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# Serological Markers for Gastric Atrophy in Asymptomatic Patients Infected with *Helicobacter pylori*

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**OBJECTIVE:** Atrophic gastritis is a precancerous condition that is commonly caused by chronic *Helicobacter pylori* (*H. pylori*) infection. This blinded, controlled study was designed to determine if serum gastrin and pepsinogens were reliable markers of atrophy in asymptomatic patients.

**METHODS:** One hundred and forty-seven asymptomatic patients underwent endoscopy with multiple gastric biopsies obtained for histology, culture, and rapid urease test. Fasting serum gastrin (total and G-17) and serum pepsinogens (I-II) were determined by standard immunoassays. Gastric atrophy was histologically assessed in accordance with internationally accepted criteria; three main patterns of gastritis were distinguished: (a) nonatrophic gastritis, (b) atrophic antrum-restricted and antrum-predominant gastritis, and (c) corpus-restricted gastritis. Receiving operating characteristic (ROC) analysis was used to determine the best cut-off for each serum test in nonatrophic gastritis *versus* antrum-restricted/antrum-predominant atrophic gastritis.

**RESULTS:** No significant differences in serum gastrin and pepsinogens I-II were detected in nonatrophic gastritis *versus* patients with antrum-restricted/antrum-predominant atrophic gastritis. The positive likelihood ratios for an abnormal serum test to detect antrum-restricted/antrum-predominant atrophy in the gastric body were total serum gastrin 2.13 (95% CI 0.99, 4.6), gastrin-17: 1.55 (95% CI 0.75, 36.17), pepsinogen I: 2.74 (1.4, 5.4), pepsinogen II: 1.74 (1.27, 2.39), and the ratio of pepsinogen I and II: 1.8 (1.2–2.8). Negative likelihood ratios ranged from 0.20 to 0.65.

**CONCLUSION:** In an asymptomatic population, serum gastrin (total and G-17) and pepsinogens I-II (and their ratio) do not discriminate nonatrophic *versus* antrum-restricted/predominant atrophic gastritis.

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## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a human pathogen causing nonatrophic gastritis, gastric atrophy (with and without intestinal metaplasia), and gastric adenocarcinoma and has been recognized as Class I carcinogen (1). Only a minority of patients infected with *H. pylori* develop gastric atrophy, which is recognized as a precursor lesion for gastric cancer (2). At present, gastric atrophy or intestinal metaplasia (another precancerous condition) cannot be identified without endoscopy and biopsy. Screening populations using endoscopy is impractical and expensive. Serologic markers for atrophy are therefore of interest but no ideal marker currently exists. Different serum markers for gastric atrophy have been proposed, including total gastrin, the circulating component of serum gastrin (G-17), pepsinogen I, pepsinogen II, and their ratio (3). It is known that gastrin circulates in at least four bioactive forms: component I, gastrin-34, gastrin-17, and gastrin-14. More than 90% of circulating gastrin consists of gastrin-34 and gastrin-17 (3 ). Hypergastrinemia related to *H. pylori* infection has been shown to be due to a selective increase in gastrin-17 (3). Total serum gastrin does not change with *H. pylori* eradication but serum values of gastrin-17 decline significantly after eradication therapy (3). Pepsinogen I is secreted only by the chief cells of corpus and its serum values decline with increasing grades of atrophy of the gastric body due to loss of oxyntic glands (4). Pepsinogen II is secreted by antral glands, corpus chief cells, and the duodenal bulb in large quantities, and therefore, pepsinogen II is not a direct measure of corpus atrophy (5).

Serum markers for gastric atrophy have frequently been studied in dyspeptic patients presenting for endoscopy but there are few data on the use of these tests in the general population. The pretest probability of atrophy may be higher

in symptomatic patients presenting for endoscopy than in the general population in whom a screening strategy using serum markers would ideally be implemented.

The aim of our study was to determine the accuracy of serum gastrin, serum gastrin-17, pepsinogen I, pepsinogen, and their ratio, in determining if gastric atrophy or intestinal metaplasia were present in an asymptomatic population.

## METHODS

### *Patients*

We studied 147 asymptomatic volunteers who participated in a long-term study of *H. pylori* eradication, which has recently been published (6). There were 74 asymptomatic, *H. pylori*-positive patients and 73 asymptomatic *H. pylori*-negative patients in our study. Patients were classified as infected with *H. pylori* when both histology and rapid urease test were positive or if culture was positive (7). All other patients were classified as being free of *H. pylori* infection. A 10-cc sample of serum was obtained from each patient after an overnight fast and stored for later analysis. The ethics committee of St. Orsola Hospital, Bologna, approved the protocol and all participants gave written informed consent.

