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**First-line eradication for *Helicobacter pylori*-positive gastritis by esomeprazole-based triple therapy is influenced by CYP2C19 genotype**

Saito Y *et al. H. pylori* eradication by esomeprazole and CYP2C19 genotype

Yoshimasa Saito, Hiroshi Serizawa, Yukako Kato, Masaru Nakano, Masahiko Nakamura, Hidetsugu Saito, Hidekazu Suzuki, Takanori Kanai

**Yoshimasa Saito, Hiroshi Serizawa, Yukako Kato, Masaru Nakano**, Division of Gastroenterology, Kitasato Institute Hospital, Minato-ku, Tokyo 108-8641, Japan

**Yoshimasa Saito, Hidetsugu Saito**, Division of Pharmacotherapeutics, Keio University Faculty of Pharmacy, Minato-ku, Tokyo 105-8512, Japan

**Yoshimasa Saito*,* Hidetsugu Saito, Hidekazu Suzuki, Takanori Kanai,**Division of Gastroenterology, Department of Internal Medicine Keio University School of Medicine, Shinjuku-ku, Tokyo 160-8582, Japan

**Masahiko Nakamura***,* School of Pharmaceutical Sciences, Kitasato University, Minato-ku, Tokyo 108-8641, Japan

**Author contributions:** Saito Y and Serizawa H designed the research; Saito Y, Serizawa H, Kato Y, Nakano M performed the clinical research; Nakamura M, Saito H, Suzuki H and Kanai T supervised the research; Saito Y and Serizawa H analyzed the data and wrote the paper.

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**Correspondence to: Yoshimasa Saito, MD, PhD,** Division of Pharmacotherapeutics, Keio University Faculty of Pharmacy, 1-5-30 Shibakoen, Minato-ku, Tokyo 105-8512, Japan. saito-ys@pha.keio.ac.jp

**Telephone:** +81-3-54002692

**Fax:** +81-3-54002692

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**Abstract**

**AIM:** To evaluate the effect of first line Esomeprazole (EPZ)-based triple therapy on *Helicobacter pylori* (*H. pylori*) eradication.

**METHODS:** A total of 80 Japanese patients with gastritis who were diagnosed as positive for *H. pylori* infection on 13C-urea breath test or endoscopic biopsy-based test were included in this study. The average age of the patients was 57.2 years (male/female, 42/38). These patients were treated by first-line eradication therapy with EPZ 40 mg/d, amoxicillin 1500 mg/d and clarithromycin 400 mg/d for 7 d. All drugs were given twice per day. Correlations between *H. pylori* eradication, CYP2C19 genotype, and serum pepsinogen (PG) level were analyzed. This study was registered with the UMIN Clinical Trials Registry (UMIN000009642).

**RESULTS:** The *H. pylori* eradication rates by EPZ-based triple therapy evaluated by intention-to-treat and per protocol were 67.5% and 68.4%, which were similar to triple therapies with other first-generation proton pump inhibitors (PPIs). The eradication rates in three different CYP2C19 genotypes; extensive metabolizer (EM), intermediate metabolizer, and poor metabolizer were 52.2%, 72.1%, and 84.6%, respectively. The *H. pylori* eradication rate was significantly lower in EM than non-EM (*p* < 0.05). The serum PG I level and PG I/II ratio were significantly increased after eradication of *H. pylori* (*p* < 0.01), suggesting that gastric atrophy was improved by *H. pylori* eradication. Thus, first-line eradication by EPZ-based triple therapy for patients with*H. pylori-*positive gastritis was influenced by CYP2C19 genotype and the eradication rate was on the same level with other first-generation PPIs in the Japanese population.

**CONCLUSION:** Unlike previous reports, the results in this study suggest that there is no advantage to EPZ-based triple therapy on *H. pylori* eradication in comparison to other first-generation PPIs.

**Key words:** *Helicobacter pylori;* esomeprazole; CYP2C19; pepsinogen; proton pump inhibitor

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**Core tip:** Esomeprazole (EPZ) is considered to be more effective for inhibition of gastric acid secretion than other first-generation proton pump inhibitors (PPIs), because its metabolism is not influenced by CYP2C19 genotype. In the present study, however, first-line eradication by EPZ-based triple therapy for patients with*Helicobacter pylori* (*H. pylori*)*-*positive gastritis was influenced by CYP2C19 genotype and the eradication rate was on the same level with triple therapies with other first-generation PPIs in the Japanese population. Unlike previous studies, our results suggest that there is no advantage for EPZ-based triple therapy on *H. pylori* eradication in comparison with other first-generation PPIs.

