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Diagnostic accuracy of GastroPanel® for atrophic gastritis in Brazilian subjects and the effect of proton pump inhibitors

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ABSTRACT – **Background** – It has been proposed that the combination of gastrin-17 (G-17), pepsinogens I and II (PGI and PGII), and anti-*Helicobacter pylori* (*H. pylori*) antibodies (GastroPanel®, BIOHIT HealthCare, Helsinki, Finland) could serve as biomarkers of atrophic gastritis. **Objective** – This study aimed to ensure the diagnostic accuracy of GastroPanel® and evaluate the effect of proton pump inhibitors (PPIs) on these biomarkers. **Methods** – Dyspeptic patients who underwent gastrointestinal endoscopy were enrolled in the present study. Histological findings, which were the gold standard to stratify groups, were as follows: no atrophy (controls); antrum atrophy; corpus atrophy; multifocal atrophy; and neoplasia. G-17, PGI, PGII, and anti-*H. pylori* immunoglobulin (Ig)G antibodies were assayed using commercially available kits. The ratio of PGI/PGII was calculated. **Results** – Among 308 patients, 159 (51.6%) were PPI users. The overall prevalence of atrophy was 43.8% (n=135). Ninety-two (29.9%) patients were *H. pylori* positive according to anti-*H. pylori* IgG levels. G-17 levels were not low in those with antrum atrophy but were high in those with corpus and multifocal atrophies. PGI levels were significantly lower in those with corpus and multifocal atrophies. The sensitivity of PGI <30 µg/L to detect corpus atrophy was 50% (95% CI 27.8–72.1%), with a specificity of 93.2% (95% CI 84.3–97.5%), a positive likelihood ratio of 7.4 (95% CI 2.9–19.2), and a negative likelihood ratio of 0.5 (95% CI 0.3–0.8). A small number of subjects (n=6) exhibited moderate to intense atrophy (4%), among whom 66.7% exhibited decreased PGI levels. PPI significantly increased the levels of G-17 and PGI, except in those with corpus and multifocal atrophies, in whom PGI levels were not increased by PPIs. **Conclusion** – GastroPanel® (Gastrin-17, PGI, and PGI/PGII ratio) did not demonstrate high sensitivity for detecting gastric atrophy.

HEADINGS – Pepsinogen A. Gastrins. Atrophic gastritis. *Helicobacter pylori*.

INTRODUCTION

The natural history of *Helicobacter pylori* (*H. pylori*) infection involves inflammation of the antrum progressing into the corpus and long-term injury, resulting in the loss of normal glandular tissue, otherwise known as multifocal atrophic gastritis[1,2]. Therefore, gastric cancer associated with *H. pylori* infection is the end phase of a long evolution process including chronic, active, non-atrophic gastritis, multifocal (antrum and corpus) atrophic gastritis without intestinal metaplasia, intestinal metaplasia of the complete type, intestinal metaplasia of the incomplete type, low-grade dysplasia, high-grade dysplasia, and, finally, cancer[2]. Thus, monitoring atrophic gastritis and intestinal metaplasia using gastrointestinal endoscopy with histological examination of the antrum and corpus is performed as a preventive measure against gastric cancer. However, upper gastrointestinal endoscopy with gastric biopsy is invasive and not accessible to all asymptomatic individuals. Thus, serological assays to detect gastric atrophy and intestinal metaplasia are essential for the early diagnosis of gastric cancer[3].

Other causes of gastric atrophy, limited to the oxyntic mucosa, include autoimmunity associated with pernicious anemia with normal antral mucosa that is not involved in the pre-cancerous cascade; however, it carries an increased risk for gastric cancer and is correlated with lower levels of pepsinogen[2]. *H. pylori* infection may trigger autoimmune gastritis by molecular mimicry between its antigens and gastric H/K ATPase[4].

Mature gastrin is synthetized by endocrine G cells of the gastric antrum in the presence of proteins and calcium in the stomach lumen. Neutralization or inhibition of acid by drugs or corpus atrophy induces the release of gastrin. After expression of the gastrin gene, the messenger RNA is translated into progastrin, which is processed along its passage through the Golgi complex, resulting in G-34 (predominant in the duodenum) and G-17 (predominant in the antrum), which are able to stimulate gastric acid secretion. Gastrin acts on the gastrin receptors on enterochromaffin cells of the gastric fundus to release histamine, which, in a paracrine action, binds to the H_2 receptors on parietal cells with the output of H^+, Cl^-, and H_2O. Other stimuli include acetylcholine and gastrin, which can directly act on the surface receptors on parietal cells and stimulate acid secretion[5-7].

