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Alimentary Tract

Clinical usefulness of serum pepsinogens I and II, gastrin-17 and anti-*Helicobacter pylori* antibodies in the management of dyspeptic patients in primary care

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Abstract

Background. Several tests have been proposed for evaluating dyspeptic symptoms and their relationship to the underlying gastric disease. Serum pepsinogens and gastrin-17 are known to be useful biomarkers for the detection of gastric pathologies.

Aim. To evaluate the capability of screening dyspeptic patients in the primary care by analyses of serum pepsinogens I (sPGI) and II (sPGII), gastrin-17 (sG-17) and the IgG anti-*Helicobacter pylori* antibodies (IgG-Hp).

Patients and methods. Three hundred and sixty-two consecutive patients with dyspeptic symptoms (208 females, mean age 50.6 ± 16 years, range 18–88 years) referred by general practitioners for upper gastrointestinal endoscopy were enrolled. A blood sample was taken from each subject for IgG-Hp, sPGI, sPGII and sG-17 analyses.

Results. Two hundred and eighty-seven patients had a complete screening; of these, 132 resulted positive for *Hp* infection. Patients with atrophic chronic gastritis showed significantly lower serum pepsinogen I levels and sPGI/sPGII ratio than patients with non-atrophic chronic gastritis. Moreover, by calculating the values of sPGI by sG-17 and sG-17 by sPGII/sPGI, subjects with atrophic chronic gastritis could be distinguished from those with non-atrophic chronic gastritis and from those with normal mucosa, respectively. sG-17 levels were found to be a useful biomarker for the detection of antral atrophic gastritis, while the combination of sPGI, the sPGI/sPGII ratio and sG-17 was found effective in identifying corpus atrophy.

Conclusion. A panel composed of PGI, PGII, G-17 and IgG-Hp could be used as a first approach in the 'test and scope' and/or 'test and treat' strategy in the primary care management of dyspeptic patients.

Keywords: Chronic gastritis; Dyspeptic patients; Gastrin-17; IgG anti-*H. pylori*; Serum pepsinogens

1. Introduction

Approximately 25–40% of the general population has experienced dyspeptic symptoms [1,2]. Management of these patients occurs at the primary care level, and as such, most patients are treated without confirmatory analyses [3–5]. *H. pylori* is known to be the causal agent for several gastroduodenal diseases [6–9]. The infection is initially confined to the antrum, causing a superficial gastritis, which then progresses to pangastritis or corpus predominant gastritis, often developing into atrophy over several years [10]. Atrophic gastritis

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can be related to autoimmune diseases, although this is less frequent in Western Europe. Several diagnostic tests are performed to evaluate dyspeptic symptoms, including upper gastrointestinal endoscopy, radiography and testing for *H. pylori* infection [11–14]. Endoscopy with biopsy remains the gold standard method for the diagnosis of most of the conditions associated with dyspepsia and provides information about *H. pylori* infection, the presence of atrophy, intestinal metaplasia or dysplasia, as well as their topographical distribution [15]. This invasive method is uncomfortable, distressing and very expensive. Current interests lie in finding rapid, reliable and inexpensive non-invasive tests for screening and monitoring patients with mild to moderate dyspeptic symptoms [16]. ^{13}C-UBT and *H. pylori* stool antigen (HpSA) analyses are often used, but they do not offer information about the morphological status of gastric mucosa [17,18].