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**Introduction**

*Helicobacter pylori* (*H. pylori*) is one of the most prevalent bacterial pathogens and is associated with upper gastrointestinal disorders such as gastritis, peptic ulcers, functional dyspepsia, gastric mucosa-associated lymphoid tissue lymphoma, and gastric cancer[[1-3](#_ENREF_1)]. Eradication of *H. pylori* infection has been reported to be an effective approach to curing or preventing these *H. pylori*-associated diseases[[4](#_ENREF_4),[5](#_ENREF_5)]. One-week of triple therapy with a proton pump inhibitor (PPI), amoxicillin (AMPC), and clarithromycin (CAM) is recommended as first-line *H. pylori* eradication therapy and covered under the national health insurance system in Japan. However, the eradication rates for *H. pylori* are declining to around 70%[[6](#_ENREF_6)].

The use of PPIs combined with antibiotics in *H. pylori* eradication therapy has been demonstrated to not only to protect the stomach, but also increase the eradication rate. As antibiotics are more stable in higher pH gastric environments, strong gastric acid inhibition increases the efficacy of *H. pylori* eradication. The metabolism of first-generation PPIs such as omeprazole (OPZ) is influenced by genetic polymorphism of CYP2C19[[7](#_ENREF_7)]. Based on the wild-type allele (\*1) and the two mutated alleles (\*2 and \*3) of the CYP2C19 gene, patients can be categorized into 3 groups: extensive metabolizer (EM, \*1/\*1), intermediate metabolizer (IM, \*1/\*2 or \*1/\*3), and poor metabolizer (PM, \*2/\*2, \*2/\*3 or \*3/\*3). As EM metabolizes OPZ rapidly, the success rate of *H. pylori* eradication by OPZ-based therapy in EM is lower than that of PM[[7-9](#_ENREF_7)].

Esomeprazole (EPZ), the S-isomer of OPZ, is the latest member of the PPI family and is a more potent acid inhibitor than other first-generation PPIs[[10](#_ENREF_10),[11](#_ENREF_11)]. The metabolism of EPZ is considered to be unaffected by CYP2C19 genotype. Indeed, recent studies have reported that there were no significant differences in *H. pylori* eradication by EPZ-based therapy among EM, IM, and PM of CYP2C19 genotype and that EPZ showed better overall *H. pylori* eradication rates than first-generation PPIs[[9](#_ENREF_9),[12-14](#_ENREF_12)]. However, Nishida *et al*[[15](#_ENREF_15)] have demonstrated that the *H. pylori* eradication rate of EPZ-based triple therapy was lower than lansoprazole (LPZ) in the Japanese population. Thus, the effect of *H. pylori* eradication by EPZ-based therapy is controversial. To evaluate the effect of first line EPZ-based triple therapy on *H. pylori* eradication, we investigated eradication rate, CYP2C19 genotype and serum pepsinogen (PG) level in Japanese patients with *H. pylori*-positive gastritis.

**Materials and Methods**

***Patients and study design***

A total of 80 Japanese patients with gastritis who were diagnosed as positive for *H. pylori* infection on 13C-urea breath test (UBT) or endoscopic biopsy-based test (*i.e.* histological examination and *H. pylori* culture) were included in this study. Patients were recruited between January and September 2013 at the Kitasato Institute Hospital (Tokyo, Japan). The average age of the patients was 57.2 years (male/female, 42/38).

These patients were treated by first-line eradication therapy with EPZ 40 mg/d, AMPC 1500 mg/d and CAM 400 mg/d for 7 d. All drugs were given twice per day. Three months after eradication, *H. pylori* infection was validated by UBT. Correlations between *H. pylori* eradication, CYP2C19 genotype, and serum PG level were analyzed. The study was approved by the ethics committee of the Kitasato Institute Hospital, and written informed consent was obtained from all patients prior to examinations. This study was registered with the UMIN Clinical Trials Registry, number UMIN000009642.

***CYP2C19 genotyping***

Blood samples were collected from the patients before eradication therapy. The CYP2C19 genotyping for wild-type allele (\*1) and two mutated alleles (\*2 and \*3) was conducted by SRL (Tokyo, Japan). The patients were categorized into 3 groups based on the CYP2C19 genotype, EM (\*1/\*1), IM (\*1/\*2 or \*1/\*3), and PM (\*2/\*2, \*2/\*3 or \*3/\*3).