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PGI and PGII are secreted by the chief cells of the oxyntic glands in the fundus and corpus. PGII is also secreted by the pyloric glands in the antrum and glands of Brunner in the proximal duodenum. Pepsinogens are stored in the form of granules and secreted into the stomach lumen in response to specific stimuli. Gastric acid converts pepsinogens into the active protein digestive enzyme, pepsin[8]; only 1% of secreted pepsinogens enter the blood stream[9]. The levels of pepsinogens are high in individuals with *H. pylori*-positive non-atrophic gastritis and decrease as inflammatory changes progress, leading to damage and loss of the gastric glands, otherwise known as atrophy[2]. Accordingly, the loss of oxyntic glands in corpus atrophy would decrease PGI levels and the PGI/PGII ratio[2,3,9-11], and antrum atrophy would decrease G-17 levels[12,13].

The performance of GastroPanel® (BIOHIT HealthCare, Helsinki, Finland) in measuring G-17, PGI, PGII, and anti-*H. pylori* antibodies has not been assessed in Brazil. Therefore, the purpose of the present study was to evaluate the diagnostic accuracy of GastroPanel® and estimate the effect of proton pump inhibitor (PPI) use on these biomarkers.

METHODS

Study population

This prospective study included consecutive dyspeptic patients who attended the gastrointestinal endoscopy division between March 2017 and July 2018. Of 340 subjects from whom blood was collected, 32 were excluded (three had underwent partial gastrectomy and 29 did not have biopsies taken according to the OLGA protocol)[14], leaving 308 subjects eligible for the study, 216 (70.1%) of whom were women. The mean (±SD) age of the study cohort was 64.6±10.3 years (range, 29 to 87 years). Individuals with systemic and psychiatric diseases, those who underwent gastrectomy, used anticoagulant drugs, and those in whom no biopsy samples were taken according to the OLGA protocol[14] were excluded. Patients answered a questionnaire surveying their consumption of medications (PPIs and H_2 receptor antagonists); those who were using PPIs were stratified separately from non-PPI users. The criteria to consider patients as non-PPI users was to have discontinued PPI and H_2 receptor antagonists for at least two weeks before testing. Individuals who underwent previous *H. pylori* eradication treatment were included. The questionnaire had no questions to select subjects with autoimmune gastritis or neuroendocrine tumors.

Ethical statement

The Ethics Committee of the Hospital approved this study protocol under the CAAE: 50561715.5.0000.0068, and all subjects provided informed written consent to participate.

Gastrointestinal endoscopy

After a 12-h fast, simethicone solution was used to improve the visibility of the mucosa, followed by 10% xylocaine spray and intravenous sedation with midazolam, fentanyl, and propofol, as previously described[15]. Endoscopies were initially performed using a standard endoscope (GIF-H180, Olympus Co., Miami, FL, USA) using white light. Subsequently, narrow-band imaging (NBI) was activated, which facilitated visualization of the mucosa and re-evaluation for the detection of macroscopically visible abnormalities. Five gastric mucosa samples were obtained according to the OLGA sampling protocol (from the corpus C1 and C2, antrum A1, A2, and the incisura angularis A3)[14], as well as from lesions detected macroscopically and by NBI.

GastroPanel® analysis

G-17, PGI, PGII, and anti-*H. pylori* IgG antibody levels were assayed using monoclonal antibodies and commercially available enzyme immunoassay kits (BioHit, Helsinki, Finland). The ratio of PGI/PGII was also calculated. Blood samples were collected in EDTA vials and centrifuged; the plasma was stored frozen until testing. Blood collection was performed at the gastrointestinal endoscopy division before sedation. Initially, the samples were diluted with diluent buffer for the assays as follows: 1:5 for G-17; 1:20 for PGI and PGII; and 1:400 for *H. pylori*. The blank solutions (for G-17, PGI, and PGII) or the sample diluent buffer (for *H. pylori*), calibrators, controls, and diluted samples were pipetted into microplate wells at a volume of 100 µL. The microplates were incubated at room temperature for 60 min with shaking (750 rpm). The microplate strips were washed three times with 350 µL of diluted wash buffer, inverted, and gently tapped a few times on a clean paper towel. Specific conjugate solutions (100 µL) were subsequently pipetted into the microplate wells and incubated for 60 min at room temperature with shaking (750 rpm). The microplate strips were washed three times with 350 µL of diluted wash buffer, inverted, and gently tapped a few times on a clean paper towel. Substrate solution (100 µL) was subsequently pipetted into the microplate wells and incubated for 30 min at room temperature while protected from light. Finally, 100 µL of stop solution was pipetted into the microplate wells. The absorbance of the microplate wells was measured at 450 nm using a microplate reader (Vivid Vision, ALKA Tecnologia, São Paulo, Brazil). Reference ranges according to the manufacturer were as follows: G-17 (1–7 pmol/mL); PGI (30–160 µg/L); PGII (3–15 µg/L); PGI/PGII ratio (3–20); and *H. pylori* IgG (<30 EIU). PGI was considered to have decreased at levels <30 µg/L, and the PGI/PGII ratio was considered to have decreased if <3. *H. pylori* IgG >30 EIU indicated positive *H. pylori* infection, although the assay did not discriminate current from pre-existing exposure to the bacteria[16].

