

Gastric Intestinal Metaplasia and Helicobacter Pylori Testing

Abstract

Gastric intestinal metaplasia (GIM) is a frequent precancerous lesion and is detected in nearly 1 of every 4 patients undergoing upper endoscopy. Helicobacter pylori (*H. pylori*) is believed to be the cause of majority of intestinal-type gastric adenocarcinoma by causing chronic active gastritis, which may evolve to atrophic gastritis, GIM, dysplasia, and cancer. Whether *H. Pylori* eradication leads to reversal of GIM remains controversial, but several studies suggest some benefit. Since *H. pylori* exhibits tissue tropism, we believe that the progression to atrophic gastritis and intestinal metaplasia drives Helicobacter pylori out of the gastric mucosa. We hypothesized that gastric biopsy alone for the detection of *H. pylori* infection may be less accurate in the context of GIM, especially if biopsies fail to sample non-metaplastic tissue. Hence, another method of *H. Pylori* testing like urease breath test (UBT) or serology must be performed to evaluate for *H. Pylori*. A retrospective chart review was conducted using Electronic Medical Records (EMR) at Dayton Veteran's Affairs Medical Center. Our study showed that pathologic testing for *H. Pylori* was completed in almost all cases of GIM and only a small proportion of patients had *H. Pylori* identified from their biopsy. This is in accordance with our hypothesis that gastric biopsy has lower accuracy in the presence of IM because of inability of *H. Pylori* to grow on metaplastic tissue. *H. Pylori* eradication could reduce the risk of further development of dysplasia and subsequent gastric malignancy. Therefore, we recommend that patients with GIM should undergo additional diagnostic tests if the initial biopsy is negative for *H. Pylori*.

Keywords: Gastric; Intestinal; Metaplasia; Helicobacter pylori; Testing; Atrophic; Precancerous; Diagnosed; Eradicated

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Abbreviations: GIM: Gastric Intestinal Metaplasia; UBT: Urease Breath Test; IRB: Institutional Review Board; EMR: Electronic Medical Records; IM: Intestinal Metaplasia

Introduction

Gastric intestinal metaplasia (GIM) is a relatively frequent precancerous lesion with a six to eleven fold increase in gastric cancer risk [1-4]. GIM is thought to be in the cascade of gastric carcinogenesis coming after multifocal atrophic gastritis but before dysplasia [1,5-7]. The prevalence of GIM depends upon geographical location and is higher in countries with high prevalence of *H. pylori* infection [3]. In the United States the overall rate of abnormal stomach mucosa increases with age, 4.9% biopsies showing GIM in a large multi-center retrospective study [8]. It is believed that the progression to atrophic gastritis and intestinal metaplasia drives *H. pylori* out of the gastric mucosa since the epithelium is no longer a suitable environment for *H. pylori* [9]. Complete intestinal metaplasia does not allow *H. Pylori* adherence [10]. Previous studies of GIM positive biopsies have shown low rates of *H. Pylori* infection [11]. It is thought that *H. Pylori* may be detected in other non-metaplastic areas of the gastric mucosa in the presence GIM if biopsies are taken from that area.

Recommendations have been previously made to determine *H. Pylori* infection status by tissue-based tests and serology [12]. Urease breath testing (UBT) or serologic testing has also been recommended as a way to diagnose *H. Pylori* infection in patients with GIM whose histological staining for *H. Pylori* is negative [13]. Furthermore, infected patients should be treated to eradicate *H. Pylori* [12,14]. Eradication is thought to lessen the occurrence of gastric cancer by preventing progression of precancerous lesions [15,16]. However, gastric cancer has been documented after eradication of *H. Pylori* [17] and some authors believe that once GIM is found there is no need to test for *H. pylori* [18]. Reversibility of GIM is controversial, but some trials suggest a benefit [19-24].

The Maastricht IV consensus report says there is no evidence that *H. pylori* eradication can lead to regression of intestinal metaplasia, leaving one to conclude that there would be no benefit to testing for *H. pylori* in patients with GIM [25]. However the report goes on to say, "the exact point of no return has not been identified" and gives a grade A recommendation to eradicate *H. Pylori* for the prevention of gastric cancer in patients with severe atrophy [25]. Meta-analyses in 2011 and 2014 suggest that *H. Pylori* eradication correlates with improvement in GIM [26,27] while a 2007 meta-analysis showed reversibility of atrophic gastritis, but not GIM [28]. These recent meta-analyses led one author to say "further prospective studies are needed to determine

the optimal strategy about *H. pylori* eradication to prevent gastric cancer" [29]. Based on the hypothesis that some patients with GIM may benefit by having *H. Pylori* infection diagnosed and then eradicated, we designed the retrospective chart review study to see what had been done in these cases at our institution over the last 10 years.

Methods

This retrospective chart review was conducted using Electronic medical records (EMR) at Dayton VA Medical Center (DVAMC). After Institutional review board (IRB) approval, a list of patients with a histological diagnosis of GIM for the last 10 years was obtained from the pathology department. Each case was reviewed individually and biopsies that were clearly labeled as "gastric" were included in this study. Any biopsies labeled "gastroesophageal junction" or "esophageal" were excluded from this study.

The EMR of each patient with biopsy proven GIM was reviewed individually. Demographic data, endoscopy reports, biopsy reports and laboratory data was reviewed and documented.