***Serum PG level***

Serum PG I and II levels were measured before and after eradication therapy. Gastric atrophy was evaluated as described previously[[16](#_ENREF_16),[17](#_ENREF_17)]: (-), PG I ≥ 70 ng/mL and PG I/PG II ratio ≥ 3.0; (1+), PGI < 70 ng/mL and PG I/PG II ratio < 3.0; (2+), PG I < 50 ng/mL and PG I/PG II ratio < 3.0; (3+), PG I < 30 ng/mL and PG I/PG II ratio < 2.0.

***Statistical analysis***

Data were analyzed using the SPSS statistics 22 software package. The data were also analyzed using *χ2* test and multiple logistic regression analysis. *H. pylori* eradication rate was evaluated by intention-to-treat (ITT) and per protocol (PP). Differences at *p* < 0.05 were considered significant.

**Results**

***Influence of CYP2C19 genotype on H. pylori eradication by EPZ-based triple therapy***

Among 80 patients who were treated by first-line eradication therapy with EPZ, AMPC, and CAM, one patient did not visit for UBT after the therapy. The *H. pylori* eradication rates of first-line therapy with EPZ, AMPC, and CAM evaluated by ITT and PP were 67.5% and 68.4%, which were similar to first-line therapy with LPZ, AMPC, and CAM (67.5%) in the Kitasato Institute Hospital. The results of CYP2C19 genotype and serum PG level in association with *H. pylori* eradication are shown in Tables 1-3. The eradication rates of first-line therapy with EPZ in three different CYP2C19 genotypes, EM, IM, and PM were 52.2% (12/23), 72.1% (31/43), and 84.6% (11/13), respectively. The *H. pylori* eradication rate of EM was significantly lower than that of non-EM (*p* = 0.048, *χ2* test).

***Influence of PG level on H. pylori eradication by EPZ-based triple therapy***

In addition to *H. pylori* infection, serum PG level is associated with gastric mucosal atrophy and gastric cancer risk, which is used for gastric cancer screening [[17-19](#_ENREF_17)]. Serum PG I level and PG I/II ratio in association with *H. pylori* eradication are shown in Tables 1, 2, and 3. Table 4 is a summary of PG I/II ratio and *H. pylori* eradication. Serum PG I level and PG I/II ratio were significantly increased after eradication of *H. pylori* (Table 4, *p* = 0.007, *χ2* test), suggesting that gastric atrophy was improved by *H. pylori* eradication therapy. We performed multiple logistic regression analysis to identify independent predictors associated with *H. pylori* eradication (Table 5). As shown in Table 5, only CYP2C19 genotype was statistically significant as an independent predictor associated with *H. pylori* eradication.

**Discussion**

EPZ is a second-generation PPI that is broadly used for the treatment of acid-peptic diseases. It is believed that EPZ is more effective for inhibition of gastric acid secretion than other first-generation PPIs, because it is the S-isomer of OPZ and its metabolism is not affected by CYP2C19 genotype. Recent studies have also shown that *H. pylori* eradication by EPZ-based therapy is not influenced by CYP2C19 genotype and that overall *H. pylori* eradication rates of EPZ-based therapy was better than first-generation PPIs[[9](#_ENREF_9),[12-14](#_ENREF_12)]. On the other hand, Hunfeld *et al*[[11](#_ENREF_11)] have revealed that the acid-inhibitory effect of EPZ was influenced by CYP2C19 genotype. Nishida *et al*[[15](#_ENREF_15)] have demonstrated that the *H. pylori* eradication rate of EPZ-based triple therapy was lower than LPZ in the Japanese population. Thus, the effect of EPZ-based therapy on *H. pylori* eradication is controversial.