Histological examination

Biopsy samples were fixed in 10% formalin and stained with hematoxylin and eosin for histological diagnosis, based on the updated Sydney System[17]; *H. pylori* was identified using Giemsa stain, indicating current infection[16]. Histological findings were considered to be the gold standard used to stratify subjects into the following categories: no atrophy, including chronic active and chronic inactive gastritis (controls); antrum and/or incisura angularis atrophy (antrum group); antrum and corpus atrophy (multifocal group); and corpus atrophy (corpus group). The neoplasia group consisted of patients who were analyzed together, with gastric cancer, mucosal low-grade neoplasia, and neuroendocrine tumor. Based on histological findings using the updated Sydney System[17], the OLGA stages[14] were determined.

Statistical analyses

Statistical analyses of categorical variables were performed using SPSS version 15.0 (SPSS, Chicago, IL, USA) for Windows (Microsoft Corporation, Redmond, WA, USA) and Fisher's exact test; differences with $P<0.05$ were considered to be statistically significant. Subjects with no atrophy were considered as the controls with which all other groups were compared. Diagnostic accuracy was determined among subjects who were non-PPI users. Each group of PPI users was compared with the non-PPI users. The levels of biomarkers were compared between the controls and the

other groups using the Mann-Whitney test. Sensitivity, specificity, positive predictive value, negative predictive value, and positive and negative likelihood ratios with 95% confidence interval (95% CI) were calculated using an online program (http://vassarstats.net/). According to McNicholl et al. (2014)[18] who analyzed the accuracy of GastroPanel® for the diagnosis of atrophic gastritis, a sample size of 90 was calculated, as they considered the prevalence of chronic atrophic gastritis to be 23% and that 20 patients would have chronic atrophic gastritis. In the present investigation, G* Power version 3.1.9.4 (Franz Faul, Universität Kiel, Germany) was used to for *post hoc* power analysis. The effect size was calculated with the means and standard deviations between two groups. The result of effect size was transferred to main window to calculate power (1- β error probability) for each one of the analysis of the study by means: Wilcoxon-Mann Whitney test (two groups). The input parameters were the effect size d, α=0.05, sample size of group 1 and sample size of group 2 to calculate power for each one of the analysis. Results are reported in accordance with the Standards for the Reporting of Diagnostic accuracy studies (STARD) checklist (2015)[19].

RESULTS

Endoscopy yielded the following findings: normal endoscopy, mild esophagitis, or minor changes, n=68 (22.1%); gastroduodenal erosions, n=78 (25.3%); atrophy, n=106 (34.4%); suspicious gastric lesions, n=7 (2.3%); gastric cancer, n=11 (3.6%); gastric ulcer, n=15 (4.9%); gastric polyps, n=15 (4.9%); and duodenal ulcer, n=8 (2.6%).

A diagram illustrating patient flow though the study, based on histological findings, is presented in FIGURE 1. Among the 308 patients, 159 were PPI users (51.6%). The overall prevalence of atrophy was 43.8% (n=135). Five groups were categorized according to the histological diagnoses as follows: controls, n=158 (non-PPI users, n=74; PPI users, n=84); antrum atrophy, n=72 (non-PPI users, n=29; PPI users, n=43); multifocal (antrum and corpus) atrophy, n=34 (non-PPI users, n=19; PPI users, n=15); corpus atrophy, n=29 (non-PPI users, n=20; PPI users, n=9); and neoplasia, n=15. The neoplasia group consisted of nine patients with gastric cancer (three non-PPI users; six PPI users), three with mucosal low-grade neoplasia (only one non-PPI user) and three with neuroendocrine tumor (all non-PPI users). Among patients with gastric cancers, three were diagnosed with poorly differentiated carcinoma, three with moderately differentiated carcinoma, and three with well-differentiated carcinoma.

