

Correlation of endoscopic and histological findings in diagnosis of gastrointestinal metaplasia in patients referred to the Clinica Colombia for upper endoscopies

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Abstract

Introduction: Intestinal metaplasia is one step towards the final process known as gastric cancer. Correct identification through a biopsy taken endoscopically is vital for histological confirmation. In our surroundings the relationship between endoscopic findings when intestinal metaplasia is suspected and histological confirmation are not understood. This study aims to determine the true correlation between endoscopic findings suggestive of metaplasia and their histological counterparts. **Methods:** This was an observational and analytical study undertaken at the Clínica Colombia. Patients who were suspected of having intestinal metaplasia following endoscopic examinations were included. Patients with prior histories of metaplasia and gastric cancer were excluded. Statistical evaluation was performed using STATA 11. **Results:** A total of 766 patients suspected of having intestinal metaplasias following endoscopic examination were included. 543 (70%) were confirmed histologically. Patients who most frequently had no correlation between suspicion following endoscopy and histological findings included those with chronic gastritis, foveolar hyperplasia, and reactive gastropathy. The positive predictive value of endoscopic findings was close to 71%. **Conclusions:** Although the correlation was close to 70%, prospective and multicenter studies, as well as studies using chromoendoscopy, are needed in order to evaluate agreement between the two methods, to determine predictive endoscopic variables for severity and for types of metaplasia, and to determine protocols for monitoring these patients.

Keywords

Metaplasia, endoscopy, correlation.

INTRODUCTION

Understanding gastric intestinal metaplasia is of vital importance for understanding gastric carcinogenesis. Over time and through Dr Pelayo Correa's work, where pre-malignant lesions, including intestinal metaplasia, are located in the pathophysiological sequence of the development of gastric cancer has been determined (1). Studies of associations, including at molecular level, have determined that intestinal metaplasia seems to emerge as a secondary adaptive response to morphological changes, and to selection pressures in the presence of *Helicobacter pylori* infection. Smoking and high salt diets also play important roles (2).

Technological advances in digestive endoscopy have allowed high degrees of correlation to be determined between some pathology observed at the endoscopic level and their histological counterparts. Histopathological study of biopsies has been considered to be the gold standard and have been the key tool for the study of anatomopathological changes that occur in gastric cancer patients and in patients with precursor lesions and/or lesions associated with them (3). As has been demonstrated over time, it is of vital importance that the diagnosis and classification of intestinal metaplasia are useful for endoscopic monitoring of patients whose have been diagnosed (4). The endoscopic and histological correlations of metaplasia have not been

fully studied, though there are studies that have attempted to determine the sensitivity and specificity of endoscopy for classification and study of different types of gastritis. The results of these studies have varied (5).

In recent times, there has been controversy regarding whether gastric cancer develops from areas of intestinal metaplasia or whether intestinal metaplasia simply represents a high risk marker for gastric cancer. Several studies have estimated that the relative risk of gastric cancer in patients with intestinal metaplasia types II and III can be 20 times higher, which means that early detection of these lesions and their proper monitoring could reduce mortality associated with this disease in our environment (6).

The following study seeks to identify the degree of correlation between endoscopic findings suggestive of intestinal metaplasia, as determined by the presence of shiny white, mother-of-pearl hue plaques in the endoscopy, and biopsies which are the gold standard for diagnosis of metaplasia. It is hoped that the results will allow us order to improve endoscopic diagnosis and develop protocols for endoscopic monitoring of these patients.