### *Endoscopy Sampling and Histology Assessment*

All patients underwent endoscopy; multiple biopsy samples were obtained for: (a) rapid urease test (n = 2, one from the antrum and one from the corpus), (b) culture (n = 2, one from the antrum and one from the corpus), and (c) histology (antrum n = 2; lesser curvature of corpus n = 1; greater curvature of corpus n = 1; *angulus* n = 2) as recently described (8).

For the histology assessment, biopsy samples obtained from each site were fixed in 5% formalin and embedded in paraffin. Multiple sections (5-$\mu$m thick) were stained with the Hematoxylin and Eosin and Giemsa modified for *H. pylori* detection. All cases of intestinal metaplasia were confirmed by appropriate histochemical stain (High Iron Diamine (HID)) (9). Two pathologists (CR and VMR), who were blinded to any clinical information, jointly examined all the specimens and reached a consensus on the score of each of the considered histological variables. Gastritis was classified as nonatrophic or atrophic, in accordance with current criteria (10, 11). Mucosal atrophy was defined as loss of appropriate glands. Inflammation (polymorphs and lymphoplasmocytic) and atrophy (subclassified as with and without intestinal metaplasia) were graded with currently accepted criteria (10, 11).

According to the topographical location of the atrophic-metaplastic changes, three main patterns of atrophic gastritis were distinguished:

- Antrum-restricted atrophic gastritis: characterized by different grades of inflammatory cells within the *lamina propria*, coexisting with loss of appropriate glands (replaced by fibrosis and/or intestinalized glands) only located in the native mucus-secreting antral mucosa.
- Antrum-predominant atrophic gastritis: characterized by different grades of inflammatory cells within the *lamina propria*, coexisting with loss of appropriate glands (replaced by fibrosis and/or intestinalized glands) in both native oxyntic and native mucus-secreting antral mucosa. All cases categorized as antrum-predominant atrophic gastritis showed extensive (*i.e.*, moderate-to-severe) mucosal atrophy in the antral specimens while patchy/small foci of atrophy (*i.e.*, mild) was detected in one of the biopsy samples obtained from the corpus mucosa.
- Corpus-restricted atrophic gastritis. This pattern, which has been considered typical of autoimmune etiology, was characterized by atrophic changes only detected in the biopsy specimens obtained from the oxyntic mucosa; in the antral specimens, no atrophic changes were detected in association with inflammatory cells within the *lamina propria*. In this study, corpus-restricted atrophic gastritis was detected in 5 patients, who were excluded from any subsequent calculation because the numbers of these patients were too small to permit meaningful calculations of predictive value.

### *Gastrin, Gastrin-17, Pepsinogen I, II, and Ratio*

Serum gastrin was measured by radioimmunoassay using a commercially available kit (ICN Orangeburg, NY). The normal range of value for serum gastrin provided by the manufacturer is 25–111 pg/ml with a mean of 49.6 pg/ml in a healthy population ranging in age from 19 to 60 yr. Gastrin-17 was assessed using a commercially available radioimmunoassay kit (DRG Instruments GmbH, Hamburg, Germany). The normal range of value for serum gastrin-17 provided by manufacturer is 25–111 pg/ml with a mean of 49.6 pg/ml in a healthy population ranging in age from 19 to 60 yr. Serum fasting pepsinogen I, II were determined by ELISA using a commercially available kit (Eiken Chemical Co., Ltd., Tokyo, Japan). According to the manufacturer, a pepsinogen I below 70 ng/ml and a pepsinogen I/pepsinogen II ratio less than 3 are suggestive of atrophic gastritis, while a pepsinogen I value less than 30 ng/ml and a ratio less than 2 is considered strongly suggestive of atrophy.