Recently, the determination of serum pepsinogens I (sPGI) and II (sPGII), gastrin-17 (sG-17) and IgG anti-*H. pylori* antibodies (IgG-Hp) by ELISA has been proposed as a series of non-invasive markers for the assessment of both morphological and functional status of gastric mucosa in subjects with dyspeptic symptoms [19,20]. PGI and PGII are both precursors of pepsin. PGI, exclusively secreted by oxyntic glands, is a specific marker of corpus secretion capacity. Conversely, PGII produced by all gastric glands (oxyntic, cardiac and pyloric) as well as duodenal (Brunner's) glands is strongly influenced by gastric inflammation [21,22]. These precursors are secreted into the gastric lumen, but only a small amount, which is measurable, leaks into the blood stream. Gastrin-17 (G-17), produced exclusively in the antrum and secreted directly in the blood, represents a specific marker of G cell functionality [23]. Studies have shown that sPGI, sPGII and sG-17 levels are high in the presence of *H. pylori* related to non-atrophic chronic gastritis (NACG) [24,25]. SPGI and sPGII concentrations are found to decrease significantly 2 months after a successful *H. pylori* cure [26–28]. Similarly, sPGI levels and the calculated value, sPGI·gastrin, are found to predict the presence of gastric cancer [29–31]. Indeed, sPGI and/or sPGI/sPGII levels are considered serological markers of atrophic body gastritis [32–34]. In the latter condition, G-17 levels are significantly high. Conversely in antral atrophy, they become very low due to the exiguity number of G cells [23].

The correlations between the above-mentioned variables and related histological patterns of gastritis could give a first selection of patients, who need an upper gastrointestinal endoscopy with multiple biopsies to identify precancerous gastric conditions or lesions [35].

The aim of the present study was to evaluate dyspeptic patients in the primary care by means of a panel of non-invasive serological tests (PGI, PGII, G-17 and IgG-Hp) and to establish the accuracy of these tests to identify patients with atrophic chronic gastritis (ACG) in whom gastroscopy and biopsy should be performed.

2. Patients and methods

2.1. Patients

This study was conducted in two gastroenterological centres in Italy (in Belluno, located in the mountains of north-eastern Italy and in Parma, located on the agricultural plain in central Italy). The policy of 'open access' to endoscopy was adopted by each centre, to which general practitioners (GP) could directly refer patients for further investigation when needed.

After a series of meetings aimed at informing the GPs about the relevance of sPGI, sPGII, sG-17 and IgG-Hp analyses in the detection of gastroduodenal pathologies, 36 GPs agreed to participate to the study (16 from Belluno and 20 from Parma). Each GP consecutively selected patients eligible for upper gastrointestinal endoscopy on the basis of the clinical picture of dyspepsia. Dyspepsia was defined as a mean chronic or recurrent pain or discomfort in the upper abdomen according to Talley et al. [36].The GPs proposed to patients a pre-endoscopy management strategy including treatment with antacids or prokinetics.

A total of 362 consecutive patients with dyspeptic symptoms (208 females, mean age 50.6 ± 16 years, range 18–88 years) were enrolled from May to October 2003.

Epidemiological data including smoking habit and alcohol intake, as well as previous diseases and NSAID consumption, were collected during structured interviews by the single GP for a period of 15 working days from the start of the study.

Patients with previous gastroduodenal surgery, malignancies of any type, hepatic or renal failure, or under therapy with proton pump inhibitors or H_2 receptor antagonists were excluded from the study.

2.2. Determination of sPGI, sPGII, sG-17 and IgG-Hp

After completing the interview, blood samples (5 ml) were drawn from each patient and sent to the respective laboratories in Parma and Belluno. Samples were stored before analysis in four centrifuged aliquots at $-20\,^{\circ}$C for determination of sPGI, sPGII, sG-17 and IgG-Hp levels by enzyme linked immunosorbent assay (ELISA), according to the manufacturer's instructions (Biohit, Helsinki, Finland).

Normal values were as follows: sPGI: 25–100 μg/L, sPGII: 2–10 μg/L, sG-17: 2.5–7.5 pmol/L and IgG-Hp titres: <44 IU.

2.3. Histological examination and assessment of H. pylori status

During the upper gastrointestinal endoscopy, sample biopsies were taken from different stomach sites (two from the antrum, two from the corpus and one from the incisura) for histological examination. Serial sections (5 μm thick) prepared from formalin-fixed biopsy samples were embedded in paraffin and stained with haematoxylin and eosin for

conventional histological analysis and with modified Giemsa for the detection of *H. pylori*.