MATERIALS AND METHODS

This observational and analytical study studied all patients suspected of having intestinal endoscopic metaplasia. Since data collection was retrospective, the criteria for suspicion of intestinal metaplasia in the gastric mucosa were determined according to the discretion of the endoscopist who did the examination. There was no established protocol for biopsy samples. However, in general they showed shiny white, mother-of-pearl colored plaques and/or a discoloration of the gastric mucosa. After applying inclusion and exclusion criteria to patients in the database of the department of gastroenterology at the Colombia University Hospital from June 2008 to December 2010, we found a total of 766 patients with endoscopically suspected intestinal gastric metaplasia. All patients who had had upper digestive endoscopy during this period of time, and who were suspected of having intestinal metaplasia by the endoscopist, were included. Patients with a previous diagnosis of intestinal metaplasia, patients with a history of gastric cancer, and patients with a previous gastrectomy were excluded. After identifying endoscopy results with suspected metaplasia, the pathology reports for those patients were found. We determined that the procedure was similar for all biopsies and that they had been preserved in formaldehyde and that slides had been stained with hematoxylin - eosin. Biopsies were read by pathologists at the Clínica Universitaria Colombia. This information was used to determine the correlation of endoscopic findings of suspected intestinal metaplasia with histology results.

Statistical analyses of patients' ages, genders, endoscopic indications, presence or absence of *Helicobacter pylori*, and other factors were performed using descriptive statistics software (STATA 11).

The study was approved by the ethics committee of the Clínica Universitaria Colombia. In accordance with Article 11 of Resolution 8430 of 1993 which defines this type of study as risk free, informed consent forms were not required. This study was also in accordance with recommendations for biomedical research of the Helsinki declaration of the World Medical Association.

RESULTS

After applying inclusion and exclusion criteria a total of 766 patients were identified with endoscopically suspected intestinal metaplasia.

Social and demographic characteristics

The gender distribution was 510 female patients (66.5%) and 256 male patients (33.4%). Table 1 describes demographic characteristics of the study population.

Table 1. Demographic characteristics of the study population (patients who had undergone digestive endoscopies which resulted in suspicion of intestinal metaplasia).

Variable	Presence of metaplasia diagnosed	Metaplasia absent according to diagnosis
Gender		
1. Female N (%)	350 (45%)	159 (20.7%)
2. Male N (%)	193 (25.1%)	64 (8.2%)
Age (years)		
1. <35	9 (0.001%)	15 (1.95%)
2. 36-49	67 (8.7%)	30 (3.9%)
3. 50-69	273 (35.6%)	125 (16.3%)
4. >70	194 (25.3%)	53 (7.3%)
H pylori infection		
1. Positive	188 (35.2%)	83 (10.7%)
2. Negative	355(64.7%)	140 (18.2%)

The four age groups in which there were the highest percentage of patients were combined to form the age group between 50 to 69 years (corresponding to 52% of patients. (Table 1).

Symptoms or clinical indications indicating the need for endoscopic study were as follows: dyspepsia (30%), gastritis (22.5%), gastroesophageal reflux (12%) and abdominal pain (12%). Other indications such as anemia, dysphagia and family histories of gastric cancer accounted for smaller percentages (Figure 1)

