Cross-sectional Study

Serum pepsinogen: A potential non-invasive screening method for moderate and severe atrophic gastritis among an asian population

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ARTICLE INFO	ABSTRACT
Keywords: Atrophic gastritis Pepsinogen Biomarker Diagnostic value Cut-off values	*Background:* Serum pepsinogen has been approved and used widely as an effective biomarker in diagnosis of atrophic gastritis and gastric cancer; however, its validity and appropriate cut-off values vary among different populations. This study aimed to initially assess the diagnostic value of the serum pepsinogen in diagnosis of moderate and severe atrophic gastritis for Vietnamese population. *Materials and methods:* A cross-sectional study enrolled 273 participants from June 2008 to November 2019. All participants underwent a gastroscopy procedure and three tests including serum PG test, pathology test, and Hp-Igg Elisa test. The Kimura-Takemoto classification and OLGA system were used to classify the mild versus moderate-severe atrophic gastritis. Receiver Operating Characteristic curve was used to assess the value of PGI, PGII and PGR. *Results:* Based on Kimura-Takemoto classification, the AUC of PGI and PGR was 0.635 ($p = 0.008$, 95% CI 0.554–0.716) and 0.766 ($p < 0.001$, 95% CI 0.676–0.857) respectively. The best cut-off values were PGI $\leq$69.0 and PGR $\leq$4.6 (sensitivity: 73%, specificity: 83.9%, positive predictive value: 41.5%, negative predictive value: 95.2%, accuracy: 82.4%). According to the OLGA system, the AUC of PGI and PGR was 0.612 ($p = 0.004$, 95% CI 0.540–0.684) and 0.689 ($p < 0.001$, 95% CI 0.621–0.758) respectively. The best cut-off values were PGI $\leq$63.5 and PGR $\leq$5.2 (sensitivity: 49.4%, specificity: 82.1%, positive predictive value: 52.1%, negative predictive value: 80.5%, accuracy: 72.9%). *Conclusions:* The serum pepsinogen II and pepsinogen I/II ratio had reliable diagnostic value for screening of moderate and severe atrophic gastritis among Vietnamese population. Further research was recommended to focus on larger scale to improve the diagnostic yield and to continue finding the cut-off values for diagnosis of gastric cancer among Vietnamese population.

1. Introduction

Gastric cancer was the fourth leading cause of cancer mortality [1–4]. However it can be well treated and have a good prognosis if it is detected early from initial likely-precancerous lesions, particularly atrophic gastritis, a common progressive disease [5–8]. Atrophic gastritis, from beginning mild lesions, may develop to moderate and severe ones which were considered as the high-risk group of gastric cancer [6]. Therefore, in order to reduce cancerous risk, the early

detection of high-risk group with moderate and severe atrophic gastritis lesions should be implemented [7]. However, these lesions are usually asymptomatic in populations, which make it difficult to be identified by recommendedly assigned modern techniques such as endoscopy or guided biopsies. Therefore, the needs for non-invasive technique for screening program of atrophic gastritis lesions among local community has been required.

Serum pepsinogen (PG) has been identified and considered the most effective non-invasive biomarker available for diagnosis of severe

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atrophic gastritis or gastric cancer in the community [9–16]. PG can be classified immunologically into two types: pepsinogen I (PGI) and pepsinogen II (PGII) and the pepsinogen ratio (PGR: PGI/PGII) was also calculated [11]. However, the use of it is still controversial [17,18], since it is also recommended to use with cautions [13] and its cut-off values vary from population to population [9,19,20]. Recently, the cut-off values of PGI ≤70 ng/ml and/or PGR ≤3 were widely accepted [12,21] while the best cut-off value for atrophy gastritis was PGI ≤50.3 ng/ml and the cut-off point for severe atrophy was PGR ≤4.28 in China [10]. In contrast, serum pepsinogen was assessed as an un-useful biomarker in Iran [18], or using serum pepsinogen alone is not enough for screening [17]. Therefore, the research on the diagnostic yield of serum pepsinogen to optimize its value for each local community population is essential.

