.128). Studying the presence of concomitant diseases in patients with esophagitis, the most common association was with cardiovascular disease.

Conclusions: Erosive esophagitis is a frequent disease, the most common forms beeing grade A and B. Male sex and hiatal hernia are risk factors for the development of erosive esophagitis, particularly severe forms.

Keywords: esophageal adenocarcinoma, Barrett's esophagus, H. pylori, erosive esophagitis