The Updated Sydney Classification System was used to assess gastritis [37]. We defined ACG as any form of moderate or severe atrophy with or without intestinal metaplasia and associated with chronic inflammation. NACG was defined as the presence of chronic inflammation with or without infiltration of polymorphonuclear cells, in the absence of moderate or severe signs of gland loss in the antrum or corpus. Patients were divided according to the topographical distribution of atrophic gastritis: antrum-predominant atrophic gastritis (APAG) when the atrophy score was higher in the antrum, multifocal atrophic gastritis (MAG) when the atrophy score was equal in the antrum and corpus and corpus-predominant atrophic gastritis (CPAG) when the atrophy score was higher in the corpus.

Both the pathologists and the biologists were masked. Blood test and histology results were sent to the clinical researchers.

2.4. Accuracy of serological tests to discriminate ACG

Patients were classified as Normal (with normal gastric mucosa), NACG and ACG in a masked way by gastroenterologists, interpreting the serological parameters by means of the following empirical criteria:

- Active *H. pylori* infection: IgG-Hp $\geq$ 38 IU and sPGII $\geq$ 16 μg/L or IgG-Hp $\geq$ 40 IU and sPGII $\geq$ 8 μg/L or IgG-Hp > 90 IU.
- CPAG: sPGI $\leq$ 25 μg/L and gastrin-17 > 10 pmol/L.
- MAG: sPGI $\leq$ 25 μg/L and gastrin-17 $\leq$ 10 pmol/L or sPGI < 50 μg/L and gastrin-17 $\leq$ 10 pmol/L in *H. pylori*+ve patients.
- APAG: G-17 $\leq$ 3 pmol/L and sPGI > 25 μg/L in *H. pylori*+ve patients.

According to the serological key of lecture described above, the histological patterns of patients with ACG were compared and classified as: a, true positive; b, false positive; c, false negative; and d, true negative. Sensitivity was calculated as a/a + c; specificity as b/b + d; positive predictive value (PPV) as a/a + b; negative predictive value (NPV) as d/d + c; overall accuracy: (a + d)/(a + b + c + d).

2.5. Statistical analysis and ethical approval

All measured parameters were expressed as means and standard deviation. The means of variables were compared by Mann–Whitney rank-sum test. The test was considered significant if the *p*-value was less than 0.05. The analysis was performed using the SPSS 10.1 Software version 2004 (Chicago 606006, Illinois, USA).

Informed consent was obtained from all participants in agreement with the Declaration of Helsinki.

3. Results

Seventy-five patients were excluded from the study because they were under therapy with proton pump inhibitors. Of the remaining 287 patients, 132 were positive for *H. pylori* infection (68 females, mean age 51.2 ± 16.1 years, range 19–83 years) and 155 were negative (mean age 48.0 ± 16.5 years, range 18–88 years). *H. pylori*-positive patients demonstrated significantly higher mean sPGI (120.6 ± 63.2 μg/L), sPGII (15.9 ± 1.0 μg/L) levels and IgG-Hp titres (73.1 ± 32.6 IU) than *H. pylori*-negative patients (sPGI: 88.2 ± 50.7 μg/L; sPGII: 8.9 ± 7.9 μg/L; IgG-Hp: 20.7 ± 21.3 IU; $p < 0.001$ for all comparisons). Conversely, the sPGI/sPGII ratio was significantly lower in positive (9.6 ± 5.6) versus negative patients (11.8 ± 7.7; $p < 0.001$). No statistically significant difference in sG-17 levels was found between the two groups (Table 1).

Histological analyses identified 138 patients with a normal gastric mucosa (84 females, mean age 46.9 ± 16.4 years, range 18–88 years), 89 patients with NACG (50 females, mean age 48.6 ± 16.4 years, range 19–81 years) and 60 patients with ACG (32 females, mean age 56.7 ± 14.3 years, range 20–83 years).