H. pylori was positive in 92 (29.9%) subjects according to anti-*H. pylori* IgG levels, and in 61 (19.8%) according to Giemsa staining of gastric samples**.** *H. pylori* infection was positive in 25.8% of the subjects who used PPIs and in 34.2% of non-PPI users. The highest prevalence of *H. pylori* infection (51.7%, $P<0.05$) was in the antrum atrophy group of non-PPI users (data not shown), who also exhibited significantly higher levels of anti-*H. pylori* IgG (power=0.70) (FIGURE 2).

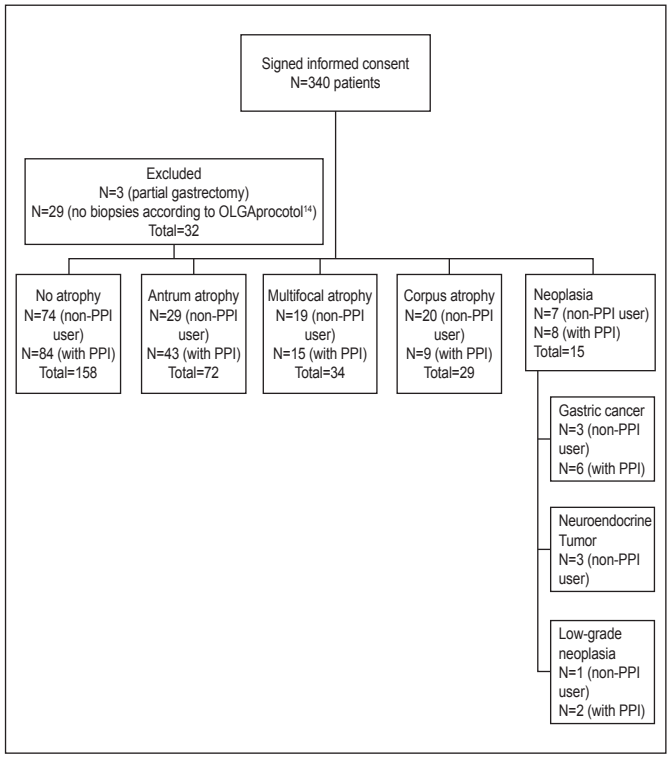

FIGURE 1. Flow chart of the subjects eligible for the study.
PPI: proton pump inhibitor.

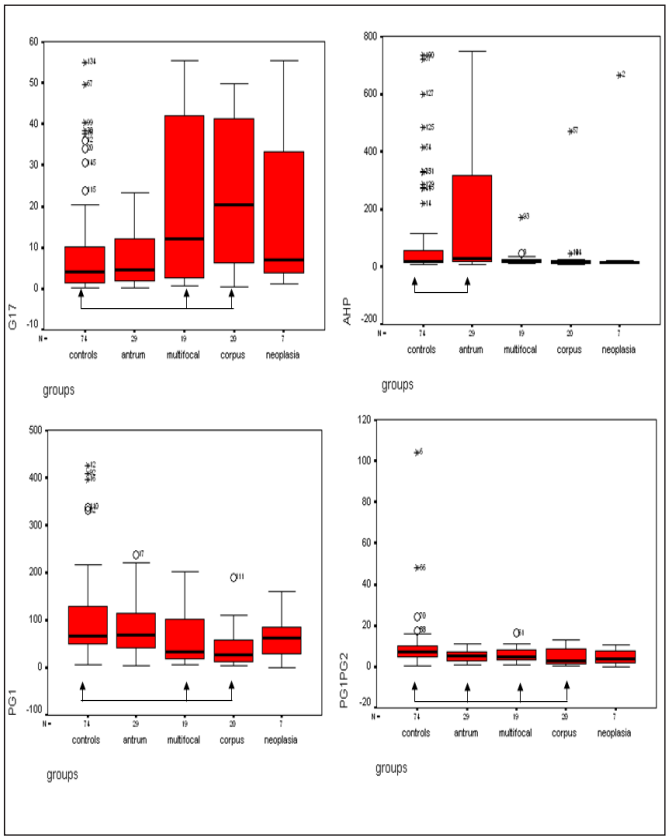

FIGURE 2. Comparison of the levels of G-17 (pmol/mL), PGI (μg/L), anti-*H. pylori* Ig(G) (EIU), and the PGI/PGII ratio of each group of non-PPI users with the controls.
The arrows indicate significance between the group and controls. The graphs indicate the medians and the boxes the 25%–75% quartiles.
$P<0.05$: statistically significant; PG1: PGI; PG2: PGII; PG1/PG2: PGI/PGII; AHP: anti-*H. pylori* Ig(G); Antrum: antrum atrophy; Multifocal: multifocal atrophy; Corpus: corpus atrophy.