In Vietnam, the incidence and mortality rate of gastric cancer was greater than 16.4 per 100 000 in males, and greater than 8.2 per 100 000 among females, which are higher than other parts of the world [1]. Additionally, *H. pylori* infection is common in Vietnam with up to 65.6%, and it was strongly related to peptic ulcer, active gastritis, atrophy, and intestinal metaplasia, which could be precancerous lesions [22]. Therefore, the screening programs with simple and non-invasive method to identify people in the high-risk group of gastric cancer, especially people with moderate or severe atrophic gastritis are important. Currently, the primary methods to diagnosis atrophic gastritis in Vietnam are gastroscopy and pathology which are infeasible for large screening in the community. To our best knowledge, there has been no any studies on serum pepsinogen and its diagnostic value adapting to Vietnamese population. This study aimed to initially assess the diagnostic value of serum pepsinogen in diagnosis of moderate and severe atrophic gastritis among Vietnamese people.

In such developing countries as Vietnam, endoscopy is more commonly used in clinical practice as the gold standard of the atrophic gastritis investigation, whereas many studies commonly use pathology results, an expensive and complex but more accurate gold-standard method. In this study, we compared the PG cut-off to both endoscopy and pathology results to identify the diagnostic value of PG. Thus, the resulting data will be useful to clinicians in practice, and could also be a reference to other studies over the world.

2. Methods

Our study has been reported in line with the STROCSS criteria [23] and has been registered at the Research Registry with the Unique Identifying Number: researchregistry7907.

This cross-sectional study enrolled 273 patients of Department of Gastroenterology and Hepatology in Bach Mai Hospital, a national and largest hospital in Vietnam in Internal Medicine area, from June 2018 to November 2019.

2.1. Participants

The inclusion criteria was patients over 40 years old who underwent gastroscopy procedure. The exclusion criteria were as the followings: patients diagnosed with gastroesophageal reflux disease, peptic ulcer or gastric cancer; patients who underwent gastric resection; patients who had unclear atrophic borders on the gastroscopy images according to Kimura Takemoto classification; and patients who could not give enough Pepsinogen serum for PG I, PG II, and *Hp*-Igg antibody tests.

2.2. Study processes

All participants were made to undergo a gastroscopy procedure and three tests including serum PG test, pathology test, and *H. pylori* test. All of these process and tests were performed within one day. All participants were also interviewed by researchers or nurses based on a designed questionnaire, in which they were asked about their eating habits, physical activity habits, comobidities, and medicine intake history.

2.3. Gastroendoscopy procedure

All gastroscopy procedures were performed by senior endoscopists who had at least five years of professional experience. Before the gastroscopy procedure, patients were checked up and made to drink a mix of 1 mg/ml Simethicone x 50 ml of water 30 min before the procedure in order to decrease gastric foam and improve the mucosal visibility [24]. Endoscopy machines Fujinon or Olympus 180 then would be used in the gastroscopy procedure to assess the atrophic gatritis level based on the Kimura-Takemoto classification [25–27]. Kimura-Takemoto classification includes 2 main types: type Close (C) and type Open (O). Type C was divided into C1, C2, and C3. Type O was divided into O1, O2, and O3. In this study, we divided gastritis into two following levels: mild atrophic gastritis (MAG) group – including C1 and C2, and moderate and severe atrophic gastritis (MSAG) group – including C3, O1, O2 and O3.

2.4. Pathology test with OLGA (Operative Link on Gastritis Assessment) staging system

During the gastroscopy procedure, the biopsy was performed in order to assess the atrophic gastritis status. The biopsy was done at five different places in stomach as the followings: 2 biopsy specimens at pyloric antrum with 2 cm from the pylorus at the front and the back of stomach wall, 2 biopsy specimens at gastric body at the front and the back of stomach wall, and 1 biopsy specimen at the lesser curvature corner. All of these biopsy specimens then were pathologically analyzed according to OLGA staging system [8,28]. Based on OLGA stages, patients were divided into two following levels: mild atrophic gastritis (MAG) group – including stages 0 and I, and moderate and severe atrophic gastritis (MSAG) group – including stages II, III, and IV.