3.1. Non-atrophic versus atrophic chronic gastritis

The NACG group had higher levels of both serum pepsinogens (sPGI: 121.5 ± 62.5 μg/L; sPGII: 15.7 ± 10.4 μg/L) and IgG-Hp titres (71.9 ± 32.8 IU) than normal patients (sPGI: 98.4 ± 49.8 μg/L; sPGII: 9.0 ± 8.0 μg/L; IgG-Hp: 21.7 ± 13.8 IU; $p < 0.001$ for all comparisons), accompanied by a significantly lower sPGI/sPGII ratio (NACG: 9.4 ± 4.8; normal: 13.1 ± 7.4; $p < 0.001$). Similarly, the ACG group had significantly higher IgG-Hp titres (58.1 ± 37.2 IU) and sPGII (13.9 ± 10.1 μg/L) levels, and a significantly lower sPGI/sPGII ratio (7.7 ± 6.6) than normal patients ($p < 0.001$ for all comparisons). Furthermore, the ACG group had a significantly lower sPGI/sPGII ratio ($p = 0.003$), sPGI levels ($p < 0.001$) and mean IgG-Hp titres ($p = 0.016$) than the NACG group. Table 2 summarises the results of serological tests in patients divided according to histological findings, as described above. Patients with ACG had a significantly lower

Table 1
Mean and standard deviation of sPGI, sPGII, sPGI/sPGII ratio, sG-17 and IgG-Hp in relation to *H. pylori* infection

H. pylori status	sPGI (μg/L)	sPGII (μg/L)	sPGI/sPGII ratio	sG-17 (pmol/L)	IgG-Hp titres (IU)
Negative ($N = 155$)	88.2 ± 50.7	8.9 ± 7.9	11.8 ± 7.7	12.8 ± 31.4	20.7 ± 21.3
Positive ($N = 132$)	120.6 ± 63.2*	15.9 ± 1.0*	9.6 ± 5.6*	8.4 ± 17.5	73.1 ± 32.6*

* $p < 0.001$ for positive vs. negative *H. pylori* status.

Table 2
Mean and standard deviation of sPGI, sPGII, sPGI/sPGII ratio, sG-17 and IgG-Hp in relation to histological findings

Histological findings	sPGI (μg/L)	sPGII (μg/L)	sPGI/sPGII ratio	sG-17 (pmol/L)	IgG-Hp titres (IU)
Normal ($N = 138$)	98.4 ± 49.8	9.0 ± 8.0	13.1 ± 7.4	6.9 ± 20.7	21.7 ± 13.8
NACG ($N = 89$)	121.5 ± 62.5[a]	15.7 ± 10.4[a]	9.4 ± 4.8[a]	8.3 ± 10.8	71.9 ± 32.8[a]
ACG ($N = 60$)	87.1 ± 66.3[c]	13.9 ± 10.1[b]	7.7 ± 6.6[b,c]	21.0 ± 41.4	58.1 ± 37.2[b,c]

NACG: non-atrophic chronic gastritis, ACG: atrophic chronic gastritis.
[a] NACG vs. Normal group ($p < 0.001$ for all parameters).
[b] ACG vs. Normal group ($p < 0.001$ for all parameters).
[c] ACG vs. NACG group (sPGI: $p < 0.001$; sPGI/sPGII: $p = 0.003$; IgG-Hp: $p = 0.016$).

Table 3
Performance characteristics of the serological parameters (IgG-Hp, sPGI, sPGII and gastrin-17) considered as a unique test to discriminate between patients with ACG and non-atrophic gastric mucosa (histological normal gastric mucosa or NACG)

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	PPV (%) (95% CI)	NPV (%) (95% CI)	Accuracy (%) (95% CI)
Serological panel test	64 (59–70)	93 (90–96)	70 (75–64)	91 (88–94)	87 (91–83)

PPV: positive predictive value; NPV: negative predictive value.

calculated sPGI·sG-17 value (495.7 ± 121) than patients with NACG (1099 ± 208; $p = 0.002$). Additionally, subjects with ACG had a significantly higher sG-17·sPGII/sPGI value (17.03 ± 15) than normal patients (0.77 ± 0.6, $p = 0.002$).