### *Anti-CagA Antibody Determination*

CagA status was determined by Western blot. A whole cell suspension of *H. pylori* CCUG 17874 (CagA-positive-type strain) was denaturized in Laemmli's solution at 100°C for 10 min, and run electrophoretically in a 10% sodium dodecylsulphate-polyacrylamide gel. Separated proteins were transferred to nitrocellulose, which was saturated for 30 min with a 3% defatted milk solution in phosphate saline buffer pH 7.5 containing 0.1% Triton X (MTB). Nitrocellulose strips were incubated with serum samples diluted 1:1000 in MTB at room temperature overnight. After washing with MTB, strips were incubated with antihuman immunoglobulin G conjugated with peroxidase at room temperature for 90 min. The strips were washed and the reaction was visualized by an enhanced chemi-luminescence assay

(Amersham, Pharmacia Biotech, Buckinghamshire, UK). As controls, the following sera provided by Drs. Covacci, Telford, and Burroni (I.R.I.S.- Biocine, Siena, Italy) were used: antirecombinant CagA, antirecombinant VacA, antipurified urease, and heat shock protein. Patients were considered to be CagA-positive if more than four bands of reaction were evident in the blots (12).

### *Statistical Analysis*

As the values of the biomarkers we studied were not normally distributed, data are expressed as median and interquartile range (IQR) and the Mann-Whitney test was used to assess statistical differences. The evaluation of the performance of biomarkers for atrophy was performed using the histological diagnosis as gold standard. The cut-off point for each of the biomarkers was determined by means of a receiving operating characteristic (ROC) curve. It was defined as the best point to discriminate between patients with antrum-restricted/predominant atrophy and patients with nonatrophic changes (13) Sensitivity, specificity, and the likelihood ratio for a positive and negative test were calculated using methods recommended by Altman (14). Multivariate logistic regression models were separately performed including age, sex, and CagA status. The best cut-off found for each biomarker was also included in the model as a dichotomous variable. Rather than using an automatic computer-defined step-down procedure to reduce the number of explanatory variables, we decided to use a two-stage elimination method, which enabled us to monitor which of the variables would be eliminated. The elimination of the variables, which did not contribute to the ability of the model to predict atrophy, was necessary also because the sample size was small (15). Thus, the rule that we adopted was to eliminate variables from the full model if the level of statistical significance was less than $p = 0.2$. The remaining variables were included in a second model, and finally, only the variables, which were statistically significant at $p < 0.05$ were included in the final one. Values of $p < 0.05$ were considered statistically significant. All statistical analysis were performed employing Intercooled STATA 8.1 (Stata Corporation, College Station, TX).

## RESULTS

Table 1 shows the demographic and histological characteristics of the patients enrolled, according to the *H. pylori* and CagA status. Three of 147 patients (1 *H. pylori*-positive female with nonatrophic gastritis, 1 *H. pylori*-positive female with antrum-restricted atrophy, and 1 *H. pylori*-negative male with nonatrophic gastritis) were excluded from the analysis because adequate serum samples were not available. In 5 patients (2 *H. pylori*-positive and 3 *H. pylori*-negative; 4 female and 1 male; mean age 43.8 ± 14.61 yr), the histology demonstrated corpus-restricted atrophic-metaplastic changes. Such a pattern was considered compatible with a chronic atrophic gastritis with autoimmune etiology. The etiological hypothesis was confirmed by appropriate serology tests in four of five cases. As a consequence, all these 5 patients were excluded by any subsequent calculation. Table 2 shows the values for the different serum markers in the overall sample studied, and according to the *H. pylori* and CagA status and to the histological diagnosis. The median values of pepsinogen I and II were significantly higher in patients infected with CagA-positive strains as well as for those with CagA-negative *H. pylori*-positive compared to patients not infected ($p = 0.001$ and $p < 0.0001$, respectively). The mean values of pepsinogen II were higher in patients with antrum atrophy compared to the normal ($p = 0.02$). The values of ratio were also significantly higher for those with antrum or corpus atrophy compared to normal patients ($p = 0.0344$ and $p = 0.02$, respectively).

### *ROC Curve Analysis*

ROC curves were plotted for each of the serum tests as a predictor of antrum or corpus atrophy and the values of the sensitivity, specificity, and likelihood ratio for a positive and negative test are shown in Table 3. Serum pepsinogen I is sensitive but not specific for the presence of antrum-restricted/predominant atrophy while total gastrin and pepsinogen II are specific but not sensitive. Using the ROC curves, the best cut-off value for each test was determined and then used for further calculations.