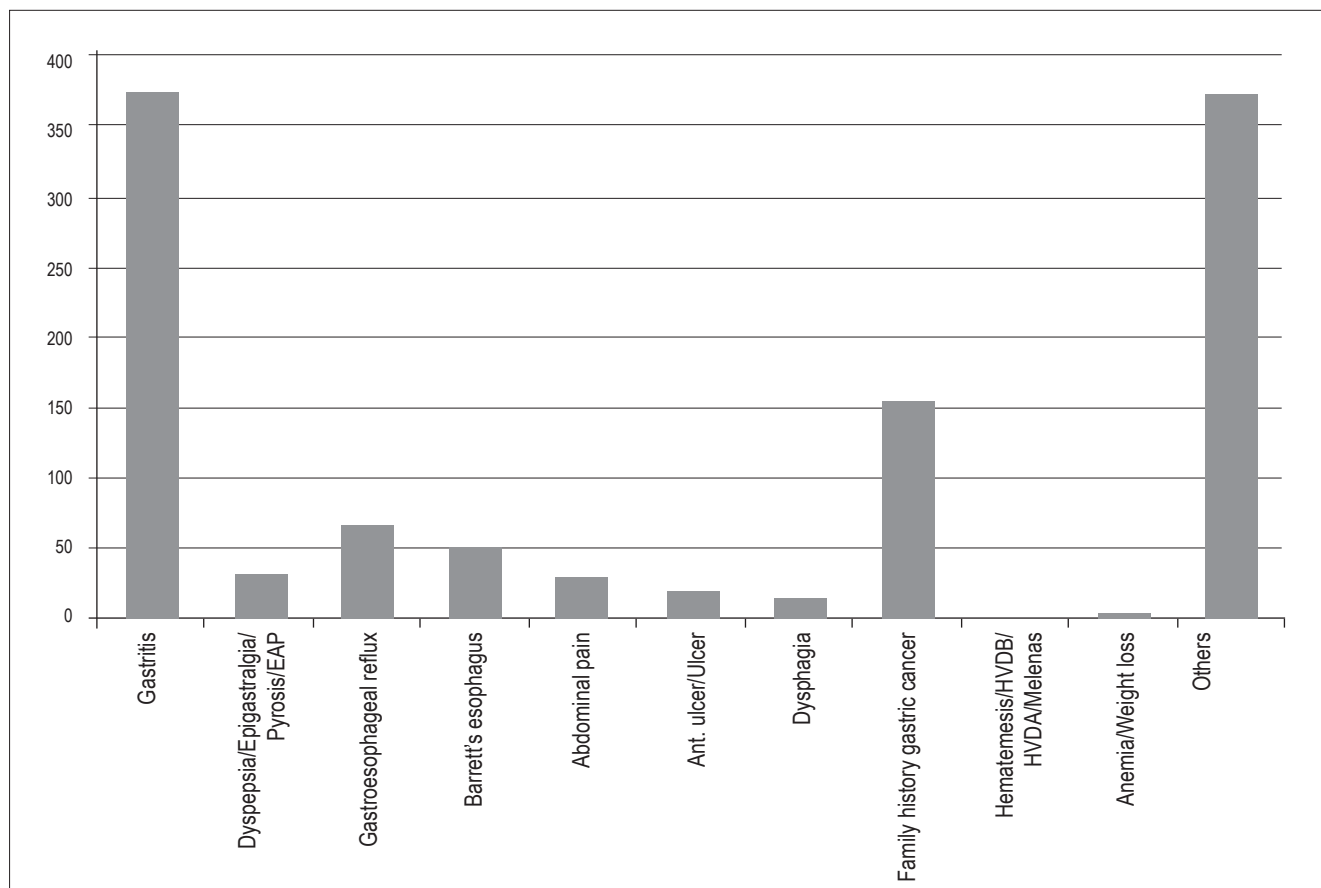


Figure 1. Indication for upper digestive endoscopy.

Helicobacter pylori infections were identified in 270 patients (35% of the sample) but were absent in 496 patients (64% of the total patient sample of the study). Our data did not include information about whether patients had received eradication treatment prior to endoscopy. Among patients whose endoscopic and histopathological diagnoses were positively correlated for intestinal metaplasia, the bacteria were identified in 188 of the 543 patients (34%). 355 patients (66%) whose endoscopic and histopathological diagnoses were positively correlated for intestinal metaplasia tested negative for the presence of the bacteria (Figure 2).

A total of 543 patients (70%) whose endoscopic evaluations led to suspicion of intestinal metaplasia had these diagnoses confirmed by histological studies for a concordance of about 70% in the sample studied (Figure 3).

Histological reports broke down diagnoses of intestinal metaplasia into the following subcategories: unspecified metaplasia (49%), incomplete metaplasia (8%), complete metaplasia 4%, mixed metaplasia 6.1%, and presence of metaplasia with any type of dysplasia 3.8% (Figure 4).

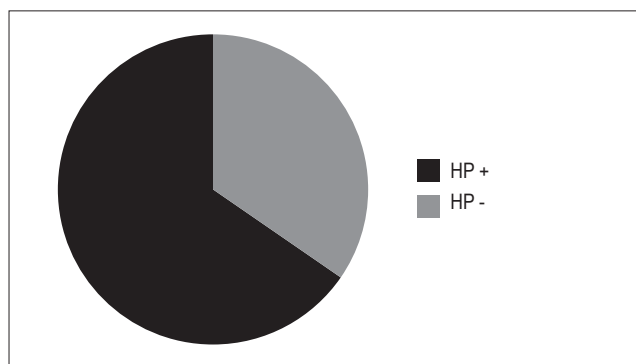


Figure 2. Presence and absence of *Helicobacter Pylori* in patients with histologically confirmed intestinal metaplasia in the study population.