With regards to age, a statistically significant difference was found between normal (46.9 ± 16.4 years) patients and the ACG (56.7 ± 14.3 years; $p < 0.001$) group, and the ACG and the NAGC (48.6 ± 16.4 years; $p = 0.004$) group.

3.2. Site-specific ACG

Regarding the 60 patients with ACG, 35 had APAG, 8 had MAG and 17 had CPAG. Positive *H. pylori* infection was found in 32/35 APAG patients (91.2%), 5/8 MAG patients (62.5%) and 2/17 CPAG patients (13.3%). The APAG group had significantly higher mean serum pepsinogen levels (sPGI: 117 ± 50.7; sPGII: 17 ± 9) and IgG-Hp titres (72.9 ± 30.3), as well as a significantly lower sPGI/sPGII ratio (9.5 ± 5.2) than normal patients (sPGI, $p < 0.03$; sPGII, $p < 0.001$; IgG-Hp, $p < 0.001$; sPGI/sPGII ratio, $p = 0.002$). Patients with APAG had significantly lower levels of sG-17 (3.8 ± 2) than patients with NACG (8.3 ± 10.8, $p = 0.01$), while no statistically significant difference was found when compared to normal patients (6.9 ± 20.7). sPGI levels were significantly lower in patients with MAG (78.9 ± 40.2) than in patients with NACG ($p = 0.02$). Additionally, patients with MAG had lower sPGI/sPGII ratio (9.2 ± 5) and higher anti-*Hp* levels (61.4 ± 25.6) than normal ($p < 0.001$ for both comparisons). Patients with CPAG had the lowest sPGI (28.1 ± 15.8) and sPGI/sPGII ratio (3 ± 2.2) levels than all the other groups ($p < 0.05$) and a significantly higher sG-17 levels (62.2 ± 30.5) compared to normal, NACG and APAG ($p < 0.001$ for all comparisons). Patients with CPAG had lower IgG-Hp titres (24.7 ± 15.6) than NACG, APAG and MAG ($p < 0.001$ for all comparisons). Fig. 1a–e illustrate the results of these serological tests in relation to site-specific atrophic gastritis.

3.3. Endoscopical and histological findings

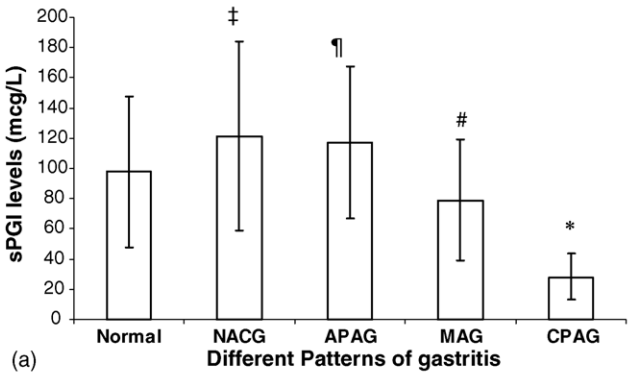
Of the 287 patients considered for the analysis, we detected 20 gastroduodenal focal lesions: five gastric erosions, six gastric ulcers, seven duodenal ulcers, one prepyloric polyp and one gastric leiomyoma. According to a 'test and scope' strategy, we missed eight (40%) and six (30%) gastroduodenal focal lesions by means of *H. pylori* serology and all four serological parameters, respectively. Endoscopies saved were similar: 57% with *H. pylori* serology and 55% with all the serological parameters. From endoscopies saved by *H. pylori* serology 24 out of 60 (33%) were ACG, of whom 15 out of 17 (88%) were CPAG. Otherwise, we missed 13 out of 60 (21.6%) of ACG, of whom only 2 out of 17 (12%) were CPAG, by means of serological parameters.