2.5. Serum pepsinogen test

Each participant was asked to give 3 ml blood for serum pepsinogen test. Blood samples were centrifuged for 10 min at 1500 RCF. Serum samples were stored at −70 °C while waiting for examination. Serum pepsinogen level was assayed by Chemiluminescent Microparticle Immuno Assay method using Architect IR 4000 (Abbott) Pepsinogen I and II Readgent Kit.

2.6. Helicobacter pylori test

H. pylori infection was determined on the results of pathology test.

2.7. Study ethics

This study was one part of the national-level research named "Apply Molecular Biology, Biochemistry, and Endoscopic techniques into Early Gastric Cancer Screening, Diagnosis, and Treatment", which was approved by Ethics Committee at Bach Mai hospital with Decision number 2795/QĐ-BM. Participants who took part in the study were explained sufficiently about the aims and the contents of the research and asked for their consent by documents.

2.8. Data analysis

We used Epidata for data entry and management. Normally distributed data were reported with mean ± Standard deviation (SD), and abnormal distributed data were reported with median (IQR). Regarding testing differences of numeric data, Independent-samples *t*-test and Mann-Whitney *U* test were employed for normally distributed and non-normally distributed data respectively. Chi-square test was employed to

assess the categorical data. The correlation between all pepsinogen parameters or between pepsinogen and other numeric variable was analyzed separately using bivariate Pearson or Spearman correlation test if applicable. Receiver Operating Characteristic (ROC) curve and AUC (area under the curve) were used to assess the value of PGI, PGII, PGR. The most appropriate cut-off values were determined by maximizing the Youden's index [29,30]. Statistical analysis was performed by SPSS statistical software (SPSS IBM 25.0). a p value < 0.05 was considered statistically significant.

3. Results

3.1. Patient characteristics

The mean (SD) age of the patients was 56.3 (9.7), ranging from 40 through 84 years old. The female: male ratio was 1.53:1, with 108 males. The *H. pylori* infection rate among the participants was 34.1% (93/273).

A majority of the patients was diagnosed with mild atrophic gastritis based on both Kimura-Takemoto classification (86.4%) and OLGA system (71.8%) (Table 1). The average age of MSAG group was significantly higher than that of MAG group according to gastroscopy images (p < 0.001). The *Hp* infection rate in the MSAG was also significantly higher than that of MAG group (Kimura-Takemoto: p = 0.017, OLGA: p = 0.006).

3.2. Different serum pepsinogen levels among AG groups

The median (IQR) of PGI and PGII were 51.4 (37.4–70.8) and 9.4 (6.4–14.4) respectively. The mean (SD) of PGR was 5.5 (1.9). There was a strong positive significant correlation between PGI and PGII (r = 0.799, p < 0.001), a negligible positive significant correlation between PGI and PGR (r = 0.129, p = 0.033) and a weak positive significant correlation between PGII and PGR (r = −0.430, p < 0.001).

The level of serum PGII was statistically significant different between patients with Hp infection and without Hp infection (p < 0.001), but there was no significant difference on serum PGI level between these two groups. There was neither correlation between PGI or PGII and age, nor significant difference between pepsinogen level between males and females.

With regards to the atrophic gastritis level, serum PGI in the MSAG group was significantly lower than that of the MAG group based on both gastroscopy images and pathology test (Kimura-Takemoto: p = 0.008, OLGA: p = 0.004). The PGR was also significantly lower in the MSAG group than the MAG group (Kimura-Takemoto: p < 0.001, OLGA: p < 0.001). The serum PGII level was similar in both the MAG and MSAG groups (Table 2).

3.3. Diagnostic value of serum pepsinogen for moderate and severe atrophic gastritis

The diagnostic value of serum pepsinogen was assessed by comparing with both gastroscopy and pathology results. According to the gastroscopy results (Kimura-Takemoto classification), the AUC of PGI and PGR was 0.635 (p = 0.008, 95% CI 0.554–0.716) and 0.766 (p < 0.001, 95% CI 0.676–0.857) respectively (Fig. 1a). According to the pathology examination (OLGA system), the AUC of PGI and PGR was 0.612 (p = 0.004, 95% CI 0.540–0.684) and 0.689 (p < 0.001, 95% CI 0.621–0.758) respectively (Fig. 1b). The PGII level did not have meaningful diagnostic value for moderate and severe atrophic gastritis.