In this study we evaluated the influence of CYP2C19 genotype in patients with *H. pylori*-positive gastritis treated by EPZ-based triple therapy. Our results demonstrated that the *H. pylori* eradication rate was significantly lower in EM than non-EM. The CYP2C19 genotype of EM patients is wild-type (\*1) on both alleles, whereas non-EM patients include the mutant alleles (\*2 and \*3) on either, or both, alleles. The result of multiple logistic regression analysis also showed that CYP2C19 genotype is an independent predictor associated with *H. pylori* eradication. These findings suggest that EM metabolizes EPZ more rapidly, and therefore plasma concentration of EPZ becomes lower, resulting in a lower *H. pylori* eradication rate than that of non-EM. Nishida *et al*[[15](#_ENREF_15)] conducted a multicenter, randomized, open-label, non-inferiority trial comparing EPZ and lansoprazole (LPZ) in triple therapy for *H. pylori* eradication in Japan. They have reported that the *H. pylori* eradication rates of EPZ-based triple therapy (69.4%/76.9%, ITT/PP) were lower than LPZ-based triple therapy (73.9%/79.8%, ITT/PP). In this study, the overall *H. pylori* eradication rates of EPZ-based triple therapy were 67.5%/68.4% (ITT/PP), which were similar to the previous report. A recent study with the Japanese population has also shown that the *H. pylori* eradication rates by the regimen with Rabeprazole (RPZ), AMPC, and CAM were 73.3%/77.2% (ITT/PP)[[6](#_ENREF_6)]. Thus, these findings indicate that the *H. pylori* eradication rate by EPZ-based triple therapy is on the same level with triple therapies with other first-generation PPIs.

Serum PG level is associated with gastric mucosal atrophy and gastric cancer risk[[17-19](#_ENREF_17)]. In the present study, the serum PG I level and PG I/II ratio were significantly increased after eradication of *H. pylori*, suggesting that gastric atrophy was improved by *H. pylori* eradication. Serum PG level and PG I/II ratio can be non-invasive biomarkers for screening of gastric atrophy and gastric cancer. *H. pylori* eradication has clinical benefit for improvement of gastric mucosal atrophy and prevention against gastric cancer.

In conclusion, first-line *H. pylori* eradication by EPZ-based triple therapy was influenced by CYP2C19 genotype and the overall eradication rate was on the same level with triple therapies with other first-generation PPIs in Japanese patients with *H. pylori-*positive gastritis. Unlike previous reports, the results in this study suggest that there is no advantage to EPZ-based triple therapy on *H. pylori* eradication in comparison to other first-generation PPIs. Further studies are needed in a large population of patients in different countries before an accurate correlation between the EPZ-based therapy and CYP2C19 genotype is completed. Evaluation of CYP2C19 genotype and serum PG level is important to develop more effective personalized *H. pylori* eradication therapy with EPZ.

**COMMENTS**

***Background***

Esomeprazole (EPZ) is a second-generation proton pump inhibitor (PPI) that is broadly used for the treatment of acid-peptic diseases. Recent studies have shown that EPZ is more effective for inhibition of gastric acid secretion than other first-generation PPIs because its metabolism is not influenced by CYP2C19 genotype. However, the effect of *Helicobacter pylori* (*H. pylori*) eradication by EPZ-based therapy is controversial.

***Research frontiers***

First-line eradication by EPZ-based triple therapy for patients with*H. pylori-*positive gastritis was influenced by CYP2C19 genotype and the eradication rate was on the same level with other first-generation PPIs in the Japanese population.

***Innovations and breakthrough***

Unlike previous reports, the results in this study suggest that there is no advantage to EPZ-based triple therapy on *H. pylori* eradication in comparison to other first-generation PPIs.

***Applications***

Evaluation of CYP2C19 genotype and serum pepsinogen level is important to develop more effective personalized *H. pylori* eradication therapy with EPZ.

***Terminology***

EPZ is the latest member of the PPI family and is a more potent acid inhibitor than other first-generation PPIs. The metabolism of first-generation PPIs is influenced by genetic polymorphism of CYP2C19. Patients can be categorized into 3 groups: extensive metabolizer, intermediate metabolizer, and poor metabolizer.

***Peer-review***

This study reports that overall eradication rate by triple therapy utilizing the second-generation PPI inhibitor, EPZ for patients with *H. pylori*-positive gastritis, which has no apparent advantage over triple therapies utilizing other first-generation PPIs. The EPZ-based therapy was influenced by CYP2C19 genotype of the studied Japanese patients.