3.4. Accuracy of serological parameters to detect ACG

Interpreting all the four serological parameters as a unique test as mentioned in the methods, the same 287 patients were distinguished in: 157 normal, 76 with NACG and 54 with ACG of whom were 35 APAG, 4 MAG and 15 CPAG. Sensitivity, specificity, positive predictive and negative predictive values and overall accuracy of the serological diagnosis in comparison to histology were 64, 93, 70, 91 and 87%, respectively (Table 3).

4. Discussion

This study was aimed to validate a non-invasive test or panel of tests to evaluate, at the primary care level, patients with dyspeptic symptoms and to select subjects in whom gastroscopy with biopsy should be done. The relationship of sPGI, sPGII, sG-17 and IgG-Hp levels to histological gastric mucosal damage was assessed. It is well known that the GP must have a fast, reliable and inexpensive test to identify

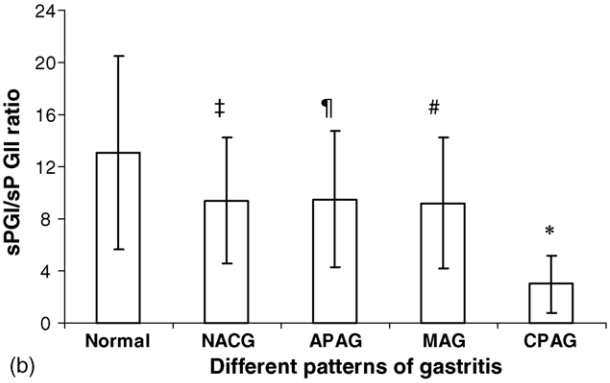


‡ NACG *versus* Normal group (p<0.001)

¶ APAG *versus* Normal group (p=0.03)

MAG *versus* NACG group (p= 0.02)

* CPAG *versus* all the other groups (p<0.05)

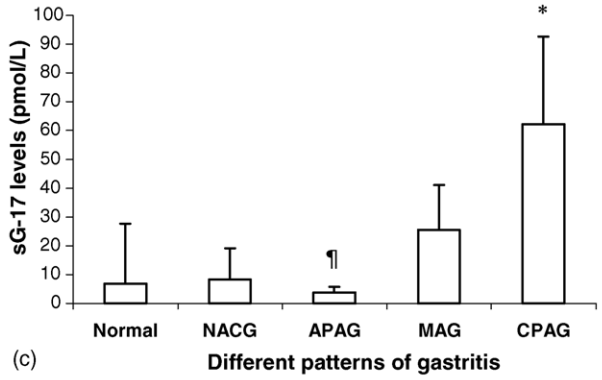


‡ NACG *versus* Normal group (p<0.001)

¶ APAG *versus* Normal group (p=0.002)

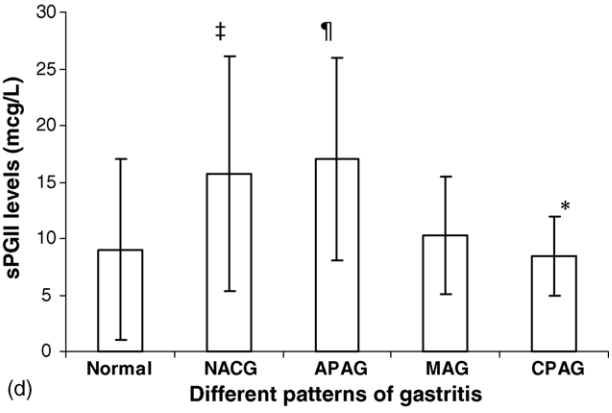
MAG *versus* Normal group (p=0.002)

* CPAG *versus* all the group (p<0.05)



¶ APAG *versus* NACG group (p=0.01)