G-17 levels were significantly higher in those with corpus (power=0.98) and multifocal (power=0.93) atrophies; however, was not lower in antrum atrophy (power=0.26). PGI was significantly lower in corpus (power=0.91) and multifocal (power=0.59) atrophies. The PGI/PGII ratio was significantly lower in all groups, except for neoplasia (antrum atrophy; power=0.66, multifocal atrophy; power=0.43, and corpus atrophy; power=0.58) compared with controls (FIGURE 2). There were no significant differences in the levels of biomarkers between women and men (data not shown). Age was not significantly different among controls and the atrophy groups (data not shown).

The performance of PGI (<30 µg/L) and PGI/PGII ratio (<3) to detect gastric atrophy with 95% confidence interval (CI) is summarized in TABLE 1 for corpus and multifocal atrophy groups. For corpus atrophy, PGI < 30 µg/L demonstrated a sensitivity of 50% (95% CI 27.8–72.1%), a specificity of 93.2% (95% CI 84.3–97.5%), a positive predictive value of 15.9% (95% CI 9.5–25.3%), a negative predictive value of 84% (95% CI 74.7–90.5%), and positive 7.4 (95% CI 2.9–19.2) and negative 0.5 (95% CI 0.3–0.8) likelihood ratios. The PGI/PGII ratio of <3 demonstrated a sensitivity of 55% (95% CI 32–76.2%), a specificity of 93.2% (95% CI 84.3–97.4%), a positive predictive value of 17% (95% CI 10.3–26.5%), a negative predictive value of 82.9% (95%CI 73.5–89.7%), and positive 8.1 (95% CI 3.2–20.7) and negative 0.5 (95% CI 0.3–0.8) likelihood ratios.

For multifocal atrophy, PGI <30 µg/L demonstrated a sensitivity of 42.1% (95% CI 21.1–66%), a positive predictive value of 13.9% (95% CI 7.9–23%), a negative predictive value of 86% (95% CI 76.9–92%), and positive 6.2 (95% CI 2.3–16.9) and negative 0.6 (95% CI 0.4–0.9) likelihood ratios. PGI/PGII ratio of <3 demonstrated a sensitivity of 21% (95% CI 6.9–46%), a positive predictive value of 9.7% (95% CI 5–18%), a negative predictive value of 90.3% (95% CI 81.9–95.2%), and positive 3.1 (95% CI 0.9–10.5) and negative 0.8 (95% CI 0.7–1.0) likelihood ratios.

The distribution of subjects who were non-PPI users according to the OLGA stage revealed that 75 (50.3%) were stage O, 68 (45.6%) stages I–II, and six (4%) stages III–IV. The PGI level was <30 µg/L in 19 (27.9%) subjects with stages I and II and four (66.7%) with stages III and IV (P<0.05) (TABLE 2). Among the subjects who exhibited gastric atrophy, 87 (58.4%) exhibited no intestinal metaplasia.

TABLE 1. The performance of PGI (<30 µg/L) and PGI/PGII ratio (<3) to detect gastric atrophy with 95% confidence interval for corpus and multifocal atrophy (non-PPI users) groups.

Parameters	PGI <30 µg/L	PGI/PGII ratio<3
Sensitivity		
Corpus atrophy	50% (27.8–72.1%)	55% (32–76.2%)
Multifocal atrophy	42.1% (21.1–66%)	21% (6.9–46%)
Specificity	93.2% (84.3–97.5%)	93.2% (84.3–97.4%)
PPV		
Corpus atrophy	15.9% (9.5–25.3%)	17% (10.3–26.5%)
Multifocal atrophy	13.9% (7.9–23%)	9.7% (5–18%)
NPV		
Corpus atrophy	84% (74.7–90.5%)	82.9% (73.5–89.7%)
Multifocal atrophy	86% (76.9–92%)	90.3% (81.9–95.2%)
+ Likelihood ratio		
Corpus atrophy	7.4 (2.9–19.2)	8.1 (3.2–20.7)
Multifocal atrophy	6.2 (2.3–16.9)	3.1 (0.9–10.5)
– Likelihood ratio		
Corpus atrophy	0.5 (0.3–0.8)	0.5 (0.3–0.8)
Multifocal atrophy	0.6 (0.4–0.9)	0.8 (0.7–1)

TABLE 2. PGI results according to OLGA stages of subjects who were non-PPI users.

