Short Communication

Agreement of Endoscopic Findings and Serum Pepsinogen Levels as an Indicator of Atrophic Gastritis[1]

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Abstract

Serum pepsinogen I and II levels have recently become popular as indicators of atrophic gastritis in epidemiological studies. Previous studies show a significant association between serum pepsinogen levels and endoscopically diagnosed atrophic gastritis. This study assesses the level of agreement between the degree of atrophic gastritis as assessed by endoscopic examination and by serum pepsinogen assays. Study subjects were 200 outpatients at Aichi Cancer Center Hospital, Nagoya, Japan, who were endoscoped between February and August 1995. Agreement of the degree of atrophic gastritis was assessed by endoscopic examination and by serum pepsinogen levels. Agreement in assessing the extent of atrophic gastritis between the two methods was 57%, and the presence of atrophic gastritis was 79%. Serum pepsinogen assays identify the majority of patients with atrophic gastritis, although they are less useful in assessing the degree of atrophy in detail.

Introduction

Atrophic gastritis is considered to be one of the most important precancerous lesions of the stomach, linked with *Helicobacter pylori* infection (1–11). There are several ways to assess the presence and severity of atrophic gastritis. Endoscopic examination has been the typical diagnostic method for atrophic gastritis in Japan. Histological examination is the most reliable way to determine atrophic gastritis, but this is not done routinely in patients without gastric cancer. Its principal use is to rule out the presence of cancer rather than to determine the presence and the extent of atrophic gastritis. Serum pepsinogen I and II levels have recently become popular as indicators of atrophic gastritis in epidemiological studies because these determinations are simpler and less invasive than endoscopy with biopsy.

A comparison between the histological findings of atrophic gastritis and the serum pepsinogen levels has been made in a previous study (12). However, a comparative study of the degree of atrophic gastritis, as determined by endoscopy alone and by serum pepsinogen I assays and/or the pepsinogen I:II ratio, has not been reported. This study was undertaken to fulfill this need.

Subjects and Methods

The test subjects were 200 outpatients at Aichi Cancer Center Hospital, Nagoya, Japan, who received gastroendoscopy between February and August 1995. Those who had been diagnosed as having gastric cancer, had undergone gasterectomy, or had been under treatment for cancer at other sites were excluded from the study. The subjects were recruited by an gastroenterologist. All subjects gave written informed consent before participating the study. Ninety % of the eligible subjects participated in the study. Blood samples were obtained from the subjects before endoscopy for measurement of the serum pepsinogen levels and anti-*H. pylori* IgG antibody titers.

The gastroendoscopic findings were evaluated by an experienced gastroenterologist at Aichi Cancer Center Hospital for degree and extent of atrophic gastritis and the presence of gastric ulcer and polyps. This was done without knowing the results of any blood tests. The degree of atrophy was classified into three levels of severity, according to the appearances of the mucosal blood vessels and the mucosal folds, as follows: mild (transparent fine blood vessels and yellowish discoloration limited to the lower body, with thick mucosal folds), moderate (clearly transparent blood vessels and yellowish discoloration up to the middle and upper body, with thinned and narrowed mucosal folds), and severe (clearly transparent large blood vessels and yellowish discoloration up to the upper body, with disappearance of mucosal folds on air insufflation). The use of these criteria is justified by the previous reports on the consistency between endoscopic and histological findings on atrophic gastritis (13).

Both serum pepsinogen I and II levels and anti-*H. pylori* IgG antibodies were measured at an external laboratory (SRL Co. Ltd.). Serum pepsinogen I and II levels (ng/ml) were measured by RIA kits (DINABOT Co. Ltd.) The degree of atrophy determined by the pepsinogen levels was classified using the criteria established as follows: ++, pepsinogen I ≤30 and pepsinogen I:II ratio ≤2.0; +, pepsinogen I ≤70 and pepsinogen I:II ratio ≤3.0 (excluding levels categorized as ++), ±, pepsinogen I ≤40 or pepsinogen I:II ratio ≤2.5 (excluding levels categorized as ++ and +); −, others. We then assumed that these categories, ++, +, ±, and − were equivalent to the degrees of atrophic gastritis categorized by endoscopy as severe, moderate, mild, and none, respectively. Serum anti-*H. pylori* IgG antibodies were measured using a semiquantitative commercial enzyme immunoassay kit (Pirika

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Table 1 Mean (± SE) and median level of serum pepsinogen I, pepsinogen II, and pepsinogen I:II ratio and anti-*H. pylori* antibody positivity (%) by the degree of atrophy estimated by endoscopic findings

Atrophic gastritis by endoscopic findings	No. of subjects		Serum pepsinogen I (ng/ml)	Serum pepsinogen II (ng/mL)	Pepsinogen I/II ratio	anti-*H. pylori* antibody positive (%)
Total	200	Mean (± SE)	56.0 (±2.2)	19.6 (±0.8)	3.2 (±0.1)	76.0
		Median	50.3	17.6	2.9	
None	83	Mean (± SE)	66.7 (±3.3)	17.7 (±1.2)	4.3 (±0.2)	62.7
		Median	58.5	16.2	4.1	
Mild	63	Mean (± SE)	57.2 (±3.4)	22.8 (±1.5)[a]	2.8 (±0.2)[a]	84.1[a]
		Median	55.1	20.5	2.5	
Moderate	35	Mean (± SE)	41.3 (±3.9)[a]	20.4 (±1.7)	2.1 (±0.1)[a]	85.7
		Median	37.9	20.0	2.1	
Severe	19	Mean (± SE)	32.4 (±7.7)[a]	15.6 (±1.5)	2.0 (±0.4)[a]	89.5
		Median	23.8	16.6	1.6	

[a] $P < 0.01$, compared with the category "none."