The histologic diagnoses found most frequently in the subgroup of patients among whom no histological diagnosis of metaplasia was considered included: chronic gastritis (20%), foveolar hyperplasia 2.6%, and reactive gastropathy 1.8%.

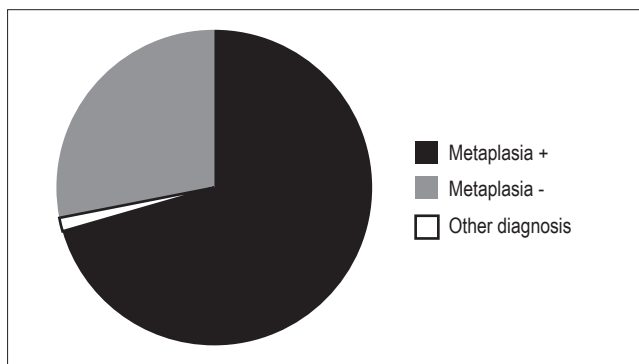


Figure 3. Endoscopic correlation with histological diagnosis of intestinal metaplasia.

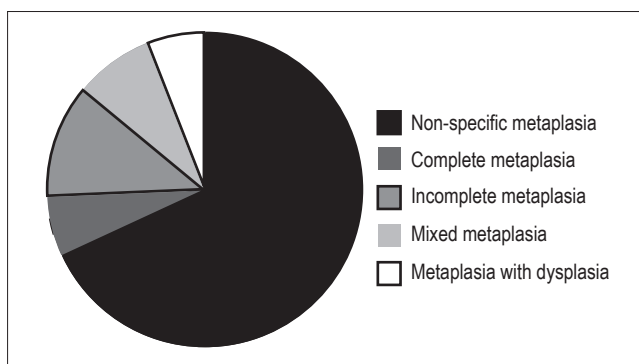


Figure 4. Histopathologic report of the metaplasia type according to pathology.

DISCUSSION

The adaptive process that leads to a histological diagnosis of intestinal metaplasia is broad and complex. With heightened knowledge that this pathological entity is part of the final process that can lead to the appearance of gastric cancer, it has been suggested this entity is pre-malignant and therefore requires strict endoscopic and histological surveillance (7).

Although the risk of gastric cancer varies depending on many risk factors including race, diet and H pylori infection, this risk may not increase at all, or may increase only minimally, in the presence of pre-malignant lesions such as intestinal metaplasia. However, the risk changes dramatically when the histological status changes to dysplasia (8).

In our environment it is important to have studies about intestinal metaplasia in order to develop better protocols for diagnosis and for proper monitoring. Such protocols have not been fully established internationally, although they are trying to develop them in order to prevent the appearance of gastric cancer on an early stage (9).

This study aimed to identify the degree of correlation between endoscopic and histological diagnoses for detec-

ting and confirming intestinal metaplasia in patients under upper digestive endoscopy.

Of the 766 patients evaluated who had been suspected of having intestinal metaplasia following endoscopies approximately 543 were confirmed by biopsy. The positive predictive value (PPV) for correct identification of metaplasia for endoscopy was 70%. Unfortunately, for adequate assessment of the correct concordance between the two studies we should also evaluate patients with confirmed histological intestinal metaplasia and the counterpart endoscopic diagnoses to allow us to establish VPN, sensitivity and specificity of endoscopy for this entity.

The use of chromoendoscopy for endoscopic diagnosis has improved the detection of suspicious malignant lesions. Better characterization of these lesions generates correct decisions and indicates the suspicious areas from which biopsies should be taken (10).