### *Univariate Logistic Analysis for Antrum-Restricted/Predominant Atrophic Gastritis*

Table 4 shows the univariate logistic model for antrum-restricted/predominant atrophic gastritis. The best cut-off value found for each test to diagnose antrum-restricted/predominant atrophy was included in the model as a dichotomous variable. Age ≥45 yr was a significant risk factor for atrophy (OR = 2.86; $p = 0.033$) as was infection with a CagA-positive strains (OR = 4.67; $p = 0.000$). The

**Table 1.** Characteristics of Patients Included in the Study

| | Overall Population | *H. pylori* +ve CagA +ve | *H. pylori* +ve CagA −ve | *H. pylori*−ve |
|---|---|---|---|---|
| Number of patients | 144 | 37 | 35 | 72 |
| Male/female | 86/58 | 18/19 | 22/13 | 46/26 |
| Age mean ± SD | 47.3 ± 10.9 | 48.29 ± 10.49 | 48.57 ± 9.94 | 46.3 ± 11.6 |
| Atrophic gastritis (antrum restricted + antrum-predominant) No. (95% CI) | 31 (21.5; 15.6–28.9) | 16 (43.2; 28.7–59.1) | 8 (21.6; 11.4–37.2) | 7 (9.7; 4.8–18.7) |
| Atrophic gastritis (corpus restricted) No. (95% CI) | 5 (3.5; 1.5–7.9) | 1 (2.7; 0.5–13.8) | 1 (2.9; 0.5–14.5) | 3 (4.2; 1.4–11.5) |

CI = confidence interval.

**Table 2.** Median and Interquartile Ranges (IQR) for Gastrin, Gastrin-17, Pepsinogen I, Pepsinogen II, and Ratio

| | No | Gastrin (pg/ml) | Gastrin-17 (pg/ml) | Pepsinogen I (ng/ml) | Pepsinogen II (ng/ml) | Ratio |
|---|---|---|---|---|---|---|
| Overall population | | | | | | |
| Median (IQR) | 144 | 43.5 (39–48) | 46.39 (39.60–55.62) | 52.45 (40.28–69.68) | 12.07 (9.01–16.24) | 4.39 (3.41–5.41) |
| *H. pylori* status | | | | | | |
| *H. pylori* +ve CagA +ve | | | | | | |
| Median (IQR) | 37 | 45 (38–49.5) | 46.96 (40.70–58.69) | 55.03* (41.66–72.14) | 16.23** (12.89–21.33) | 3.67 (2.44–4.69) |
| *H. pylori* +ve CagA −ve | | | | | | |
| Median (IQR) | 35 | 43 (41–48) | 45.6 (38.05–53.17) | 66.78** (50.17–78.33) | 13.37** (11.62–19.518) | 4.50 (3.56–5.45) |
| *H. pylori* −ve | | | | | | |
| Median (IQR) | 72 | 43 (39–48) | 46.5 (39.11–55.23) | 43.62 (36.21–56.81) | 9.58 (7.34–12.08) | 4.56 (3.55–6.07) |
| Histological diagnosis | | | | | | |
| Atrophic gastritis (antrum restricted + antrum predominant) | | | | | | |
| Median (IQR) | 31 | 43 (37–49) | 50.07 (38.5–59.16) | 53.66 (40.99–66.79) | 13.92† (9.45–21.74) | 3.70‡ (2.96–4.84) |
| Normal | | | | | | |
| Median (IQR) | 108 | 44 (40–48) | 46.39 (39.87–53.57) | 51.96 (39.68–69.68) | 11.96 (8.55–15.03) | 4.40 (3.50–5.66) |

*$p = 0.0012$ compared to *H. pylori*-negative; **$p < 0.0001$ compared to *H. pylori*-negative;
†$p = 0.0223$ compared to normal; ‡$p = 0.0344$ compared to normal.

absence of infection was protective against the antrum atrophy (OR = 0.21; $p = 0.001$). Table 3 shows the likelihood ratios for a positive and a negative test with each of the biomarkers with the cut-off value determined by ROC analysis.

### *Multivariate Logistic Models for Antrum-Restricted/Predominant Atrophic Gastritis*

The multivariate logistic models for antrum-restricted/predominant atrophy are shown in Table 5. All the variables used for the univariate analysis were also used for the first multivariate analysis. Following the first regression, the variables sex, age, *H. pylori*-positive CagA-positive status, *H. pylori*-positive CagA-negative status, total gastrin, gastrin-17, and ratio were included in the second model because their $p$ values were <0.2. Subsequently, in the second regression, only sex and *H. pylori*-positive CagA-positive status were included in the third model because their $p$ values were <0.05. In the third analysis, the only variable still significant was *H. pylori*-positive CagA-positive status with an odds ratio (OR) of 5.40 (95% CI: 2.22–13.14).