OLGA	PGI <30 µg/L	PGI ≥30 µg/L	Total
Stage 0	5 (6.7%)	70 (93.3%)	75 (50.3%)
Stages I and II	19 (27.9%)	49 (72.1%)	68 (45.6%)
Stages III and IV	4 (66.7%)	2 (33.3%)	6 (4%)
Total	28 (18.8%)	121 (81.2%)	149 (100%)

P<0.05.

Comparison of the levels of G-17, PGI, anti-*H. pylori* IgG, and the PGI/PGII ratio of each group of PPI-users with its counterpart non-PPI users (FIGURE 3) revealed that PPI use significantly increased the levels of G-17 in controls (power=0.97) and

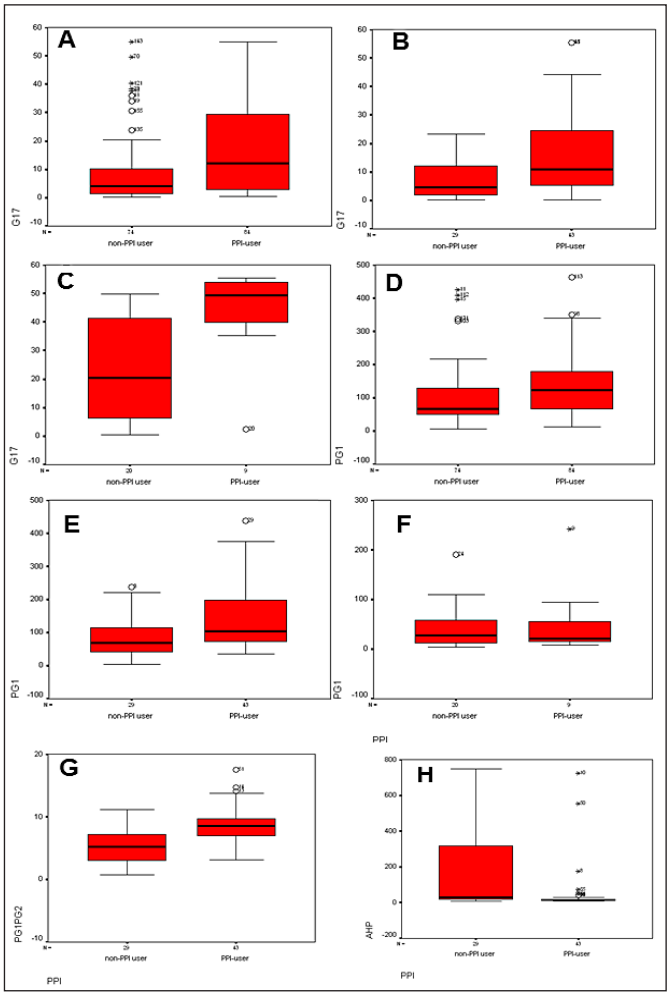

FIGURE 3. Comparison of the levels of G-17 (pmol/mL) and PGI (µg/L) of PPI-users with its counterpart non-PPI users in controls (A, D), corpus atrophy (C, F) and antrum atrophy (B, E, G, H) and anti-*H. pylori* Ig(G) (EIU), and the PGI/PGII ratio in antrum atrophy.
The graphs indicate the medians and the boxes the 25%–75% quartiles. PG1: PGI; PG1/PG2: PGI/PGII; AHP: anti-*H. pylori* Ig(G); PPI: Proton pump inhibitors.
A, B, C, D, E, G, H: P<0.05; F: P>0.05.

in those with corpus atrophy (power=0.81) and antrum atrophy (power=0.95). PPI use did not increase the levels of PGI in corpus atrophy (power=0.11) and in multifocal atrophy (power=0.25) (data not shown); however, increased the levels of PGI in controls (power=0.78) and in those with antrum atrophy (power=0.89). The PGI/PGII ratio was significantly higher in the antrum atrophy group that were PPI-users in relation to the antrum group that were non-PPI users (power= 0.99). The levels of anti-*H. pylori* IgG were significantly higher in the antrum atrophy non-PPI user group compared with the antrum atrophy PPI user group (power=0.87).

DISCUSSION

The simultaneous quantification of G-17, PGI, PGII, and anti-*H. pylori* IgG levels using GastroPanel® was designed in the late 1990s to evaluate the structure and function of the entire stomach mucosa, antrum, and corpus. Since then, several studies from different countries have tested GastroPanel®, mainly in dyspeptic subjects with atrophic gastritis, to ascertain its application as a noninvasive screening test for pre-neoplastic conditions in gastric cancer[11]. GastroPanel® is not indicated for diagnosing gastric cancer but for selecting subjects with atrophic gastritis in whom gastrointestinal endoscopy is necessary to search for cancerous lesions[3,9,11,16].