Our study was based on biopsies taken at the moment the endoscopist became suspicious of probable presence of intestinal metaplasia. Usually endoscopic descriptions were based on the presence of shiny white, mother-of-pearl colored plaques, changes in color, and nonspecific mucosal irregularity. Nevertheless, these factors were always evaluated according to the criteria of the person who did the endoscopy without any prior protocol defining symptoms. Biopsies were always taken from lesions rather than taking them randomly from the gastric mucosa. Similarly, conventional upper digestive endoscopy was used without special stains or magnification. If these techniques are used, better results for endoscopic and histological correlation might be obtained in future studies.

While it is true that the production of mucins and their coloration at the histopathological level helps classification of the type of metaplasia (11), its use is not routinely performed by pathologists. In our study, detection was performed by normal hematoxylin - eosin staining.

It is noteworthy that when we histologically identified the presence of intestinal metaplasia in about 50% of patients, the pathologist did not report the type of intestinal metaplasia. This shows that there is still no specific consensus for determining whether it is necessary for pathologist to report the type of intestinal metaplasia. Though many pathologists believe the final report confirming intestinal metaplasia should include the type of it (complete, incomplete or mixed), others do not. Since this issue is still controversial, until there is a final protocol, monitoring of patients at risk for gastric cancer and with incomplete type metaplasia should be more stringent (12).

Although the important role played by the Helicobacter Pylori in changes of the gastric mucosa and the bacteria's frequent association with pathological conditions such as chronic gastritis and intestinal metaplasia are already well

known in the literature (13), our study found a significant number of patients with confirmed intestinal metaplasia without the presence of *Helicobacter Pylori*. About 35% of patients with suspected intestinal endoscopic metaplasia and histologic confirmation of intestinal metaplasia were negative for the presence of the bacteria.

We could generate several hypotheses regarding these findings. The first is that nearly 232 patients (30%) were grouped in the dyspepsia group following endoscopic diagnoses. We do not know whether or not these patients had received prior treatment for *Helicobacter pylori*. Such prior treatment could have led to the absence of the bacteria in the pathology samples. Similarly, many studies that have attempted to validate the use of only a few biopsies, and which have attempted to indicate from which areas biopsies should be taken for correct identification of metaplasia, have had biases and are not entirely uniform in their conclusions. Some use biopsy of suspected lesions while others use the Sydney protocol. There are even studies that conclude two antral biopsies and one biopsy from the sulcus angularis should be taken for proper detection of intestinal metaplasia in up to 90% of the cases (14-15).

The other thing that could explain the significant number of patients with confirmed intestinal metaplasia without the presence of *Helicobacter Pylori* is the possibility of bacterial migration patterns that were not detected by routine biopsy, but which generate changes in the mucosa associated with subsequent development of pre-neoplastic lesions and subsequent development of cancer.

CONCLUSIONS

This study found a correlation between endoscopically generated suspicion of intestinal metaplasia and histological diagnosis of intestinal metaplasia of about 70% among patients who had undergone upper endoscopy, regardless of the initial indication.

Although there are several biases, such as the lack of data for estimating the correlation (biopsy - endoscopy) in intestinal metaplasia, there are necessary semiotic protocols for suspicious areas and determinant protocols for biopsies which can provide information regarding sensitivity, specificity and negative predictive value of endoscopy for intestinal metaplasia. The study shows a positive predictive value of about 70% for the correct identification of metaplasia in gastric samples using routine endoscopy without coloration or magnification.

We believe that this study provides the basis for the development of a prospective study with appropriate protocols for taking biopsies, using chromoendoscopy and/or magnification, and for pathology studies with defined criteria prior to sample evaluation with intraobserver and

interobserver measurement variability. Such a study could include monitoring to define prevalence, operational characteristics, and if necessary concordance rates. For our country, this would create a big impact. To follow up on the findings of this study, it is necessary to conduct prospective, multicenter studies with established defined protocols for proper appreciation of the role of endoscopy in identifying patients with suspected intestinal metaplasia. This should be done so that in the future we will be able to determine how to endoscopically monitor this type of patient.

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