Plate G *Helicobacter*). Semiquantitative titers +++, ++, +, and ± were assigned to the ratios of the positive control sera to the negatives derived from 1 in 2, 1 in 4, 1 in 8, and 1 in 16 positive control dilutions, respectively. Semiquantitative titers +++, ++, and + were considered positive, whereas ± or values below that of the 1 in 16 dilution of positive control sera were considered negative.

Mean levels of the serum pepsinogen I, pepsinogen II, and pepsinogen I:II ratio were compared to the degree of atrophic gastritis as determined by endoscopy. Sex and age groups were combined in the analyses because only four subjects were under 40 years of age (one male and three females), and no statistical differences were observed between sexes in the distribution of age and pepsinogen levels for each degree of atrophic gastritis.

The statistical significance of differences in the mean values of serum pepsinogen levels between normal and each degree of atrophic gastritis by endoscopic findings was assessed by *t* test for independent samples. The difference in the proportion of anti-*H. pylori* IgG antibody-positive subjects by endoscopic findings was assessed by Fisher's exact test. The agreement of the presence and the degree of atrophic gastritis by endoscopic findings and by serum pepsinogen levels was assessed by percentage of agreement, as well as sensitivity and specificity of classification by pepsinogen levels; endoscopic findings were regarded as real conditions of atrophic gastritis. The STATA program (14) was used for statistical analysis in this study.

Results

A total of 200 subjects (91 males and 109 females) were recruited into the study; they were ages 34–81 years (mean, 60.5 years). Almost 60% of subjects had atrophic gastritis, based on either endoscopic findings or serum pepsinogen levels. More than 75% of study subjects were anti-*H. pylori* IgG antibody positive, with a larger proportion of males testing positive.

The mean levels of serum pepsinogen I and pepsinogen I:II ratio decreased with the extent of the atrophy based on endoscopy results, but those of serum pepsinogen II did not show increasing or decreasing trends (Table 1). The proportion of anti-*H. pylori* IgG antibody-positive subjects was lower among the subjects without atrophic gastritis than among those with atrophic gastritis. A similar tendency was observed when the anti-*H. pylori* IgG antibody-negative subjects were excluded from the analysis.

Table 2 Comparison of classification of atrophic gastritis by endoscopic findings and by serum pepsinogen levels

Classification by endoscopic findings	Classification by serum pepsinogen I level and pepsinogen I:II ratio				
	n	None	Mild	Moderate	Severe
None	83	62	15	6	0
Mild	63	18	16	24	5
Moderate	35	2	3	24	6
Severe	19	1	1	6	11

Classification by serum pepsinogen levels correctly matched endoscopic classifications for 113 of 200 patients, or 56.5%, as shown in Table 2. It correctly predicted the presence or absence of atrophic gastritis in 158 of the 200 cases, or 79.0%. Sensitivity is the percentage of subjects with atrophic gastritis by endoscopy who have an abnormal pepsinogen test (*i.e.*, 96 of 117, or 82.1%). Specificity is the percentage without atrophic gastritis who have a normal pepsinogen test (*i.e.*, 62 of 83, or 74.7%). Positive predictive value is the percentage with a positive pepsinogen test who have atrophic gastritis (*i.e.*, 96 of 117, or 82.1%). Negative predictive value is the percentage with a normal pepsinogen test who do not have atrophic gastritis (*i.e.*, 62 of 83, or 74.7%). When regarding the misclassification within the neighboring categories as correct classification, the agreement of the two classifications was 92.0% (Table 2). When the analyses were limited to anti-*H. pylori* IgG antibody-positive subjects, the agreements were similar to those conducted using all subjects.

Discussion

In this study, endoscopic findings were evaluated only by one examiner to eliminate variation of classification between examiners. We tried to diminish variation of classification within the examiner as much as possible, by choosing an examiner with experienced and stable classification skills of endoscopic examination and by using classification guidelines and fixed forms for filling out the results. Both classifications were carried out without the information on the results by other methods, which suggests that misclassifications were not systematic.

Our study population was chosen from hospital outpatients who underwent endoscopy and was not derived from the general population, which raises questions about the degree to

which the present study may be generalized. In this study, however, we did not focus on clarifying the distribution of atrophic gastritis or serum pepsinogen levels among the Japanese population but on the agreement of classification by the two different methods. Therefore, as long as our study population itself does not affect the association between endoscopic findings and serum pepsinogen levels, the selection of our study population is not an issue.

The cutoff values of serum pepsinogen levels for extensive atrophic gastritis used in this study were based on previous studies (2, 12). Cutoff values for mild atrophic gastritis, however, have not been established as extensive ones, and therefore, we have applied the values recommended by the DINABOT Co. Ltd., which offers the kits for the measurement of pepsinogen levels. In our study, the combination of serum pepsinogen levels gave 57% perfect agreement with endoscopic findings. Misclassification mainly derived from the misclassification within the neighboring categories, especially mild atrophy to none and moderate atrophy to mild. These results suggest that the predictive ability of the serum pepsinogen levels for mild atrophic gastritis is unreliable because of the difficulty in establishing reliable cutoff values. Also, because the pepsinogen I levels reflect the extent of disease in the corpus of the stomach, they may not be used to assess the extent of early atrophic gastritis, which may affect only the mucosa at the antrocorpus junction. Taking this feature into consideration, we suggest that the agreement obtained in this study is reasonable, and serum pepsinogen assays may identify many patients with atrophic gastritis, but they are less useful in estimating its extent.

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