Results

A total of 54 patients were identified with histological diagnosis of gastric intestinal metaplasia (GIM). The median age was 68 years, 51 (94.4%) were male, 45 (83.3%) were caucasian, 43 (79.6%) were present or former smokers. Documentation of testing for *H. Pylori* was found for all (100%) patients with 12/54 (22.2%) testing positive in pathology specimen. Of the remaining 42 patients with histological absence of *H. Pylori*, serologic testing was done in 8/42 (19%): 4/8 (50%) tested positive, 2/8 (25%) tested negative and 2/8 (25%) were equivocal. No other diagnostic method is available in this hospital for *H. Pylori*. There were 34/42 (81%) patients with GIM and *H. pylori* negative biopsies who did not have serological testing done, but 2 of them had anti-*H. Pylori* treatment given empirically and 2 had protocol biopsies done 2 years later. Both the patients who had equivocal results on serological testing had protocol biopsies done 1-2 years later. Only 14/54 (25.9%) patients were treated for *H. Pylori* eradication after the diagnosis of GIM.

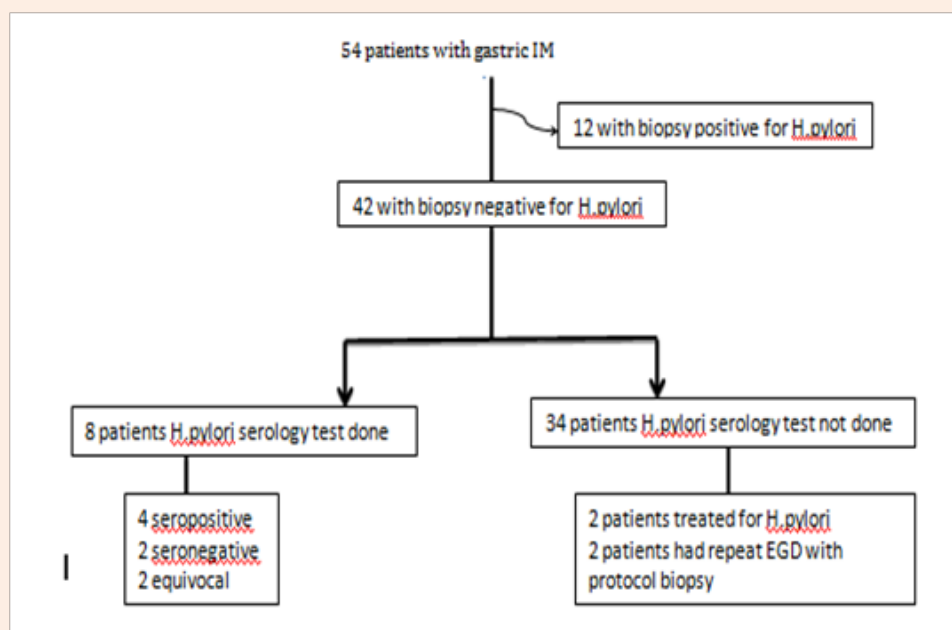


Figure 1: Flow diagram of patients included in the study.

IM: Intestinal Metaplasia

Discussion

Gastric intestinal metaplasia can be a precursor to gastric cancer caused by *H. Pylori* infection. Histology is considered to be the "gold standard" test for *H. pylori* [30]. However, if the metaplastic tissue is no longer a suitable host for *H. Pylori* and it migrates to a more histological normal gastric tissue, then we

may miss diagnosing some cases of *H. Pylori* infection in patients with GIM. There is a difference in opinion among experts about whether *H. pylori* eradication is beneficial in patients with GIM. If *H. Pylori* is eradicated and further pre-malignant cellular changes are prevented we believe that we should test for and eradicate *H. Pylori* in patients with GIM. Which test is best to look for *H. Pylori*

infection in the setting of GIM and negative histology is a question that remains to be answered. In our institution *H. Pylori* serology is the only other available test. Lower diagnostic accuracy of *H. pylori* with histologic examination has been described in the setting of GIM [12]. Urea breath testing (UBT) in the setting of GIM and *H. Pylori* negative biopsies has been studied retrospectively. UBT has decreased sensitivity if the patient is on proton pump inhibitor; therefore stool antigen test or serology should be considered as alternatives [12, 13]. Arguments have been made advocating for UBT as the most sensitive and specific test for *H. Pylori* [31]. We are not advocating the use of serology over UBT, just that further testing should be done in patients with IM and *H. Pylori* negative biopsies.

Our study shows that pathologic testing for *H. Pylori* was completed in almost all cases of GIM and only a small proportion (22.2%) of patients had *H. Pylori* identified from their biopsy. This is in accordance with our hypothesis that gastric biopsy has lower accuracy in the presence of GIM because of the inability of *H. pylori* to grow on intestinal metaplastic tissue. While only 8 out of 42 patients with negative biopsies had serological testing performed, 4 out of those 8 (50%) had positive serology. It is unclear if this represents the whole population of our patients with biopsy proven GIM and negative *H. Pylori* histologic staining. Larger studies from multiple centers are warranted. If we identified more patients with continued active infection, *H. Pylori* eradication could reduce the risk of further development of dysplasia and subsequent gastric malignancy. Currently there is no evidence to support that GIM is reversible, but it is reasonable to suggest that if active *H. Pylori* infection can be identified and treated, further cellular changes could be limited. Therefore, we recommend that patients with gastric intestinal metaplasia should undergo additional diagnostic tests for *H. Pylori* if the biopsy is negative.

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