By using the Youden's index, we determined the most appropriate cut-off values of PGI and PGR for moderate and severe gastritis (Table 3). Based on the Kimura-Takemoto classification, the best cut-off point of the serum PGI was ≤69.0 (sensitivity: 100%, specificity: 30.5%), the best cut-off point for the PGR was ≤4.6 (sensitivity: 73%, specificity: 75.8%). If combining both PGI ≤69.0 and PGR ≤4.6, it would give the accuracy of 82.4% (sensitivity: 73%, specificity: 83.9%, positive predictive value: 41.5%, negative predictive value: 95.2%). When considering the OLGA system, the best cut-off point of the serum PGI was ≤63.5 (sensitivity: 79.2%, specificity: 41.3%), the best cut-off point for the PGR was ≤5.2 (sensitivity: 61%, specificity: 68.9%). If combining these both cut-off values, PGI ≤63.5 and PGR ≤5.2, it would give the highest accuracy of 72.9% (sensitivity: 49.4%, specificity: 82.1%, positive predictive value: 52.1%, negative predictive value: 80.5%) (Table 3).

4. Discussion

Serum pepsinogen has been used widely as an effective biomarker in diagnosis of atrophic gastritis or gastric cancer; however, its validity and appropriate cut-off values vary among different populations. According to the authors, the differences could be explained, besides by various demographic characteristics, as follow: PG can be classified immunologically into two types: pepsinogen I (PGI) and pepsinogen II (PGII) and the pepsinogen ratio (PGR: PGI/PGII) was also calculated. While PGII is less affected as it is also produced by the Brunner's glands, PGI cut offs varies among reported studies because of different levels of fundus gastritis, from which PGI is secreted, which are caused by different subtypes of helicobacter pylori, the main reason of atrophic gastritis or gastric cancer, among populations [31].

This current study aimed to assess the diagnostic value of serum pepsinogen in diagnosis of moderate and severe atrophic gastritis among Vietnamese population. As the results, 13.6% of all participants were diagnosed with MSAG based on gastroscopy images with Kimura-Takemoto classification, and 28.2% were diagnosed with MSAG based on pathology examination with OLGA system. We found that serum pepsinogen had a good diagnostic value for the diagnosis of moderate and severe atrophic gastritis among Vietnamese people based on both gastroscopy image with Kimura-Takemoto classification and pathology result with OLGA system. In which the PGI level and the PGI/II ratio were detected as meaningful biomarkers for diagnosis of atrophic gastritis, the serum PGII did not have diagnostic value. The best cut-off values for MSAG diagnosis were PGI ≤69.0 and PGR ≤4.6, which may return the sensitivity of 73%, the specificity of 83.9%, the positive predictive value of 41.5%, the negative predictive value of 95.2% and the final accuracy of 82.4% based on gastroscopy images. The best cut-off values for MSAG diagnosis were PGI ≤63.5 and PGR ≤5.2, which may return the sensitivity of 49.4%, the specificity of 82.1%, the positive predictive value of 52.1%, the negative predictive value of 80.5% and the final accuracy of 72.9% based on pathology test. The study results also confirmed that age and gender factors were not relevant to pepsinogen level.

The findings of this study suggested that the serum pepsinogen has its value in the diagnosis of atrophic gastritis among Vietnamese

Table 1
Age, gender, and *Hp* infection characteristics among MAG group and MSAG group based on Kimura-Takemoto classification and OLGA system.