The purpose of the present study was to evaluate the utility of the serological markers G-17, PGI, PGII, and the ratio of PGI/PGII for the diagnosis of gastric atrophy, to identify individuals who should undergo upper gastrointestinal endoscopy. The overall prevalence of gastric atrophy (43.8%) was higher than the median prevalence of atrophic gastritis (27%) across studies described elsewhere[3]. The prevalence of intestinal metaplasia in countries around the world increases with age and the presence of *H. pylori* infection and is as high as 45.2% in the elderly in the high-risk gastric cancer region of Colombia[20]. Moreover, gastric atrophy in Japan and China may reach prevalences >50%[21]. Atrophy and intestinal metaplasia tend to be more common among elderly individuals in most studies, reflecting a progression of gastritis with age[3,9,20,21]; however, age was not significantly different among controls and the atrophy groups. There were no statistically significant differences between women and men, although women with atrophy were found to have a lower risk for developing gastric cancer than men[21].

Unexpectedly, the prevalence of *H. pylori* infection (29.9%) was lower than that in 2005 (53%)[22], except for the non-PPI group with antrum atrophy which had the significantly highest prevalence (51.7%) similar to that report[22]. *H. pylori* eradication regimens have since been widely used. The difference in the prevalence of *H. pylori* infection (29.9%) according to the serological assay and Giemsa stain (19.8%) may be due to over-diagnosis in the serological assay, which does not discriminate current from previous infection[16]. Nevertheless, serology has the advantage of not being affected by changes in bacterial load in the stomach from the action of antisecretory drugs or recent antimicrobial treatment that may lead to false-negative results in other tests[16].

G-17, which is secreted into the circulation only by G cells in the antrum, may indicate atrophy in the antrum of the stomach because the loss of G cells due to the atrophy process should reduce the levels of G-17[3,5,10-13]. However, the regulation of levels of G-17 are far more complex, as gastric acid output downregulates G-17 levels when is high and upregulates when is low[5]. Consequently, prolonged use of PPIs[23] and corpus atrophy tend to increase G-17 levels[10,11]. In fact, the use of PPIs significantly increased G-17 levels among the controls and the antrum and corpus atrophy groups as a result of hypochlorhydria. Unexpectedly, G-17 was not significantly decreased in those with antral lesions, as previously reported[3,10]; however, other authors[12] did not describe its decrease in the antrum atrophy either. Furthermore, the levels of G-17 were significantly higher in those with corpus and multifocal lesions due to an upregulation of G-17 by low acid output of the gastric glands[3,18]. Although women have significantly higher values of basal gastrin[24], statistically significant differences between men and women were not observed in the current study. Women also exhibit lower acid output than men[7], which may explain the higher levels of gastrin[24].

PGI levels were significantly lower in those with corpus atrophy and multifocal atrophy; nevertheless, sensitivities of 50% and 42.1%, respectively, were lower than those in a previous report (84%)[10] but similar to others[18] that did not recommend GastroPanel® for clinical practice. One explanation for this lower sensitivity in the present study was the small number of subjects with moderate to intense atrophy, different from the study that tested subjects with higher grades of atrophy[10].

The distribution of patients with gastric atrophy according to the OLGA stage[14] was comparable to that from Latin America, where most patients (50.2%) had OLGA stages I and II[25]. Similar to other studies[9], patients with a higher OLGA stage demonstrated a higher prevalence of decreased PGI levels; nevertheless, in this study, only 66.7% of patients with stages III and IV had decreased PGI levels. The risk for developing gastric cancer is higher in this group of patients who need to undergo endoscopy with careful follow-up[25]; therefore, the serological quantification of PGI was not accurate for atrophic gastritis screening.

The PGI/PGII ratio was significantly lower in all groups, except for neoplasia, of non-PPI users compared with controls. Conversely, the sensitivity was low (21–55%), which was in line with the results of previous reports that concluded that PGI/PGII ratio had little to no diagnostic accuracy[18]. The group with antrum atrophy, which had the highest prevalence of *H. pylori* infection, also exhibited a PGI/PGII ratio that was significantly lower than that of the controls. *H. pylori*-positive patients exhibited a lower PGI/PGII ratio[9,26] because PGI was reduced in relation to PGII, which increased due to infiltration by neutrophils and mononuclear cells in the antrum by *H. pylori* bacteria[26].