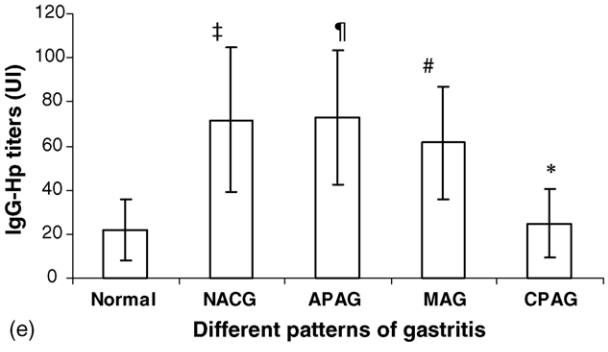
* CPAG *versus* Normal, NACG and APAG group (p<0.001)



‡ NACG *versus* Normal group (p<0.001)

* CPAG *versus* NACG and APAG group (p<0.001)

¶ APAG *versus* Normal group (p<0.001)



‡ NACG *versus* Normal group (p<0.001)

¶ APAG *versus* Normal group (p<0.001)

MAG *versus* Normal group (p<0.001)

* CPAG *versus* NACG, APAG and MAG group (p<0.001)

Fig. 1. sPGI (a), sPGI/sPGII ratio (b), sG-17 (c), sPGII (d) and IgG-Hp (e) levels in relation to the histological group. Normal, normal histology ($n = 138$); NACG, non-atrophic chronic gastritis ($n = 89$); APAG, antrum-predominant atrophic gastritis ($n = 35$); MAG, multifocal atrophic gastritis ($n = 8$); CPAG, corpus-predominant atrophic gastritis ($n = 17$).

patients with dyspepsia who are in need of a more thorough, yet invasive and costly, diagnostic confirmation. The present study involved a sample of dyspeptic patients with not improved moderate or severe symptoms after a trial of empiric therapy that warranted upper gastrointestinal endoscopic examination to exclude organic diseases. We decided, in this preliminary study, to exclude 75 out of 362 (21%) patients under gastric antisecretory therapy because of the potential influence of these drugs on serum pepsinogens and G-17 levels [38]. However, in our mind, this serological approach could be also extended to these kinds of patients, although modifying the key lecture of serological parameters. This aspect will be analysed elsewhere.

ELISA techniques, performed in most medical laboratories, were used for the determination of serum pepsinogens, sG-17 and IgG-Hp titres. These simple and widely available serological tests were shown to accurately reflect true histological status in patients with un-alarming dyspeptic symptoms (i.e. no weight loss, anaemia, vomiting, etc.). In accordance with a previous report by Plebani et al. [24], serum pepsinogen levels were significantly higher, and the relative sPGI/sPGII ratio lower in *H. pylori*-positive versus negative subjects. IgG-Hp levels demonstrated 85% sensitivity and 79% specificity for the detection of *H. pylori* infection [39]. Furthermore, high levels of serum pepsinogens, and in particular sPGII levels, accompanied by positive serology for *H. pylori*, supported the diagnosis of *H. pylori*-related chronic gastritis. Serum pepsinogens and IgG-Hp were found to be useful in distinguishing subjects with non-atrophic gastritis (NACG) from those with normal mucosa, who were found to have significantly lower values. This finding was confirmed by a recent study reported by Väänänen et al. [40]. Independent from the site of the atrophic lesion, ACG subjects had lower mean sPGI levels and a lower sPGI/sPGII ratio than NACG subjects. Interestingly, the calculated values, sPGI·sG-17 and sG-17·sPGII/sPGI, were found to be clinically significant in discriminating subjects with ACG from those with NACG and from those with normal mucosa, respectively. Furthermore, we obtained a very good accuracy to discriminate ACG from NACG or normal patients interpreting all the four serological parameters simultaneously. Patients with serological markers indicative of ACG were significantly older than patients with normal mucosa and with NACG. This was to be expected since it is well known that ACG develops approximately 20 years after *H. pylori* acquisition, and that the prevalence of *H. pylori* infection in this age group is about 60%. High positivity for anti-*H. pylori* antibodies in the ACG group suggests that this gastritis phenotype is a sequela of a long term *H. pylori* infection [41,42]. As recommended by the Consensus Conference of Maastricht 2000 [43], patients with a positive *H. pylori* infection in combination with high levels of sPGII were prescribed *H. pylori* eradication therapy.