	Kimura-Takemoto			OLGA		
	MAG	MSAG	p	MAG	MSAG	p
N (%)	236 (86.4)	37 (13.6)		196 (71.8)	77 (28.2)	
Age (mean, SD)	55.1 (9.0)	63.9 (10.1)	**<0.001**	55.8 (9.8)	57.7 (9.3)	0.152
Gender (n, %)						
Male	96 (88.9)	12 (11.1)	0.340	83 (76.9)	25 (23.1)	0.133
Female	140 (84.8)	25 (15.2)		113 (68.5)	52 (31.5)	
Hp infection (n, %)	74 (31.4)	19 (51.4)	**0.017**	57 (29.1)	36 (46.8)	**0.006**

OLGA: Operative Link on Gastritis Assessment, MAG: mild atrophic gastritis, MSAG: moderate and severe atrophic gastritis, Hp: Helicobacter pylori.
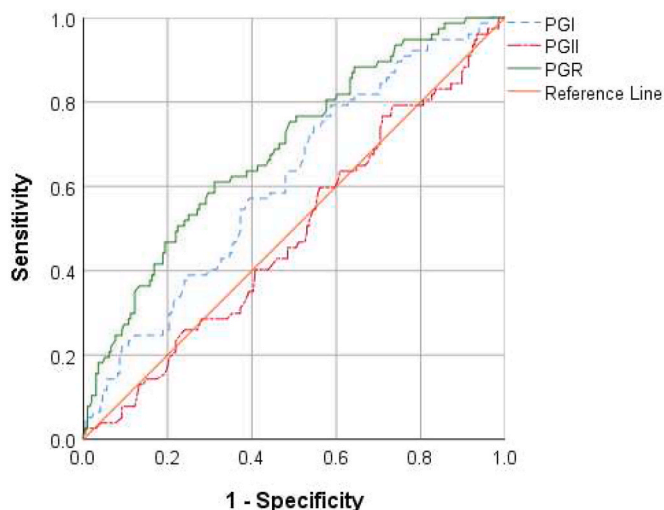
Table 2

Differences in serum PG level between MAG group and MSAG group based on Kimura-Takemoto and OLGA classifications.

	Kimura-Takemoto			OLGA		
	MAG	MSAG	p	MAG	MSAG	p
PGI (ng/ml)	52.7 (28.1–75.5)	42.4 (34.9–57.7)	**0.008**	53.2 (39.1–77.5)	44.0 (33.9–60.1)	**0.004**
PGII (ng/ml)	9.1 (6.3–13.8)	10.9 (7.8–16.4)	0.085	9.2 (6.4–14.6)	9.7 (6.3–13.6)	0.768
PGR	6.0 (1.7)	4.1 (1.9)	**<0.001**	6.1 (1.8)	4.8 (1.6)	**<0.001**

Data was reported with mean (SD) for normal distributed data or median (IQR) for abnormal distributed data. OLGA: Operative Link on Gastritis Assessment, MAG: mild atrophic gastritis, MSAG: moderate and severe atrophic gastritis, PGI: Pepsinogen I, PGII: Pepsinogen II, PGR: PGI/PGII ratio.
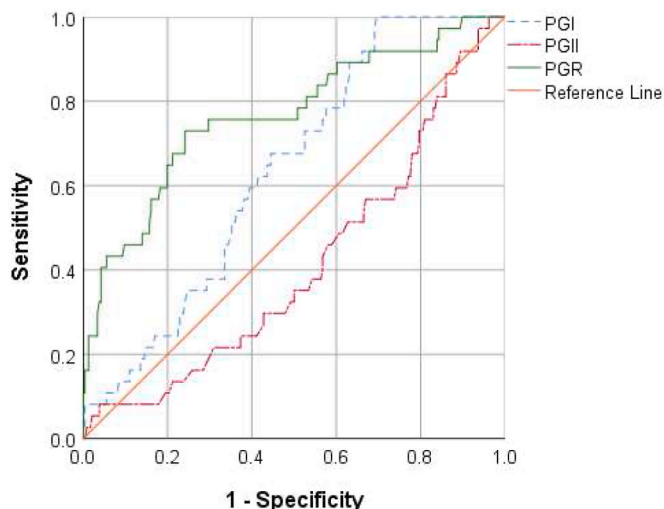
Fig. 1a. Receiver Operating Characteristic (ROC) curve for PGI, PGII, and PGR for diagnosis of moderate-severe atrophic gastritis based on Kimura-Takemoto classification. PGI: AUC = 0.635 (p = 0.008, 95% CI 0.554–0.716); PGII: AUC = 0.412 (p = 0.085, 95% CI 0.315–0.508); PGR: AUC = 0.766 (p < 0.001, 95% CI 0.676–0.857).