## DISCUSSION

Gastric cancer is the second largest cause of cancer death throughout the world (16). *H. pylori*-related gastric atrophy (mostly coexisting with intestinal metaplasia) has been shown to be a major risk factor for the development of gastric cancer (2). Gastric atrophy has been shown to regress after *H. pylori* eradication and it may therefore represent a potentially reversible step on the path of carcinogenesis (17–19). Endoscopy and histological examination of biopsy specimens are the most reliable methods of detecting gastric atrophy but are unsuitable for screening large populations because they are invasive and expensive. Serum markers that are predictive of gastric atrophy are of interest because they could identify a population at risk at a potentially treatable stage and allow intervention in this select group of patients. The ability to identify a subgroup of infected patients at risk for gastric cancer may help to target national eradication strategies by limiting intervention to a group of high-risk patients. Screening and eradication of *H. pylori* in the general population may have unforeseen consequences such as the emergence of resistant strains of *Helicobacter* or other species and has not yet been adopted even in countries with a high incidence of gastric cancer while noninvasive methods to identify high-risk patients are being developed (20, 21). In individual cases, noninvasive screening tests may also be helpful to detect patients at high risk for the development of gastric cancer, for example, first-degree relatives of patients with gastric cancer.

**Table 3.** Accuracy of Serological Markers for Antrum-Restricted/Antrum-Predominant Atrophic Gastritis in 31 Asymptomatic Patients

| | Sensitivity (%) (95% CI) | Specificity (%) (95% CI) | LR +ve (95% CI) | LR −ve (95% CI) | Best Cut-Off |
|---|---|---|---|---|---|
| Gastrin pg/ml | 35.5 (21.1–53.1) | 81.4 (73.3–87.5) | 1.909 (1.036–3.520) | 0.792 (0.602–1.044) | ≤38 pg/ml |
| Gastrin-17 pg/ml | 48.4 (32–65.2) | 72.6 (63.7–79.9) | 1.764 (1.101–2.826) | 0.711 (0.497–1.019) | >52.03 pg/ml |
| Pepsinogen I ng/ml | 90.9 (76.4–96.9) | 9.9 (5.6–16.9) | 1.009 (0.891–1.143) | 0.917 (0.272–3.095) | >32.98 μg/ml |
| Pepsinogen II ng/ml | 48.4 (32–65.2) | 76.1 (67.5–83) | 2.025 (1.24–3.307) | 0.678 (0.475–0.968) | >15.16 μg/ml |
| Ratio | 54.8 (37.8–70.8) | 68.1 (59.1–76) | 1.721 (1.123–2.615) | 0.663 (0.441–0.997) | ≤3.71 |

CI = confidence interval; LR +ve, likelihood ratio for a positive test; LR −ve, likelihood ratio for a negative test.

**Table 4.** Univariate Logistic Analysis for Antrum-Restricted/Antrum-Predominant Atrophic Gastritis in 31 Asymptomatic Patients

| Variables | OR (95% CI) | *p*-Values |
|---|---|---|
| Sex* | 0.64 (0.27–1.49) | 0.306 |
| ≥45 yr | 2.86 (1.08–7.52) | 0.033 |
| *H. pylori* –ve | 0.21 (0.085–0.54) | 0.001 |
| *H. pylori* +ve CagA +ve | 4.67 (1.99–10.92) | 0.000 |
| *H. pylori* +ve CagA −ve | 1.10 (0.44–2.76) | 0.826 |
| Gastrin cutoff antrum | 2.40 (1–5.78) | 0.049 |
| Gastrin-17 cutoff antrum | 2.47 (1–5.61) | 0.029 |
| Pepsinogen 1 cutoff antrum | 4.12 (0.48–31.04) | 0.198 |
| Pepsinogen 2 cutoff antrum | 2.98 (1.30–6.82) | 0.009 |
| Ratio—cutoff antrum | 2.59 (1.154–5.84) | 0.021 |

CI = confidence interval.
*Female compared to male.