Patients were further studied by subdividing atrophic gastritis cases by site of gland loss. sG-17 levels were found to be a good marker for detecting APAG. Furthermore, a significant increase of both serum pepsinogens and IgG-Hp in this group of patients reflected the presence of an active *H. pylori* infection. In fact, 32/35 APAG patients had histological evidence of *H. pylori* infection. This finding was confirmed by a previous study [44].

Patients with MAG had significantly lower sPGI levels as compared to NACG patients, and slightly high sG-17 levels, but neither statistically different from APAG or from CPAG. In our mind and according to the results of Sipponen et al. [23], serological MAG could be distinguished by low levels of both sPGI and G-17. Furthermore, sPGII, known to be produced both in the antrum and corpus, was in the normal range. Samloff et al. [45] also reported that sPGII levels were normal in severe atrophic gastritis. This lack of an association with atrophic gastritis is probably due to the fact that sPGII is also produced by metaplastic pyloric glands.

As reported by other studies, sG-17 and sPGI levels and the sPGI/sPGII ratio remain optimal biomarkers for the detection of CPAG. Conversely, mean sPGII and IgG-Hp levels were in the normal range, indicating the absence of an *H. pylori* infection. In fact, only 2/17 CPAG patients had histological evidence of *H. pylori* colonisation. Karnes et al. and Annibale et al. reported the inverse correlation between the histological gastric atrophy score and IgG-Hp levels. Both the studies found that in patients with corpus atrophic gastritis, the greater the degree of glandular loss, the lower the IgG-Hp levels [46,47]. Recently, Kokkola et al. followed 47 patients with atrophic body gastritis for 6 years endoscopically, as well as an additional 4 years using serum IgG-Hp. None of these patients was treated for *H. pylori* infection during the 10-year period. They concluded that *H. pylori* antibodies disappear spontaneously within 10 years in almost one-fourth of patients with severe atrophic corpus gastritis [48].

With regards to the macroscopic aspects of gastric mucosa, we found similar results about both missing gastro-duodenal focal lesions and upper endoscopies saved by means of serological parameters and *H. pylori* serology, respectively. However, our aim is to search also for histological gastric mucosa damage and not simply to know if the patients are or not *H. pylori* infected. In this way, in our results, from endoscopies saved by *H. pylori* serology we missed 88% of CPAG, whereas only 12% were missed by means of serological parameters.

From a cost-effective perspective, endoscopy with histological examination is three to four times more expensive than the ELISA test for the determination of serum pepsinogens, gastrin-17 and IgG-Hp: an ELISA assay costs approximately €30, while endoscopy with biopsy/histology costs approximately €130. With the current interest in cost reduction and the required justification of expenditures in health care, inexpensive diagnostic tests are a growing necessity in primary care medicine.

In summary, analyses of serum pepsinogen, sG-17 and IgG-Hp levels offer important information regarding the presence of *H. pylori*-related chronic gastritis as well as the site of the gastric atrophy. Patients with normal sPGI, sPGII, sG-17

and IgG-Hp can be reassured that they do not have an ulcerative disease, and can be treated symptomatically. Patients with panel test results indicating the presence of *H. pylori*-related chronic gastritis, with or without atrophic lesions, should be prescribed *H. pylori* eradication therapy to cure the underlying ulcerative process [49]. This series of tests could be recommended as a first approach to dyspeptic patients, once the presence of alarming symptoms is excluded. Thus, in our mind, this panel of tests could provide more complete information than a simple test searching for *H. pylori* infection in the management of patients with dyspeptic symptoms.

Studies are needed to confirm these results and before recommending their widespread clinical application as non-invasive first-pass markers of gastric disease.

Conflict of interest statement

None declared.

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