Fig. 1b. Receiver Operating Characteristic (ROC) curve for PGI, PGII, and PGR for diagnosis of moderate-severe atrophic gastritis based on OLGA system. PGI: AUC = 0.612 (p = 0.004, 95% CI 0.540–0.684); PGII: AUC = 0.489 (p = 0.768, 95% CI 0.413–0.564); PGR: AUC = 0.689 (p < 0.001, 95% CI 0.621–0.758).

Table 3

Cut-off values of PGI and PGR for diagnosis of moderate and severe atrophic gastritis.

Cut-off	Sensitivity %	Specificity %	PPV %	NPV %	Accuracy %
Kimura-Takemoto					
PGI ≤69.0	100	30.5	18.4	100	39.9
PGR ≤4.6	73.0	75.8	32.1	94.7	75.5
PGI ≤69.0 & PGR ≤4.6	73.0	83.9	41.5	95.2	82.4
PGI ≤69.0 or PGR ≤4.6	100	22.5	16.8	100	33.0
OLGA					
PGI ≤63.5	79.2	41.3	34.7	83.5	52.0
PGR ≤5.2	61.0	68.9	43.5	81.8	66.7
PGI ≤63.5 & PGR ≤5.2	49.4	82.1	52.1	80.5	72.9
PGI ≤63.5 or PGR ≤5.2	90.9	28.1	33.2	88.7	45.8

PGI: Pepsinogen I, PGII: Pepsinogen II, PGR: PGI/PGII ratio, PPV: positive predictive value, NPV: negative predictive value.

Mansour-Ghanaei et al. (2019) that only PGI and PGR are specific and sensitive to screen gastric cancer [14].

Comparing to PGI, PGR gave a better diagnostic yield than the serum pepsinogen I level (AUC 0.766 versus AUC 0.635 based on Kimura-Takemoto classification, and AUC 0.689 versus AUC 0.612 based on OLGA system). This was similar to the finding in the research of Miftahussurur et al. (2020) that reported within three pepsinogen values, pepsinogen I/II ratio was the most reliable biomarker [13]. Another point when using serum pepsinogen in diagnosis is that PGI and PGR should be combined instead of applying them separately. To specify, both cut-off value of PGI and PGR should be evaluated simultaneously in diagnosis to receive the highest sensitivity and specificity compared to PGI or PGR alone. For instance, to achieve highest sensitivity, physicians should use either PGI ≤69.0 or PGR ≤4.6 to classify MSAG patients. On the other hand, both PGI ≤63.5 and PGR ≤5.2 should be used together for highest specificity (Table 3).

With regards to the cut-off values of the PGI and PGR, the cut-off values of these two biomarkers were quite similar between the gastroscopy results and pathology results (PGI ≤69.0 vs PGI ≤63.5, and PGR ≤4.6 vs PGR ≤5.2). This result reflects the correlation of Kimura-Takemoto classification by gastroscopy and OLGA system by pathology test, which has been proved by previous research [26]. The cut-off value of PGI was also similar to the commonly accepted value (PGI ≤69.0 vs PGI ≤70.0) while the cut-off value of PGR was higher than the commonly accepted value (PGR ≤4.6 versus PGR ≤3.0, or PGR ≤5.2 versus PGR ≤3.0) [26]. In other populations, the cut-offs of PGI <30 ng/ml or PGI/PGII <3.0 were used for atrophic gastritis screening among Jews and Arab people [32], whereas in South and Southeast countries PGR was determined as a robust biomarker for chronic and atrophic gastritis screening with the cut-off values of 4.65 and 4.95 respectively [13]. Research on pepsinogen as markers of atrophic chronic gastritis in European dyspeptics showed mean PGI was 77 ng/ml and PGR was 5.6 [33]. These cut offs are higher than those in our study since we used PG to screen moderate and severe atrophic gastritis

population. This finding was in line with the results of other studies in the South and Southeast Asia [13], China [10], Japan and other areas [9, 16]. Within the three biomarkers PGI, PGII, and PGR, only PGI and PGR had the diagnostic value while PGII did not have meaningful value in diagnosis. This result was similar to the research result of

instead of only atrophic lesions.