Previous studies have yielded conflicting results with regard to biomarkers. In a large study of patients with dyspeptic symptoms, Broutet *et al.* (22) evaluated pepsinogen I, pepsinogen II, the ratio of pepsinogen I and II, and serum gastrin and concluded that only the ratio of pepsinogen I and II was reliable with a sensitivity of 77% and a specificity of 87% in the detection of atrophic gastritis of the corpus. They suggested that it may be a useful screening test. The study was limited by the patient sample (dyspeptic patients presenting for endoscopy), which could increase the pretest probability of gastric atrophy in the patients studied. Sipponen *et al.* have recently reported a cohort of dyspeptic patients with and without atrophic gastritis (23). They found that mean serum pepsinogen I and serum gastrin-17 were lower in patients with corpus atrophy than in patients who did not have atrophy. Analysis of a smaller subgroup of patients with atrophic gastritis or resection of the antrum compared to infected patients without atrophy suggested that serum gastrin (G-17) levels with an arbitrarily determined cut-off of 5 pmol/L could predict atrophy or the absence of an antrum with a sensitivity of 86% and a specificity of 90%. However ROC curves were not plotted and the optimal cut-off was not determined. It is also arguable whether resection of the antrum is an acceptable surrogate for chronic atrophic gastritis. Two other studies have evaluated serum markers in populations. Miki *et al.* (24) studied a group of factory workers undergoing radiographic mass screening for gastric cancer and evaluated serum pepsinogen I and II as a predictor of gastric cancer. The positive predictive value of serum pepsinogen for gastric cancer was very low (1.4%). In a study of 29 asymptomatic working patients, Wyatt *et al.* (25) found 9 patients with gastric atrophy. Pepsinogen I values below 80 ng/ml had a sensitivity of 89% and a specificity of 92% in detecting atrophy but the sample size was very small.

The advantages of our study are that we: (a) studied asymptomatic patients, (b) tested several markers, (c) applied a standardized protocol of gastric biopsy sampling, and (d) evaluated histology using the most recently codified morphological criteria (with blinding of the pathologists to the serum values). In addition, to decrease error caused by observer bias, two pathologists were involved in the assessment of all the specimens. In our population of asymptomatic patients, which can be considered representative of western European epidemiological context, this study demonstrates that serum pepsinogens, their ratio, and serum gastrin (G-17) are not reliable tests for atrophic gastritis (antrum restricted/antrum predominant). In different epidemiological settings, the patterns and severity of gastritis may be different and serum markers may have different performances. Similarly, serum markers are not reliable as a diagnostic test for gastric atrophy or intestinal metaplasia in patients who are known to be infected with *H. pylori*. Population-based screening strategies to identify patients with atrophy and intestinal metaplasia using these serum markers are unlikely to be successful.

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**Table 5.** Multivariate Logistic Analysis for Antrum-Restricted/Antrum-Predominant Atrophic Gastritis in 31 Asymptomatic Patients

| | Multivariate Logistic Model Including Each Variable | | Multivariate Logistic Model Including Variables with $p < 0.2$ | | Multivariate Logistic Model Including Variables with $p < 0.05$ | |
|---|---|---|---|---|---|---|
| Variables | OR (95% CI) | *p*-Values | OR (95% CI) | *p*-Values | OR (95% CI) | *p*-Values |
| Sex* | 0.32 (0.10–1.02) | ***0.056*** | 0.29 (0.09–0.92) | ***0.037*** | 0.47 (0.18–1.18) | 0.112 |
| ≥45 yr | 2.91 (0.94–9) | ***0.064*** | 2.98 (0.98–9.03) | 0.053 | – | – |
| *H. pylori* +ve CagA +ve** | 5.41 (1.57–18.6) | ***0.007*** | 6.60 (0.89–20.69) | ***0.001*** | **5.40 (2.22–13.14)** | **0.000** |
| *H. pylori* +ve CagA −ve | 2.35 (0.68–8.14) | ***0.176*** | 2.95 (0.89–9.69) | 0.074 | – | – |
| Gastrin cutoff antrum** | 2.91 (0.96–8.76) | ***0.057*** | 2.80 (0.95–8.25) | 0.061 | – | – |
| Gastrin-17 cutoff antrum | 2.26 (0.83–6.15) | ***0.108*** | 2.54 (0.96–6.74) | 0.060 | – | – |
| Pepsinogen I cutoff antrum | 4.41 (0.45–43.21) | 0.202 | – | – | – | – |
| Pepsinogen II cutoff antrum | 1.30 (0.43–3.89) | 0.632 | – | – | – | – |
| Ratio cutoff antrum | 2.91 (0.90–9.40) | ***0.074*** | 2.51 (0.84–7.44) | 0.097 | – | – |

CI = confidence interval.
*Female compared to male.
**Compared to *H. pylori*-negative patients.

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