Previous studies[23] have shown that PPI use increases the levels of PGI; nevertheless, antacids/alginates or H_2 receptor antagonists did not influence G-17 and PGI serum levels. In the present study, PPIs increased the levels of PGI in controls and in the antrum atrophy group. Subjects with corpus and multifocal atrophies that were associated with decreased levels of PGI did not exhibit increased PGI levels with PPI use. The mechanism underlying the increase in PGI by PPI is unclear[8,23]; however, it has been suggested that PPIs stimulate PGI release directly from the gastric mucosa or through a gastrin link[23]. Results of the current study suggest that the corpus must be intact because, even with higher G-17 levels in corpus and multifocal atrophies, PPIs did not increase PGI levels.

The present study had limitations, including the lower sensitivity of PGI to indicate gastric atrophy compared with that of previous reports (84%)[10], which may be due to the small number of patients with moderate to intense atrophy (n=6). The group of patients with neoplasia was heterogeneous and small; however, GastroPanel® was not designed to diagnose gastric cancer. The *post*

hoc power was low for some analysis; thus, further study in a new cohort with antrum atrophy may clarify the role of G-17 reduced levels to indicate antrum atrophy, and the effect of PPI on serum levels of PGI in corpus and multifocal atrophies.

CONCLUSION

GastroPanel® (Gastrin-17, PGI, and PGI/PGII ratio) did not demonstrate high sensitivity in detecting gastric atrophy. Further studies involving a larger number of subjects with moderate to intense atrophy may improve accuracy of the results.

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Authors' contribution

RM Mattar R: study design, ELISA tests, data management, statistics, writing the article. Marques SB: study design, patient inclusion, gastrointestinal endoscopy, collected gastric biopsy samples, data management. Ribeiro IB, Visconti TAC, Funari M: patient inclusion, gastrointestinal endoscopy, collected gastric biopsy samples. de Moura EGH and all the other authors read and approved the final version of the manuscript.

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Mattar R, Marques SB, Ribeiro IB, Visconti TAC, Funari M, de Moura EGH. Acurácia diagnóstica do painel gástrico para gastrite atrófica em brasileiros e o efeito dos inibidores de bomba de prótons. Arq Gastroenterol. 2020;57(2):154-60.

RESUMO – **Contexto** – Foi proposto que a combinação de gastrina 17 (G-17), pepsinogênios I e II (PGI e PGII), e anticorpos anti-*Helicobacter pylori* (*H. pylori*) (GastroPanel®, BIOHIT HealthCare), poderiam indicar gastrite atrófica. **Objetivo** – Portanto, o objetivo foi averiguar a acurácia diagnóstica do painel gástrico e avaliar o efeito dos inibidores de bomba de prótons (IBP) nesses marcadores. **Métodos** – Pacientes dispépticos que se submeteram à endoscopia gastrointestinal entraram no estudo. Os achados histológicos foram o padrão ouro para estratificar os grupos: sem atrofia (controles), atrofia de antro, atrofia de corpo, atrofia multifocal e neoplasia. G-17, PGI, PGII, e anticorpos IgG anti-*H. pylori* foram determinados por kits comerciais. A razão PGI/PGII foi calculada. **Resultados** – Entre 308 pacientes que foram incluídos, 159 estavam usando IBP (51,6%). A prevalência de atrofia foi de 43,8% (135 pacientes). *H. pylori* foi positivo em 92 (29,9%) pacientes por IgG anti-*H. pylori*. G-17 não estava diminuída na atrofia do antro, mas estava elevada nas atrofias do corpo e multifocal. PGI estava significantemente menor nas atrofias de corpo e multifocal. A sensibilidade da PGI <30 µg/L de indicar atrofia do corpo foi 50% (95%IC 27,8–72,1%) com especificidade de 93,2% (95%IC 84,3–97,5%), razão de verossimilhança positiva de 7,4 (95%IC 2,9–19,2) e razão de verossimilhança negativa de 0,5 (95%IC 0,3–0,8). O número de indivíduos com atrofia moderada para intensa foi pequeno (n=6; 4%), dos quais 66,7% tinham diminuição dos níveis de PGI. IBP significantemente aumentou os níveis de G-17 e PGI, exceto nas atrofias de corpo e multifocal que não apresentaram aumento de PGI. **Conclusão** – O painel gástrico não teve alta sensibilidade de indicar gastrite atrófica.

DESCRITORES – Pepsinogênio A. Gastrinas. Gastrite atrófica. *Helicobacter pylori.*

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