All the findings of this current study must be interpreted considering both strengths and limitations. The most prominent strength of this study is that the diagnostic value of serum pepsinogen was compared and considered based on both gastroscopy image and pathology examination test, which reflects both the width and the depth of the atrophy. Kimura-Takemoto classification was an effective preliminary tool to identify the high-risk people of gastric cancer, moderate and severe atrophic gastritis in daily practice. It is also reported to well correlate with histological assessment according to OLGA system [26].

The results of this study not only contribute to the pooled data and evidence of diagnostic value of the serum pepsinogen for diagnosis of atrophic gastritis and gastric cancer globally, but also establish an initial evidence of applying the serum pepsinogen for diagnosis of atrophic gastritis among Vietnamese people. Currently, Vietnamese people must take both gastroscopy procedure and pathology test in order to diagnose atrophic gastritis or screen gastric cancer. However, the out-of-pocket money that patients have to pay for those services is pretty high compared to the average income of Vietnamese people. Therefore, these methods are not applicable to use for large-scale screening programs based on community. The more economical method, serum pepsinogen with its cut-off values, would be an efficient and conveniently non-invasive approach to detect patients at high risk of gastric cancer in large screening programs in local communities.

With regards to limitations, this study only employed a small sample size. We did not assess the difference of serum pepsinogen in each group with H. pylori infected group due to this small sample. Besides that, we did not have the serum pepsinogen level of a control group who have not suffered from atrophic gastritis to compare. This revealed that a large-scale study as a screening program in community with a control group may improve the results of the study.

5. Conclusions

In conclusion, the serum pepsinogen I and the pepsinogen I/II ratio showed a reliable diagnostic value for the investigation of moderate and severe atrophic gastritis among Vietnamese population, in which the pepsinogen I/II ratio is favourable. The best cut-off values were PGI ≤69.0 and PGR ≤4.6. We recommend conducting further research with larger scale and including non-atrophic gastritis people for a better assessment of diagnostic yield and standardizing the cut-off values in diagnosis of atrophic gastritis and gastric cancer for Vietnamese population.

Ethical approval

This study was one part of the national-level research named "Apply Molecular Biology, Biochemistry, and Endoscopic techniques into Early Gastric Cancer Screening, Diagnosis, and Treatment", which was approved by Ethics Committee at Bach Mai hospital with Decision number 2795/QĐ-BM. Participants were explained sufficiently about the study and asked for their consent by documents.

Sources of funding

Author contributions

LCN: creating study concept and design and writing the paper.
TTD, NTTP,: data collection, data analysis.
PTN and TVP: data interpretation.
KTV: writing and proofreading the paper.

Registration of research studies

1. Name of the registry: Research Registry.
2. Unique Identifying number or registration ID: researchregistry7907.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): https://researchregistry.knack.com/research-registry#home/registrationdetails/627e32468dd34e001eb30ea3/

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Provenance and peer review

Not commissioned, externally peer-reviewed.

Consent

Written informed consent was obtained from the patients for publication of this study and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

The authors have no conflicts of interest to declare.

Acknowledgements

Abbreviations

MAG	Mild Atrophic Gastritis
MSAG	Moderate and Severe Atrophic Gastritis
PG	Pepsinogen
PGI	Pepsinogen I
PGII	Pepsinogen II
PGR	PGI/PGII ratio
Hp	Helicobacter pylori
OLGA	Operative Link on Gastritis Assessment
IQR	interquatile range
ROC	Receiver Operating Characteristic
PPV	positive predictive value
NPV	negative predictive value

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103844.

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