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**Table 1 CYP2C19 genotype, serum pepsinogen level, and *Helicobacter pylori*  eradication in the extensive metabolizer group (genotype: \*1/\*1)**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Age** | **Sex** | **CYP2C19** | | **PG I/II1** | | | | **UBT** | **Eradication** |
| **Before eradication** | | **After eradication** | |
| E1 | 45 | F | \*1/\*1 | EM | 3.6 | - | 5 | - | 0.1 | ○ |
| E2 | 39 | M | \*1/\*1 | EM | 3.3 | - | 6.7 | - | 0.4 | ○ |
| E3 | 59 | M | \*1/\*1 | EM | 3.1 | - | 5.2 | - | 0.5 | ○ |
| E4 | 58 | M | \*1/\*1 | EM | 2.9 | - | 7.1 | - | 0.4 | ○ |
| E5 | 50 | F | \*1/\*1 | EM | 2.2 | 1+ | 5.1 | - | 0.3 | ○ |
| E6 | 43 | F | \*1/\*1 | EM | 2.2 | 1+ | 4.9 | - | 0.3 | ○ |
| E7 | 63 | F | \*1/\*1 | EM | 1.6 | 1+ | 4.1 | - | 0 | ○ |
| E8 | 56 | F | \*1/\*1 | EM | 2.8 | 2+ | 4.1 | - | 0.3 | ○ |
| E9 | 36 | F | \*1/\*1 | EM | 2.2 | 2+ | 4.6 | - | 0 | ○ |
| E10 | 75 | F | \*1/\*1 | EM | 2.5 | 2+ | 4.8 | - | 0.9 | ○ |
| E11 | 67 | M | \*1/\*1 | EM | 3.7 | - | 2.2 | 2+ | 0 | ○ |
| E12 | 64 | M | \*1/\*1 | EM | 0.8 | 3+ | 2.2 | 2+ | 1.3 | ○ |
| E13 | 48 | M | \*1/\*1 | EM | 3.4 | - | 3.1 | - | 12.7 | × |
| E14 | 50 | F | \*1/\*1 | EM | 4.3 | - | 6.4 | - | 12.7 | × |
| E15 | 67 | M | \*1/\*1 | EM | 3.5 | - | 3.7 | - | 41.6 | × |
| E16 | 34 | F | \*1/\*1 | EM | 3 | - | 3.4 | - | 19.5 | × |
| E17 | 63 | M | \*1/\*1 | EM | 3.1 | - | 3 | - | 26.8 | × |
| E18 | 71 | F | \*1/\*1 | EM | 1.2 | 3+ | 3.1 | - | 11 | × |
| E19 | 55 | M | \*1/\*1 | EM | 2.4 | 1+ | 2.6 | 1+ | 24.6 | × |
| E20 | 56 | M | \*1/\*1 | EM | 2 | 2+ | 2.2 | 1+ | 24.9 | × |
| E21 | 80 | M | \*1/\*1 | EM | 1.7 | 2+ | 1.8 | 2+ | 20.9 | × |
| E22 | 53 | M | \*1/\*1 | EM | 2.2 | 2+ | 2.2 | 2+ | 26.6 | × |
| E23 | 43 | F | \*1/\*1 | EM | 2.2 | 2+ | 2.3 | 2+ | 11.5 | × |

1(-), PG I ≥ 70 ng/mL and PG I/PG II ratio ≥ 3.0; (1+), PG I < 70 ng/mL and PG I/PG II ratio < 3.0; (2+), PG I < 50 ng/mL and PG I/PG II ratio < 3.0; (3+), PG I < 30 ng/mL and PG I/PG II ratio < 2.0. Eradication rate = 12/23 (52.2%). PG: pepsinogen; EM: extensive metabolizer; UBT: 13C-urea breath test.

**Table 2 CYP2C19 genotype, serum pepsinogen level, and *Helicobacter pylori* eradication in the intermediate metabolizer group (genotype: \*1/\*2, \*1/\*3)**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Age** | **Sex** | **CYP2C19** | | **PG I/II1** | | | | **UBT** | **Eradication** |
| **Before eradication** | | **After eradication** | |
| I1 | 61 | F | \*1/\*2 | IM | 2.6 | - | 4.5 | - | 1.1 | ○ |
| I2 | 66 | M | \*1/\*2 | IM | 3.6 | - | 6 | - | 0 | ○ |
| I3 | 65 | F | \*1/\*2 | IM | 2.5 | - | 4.1 | - | 0.2 | ○ |
| I4 | 71 | F | \*1/\*2 | IM | 3.5 | - | 7.4 | - | 0.9 | ○ |
| I5 | 59 | M | \*1/\*3 | IM | 2.2 | - | 5.3 | - | 1.1 | ○ |
| I6 | 62 | M | \*1/\*3 | IM | 3.3 | - | 8.3 | - | 0 | ○ |
| I7 | 67 | M | \*1/\*2 | IM | 4.9 | - | 5 | - | 0.3 | ○ |
| I8 | 64 | F | \*1/\*2 | IM | 2.8 | - | 5.2 | - | 0.5 | ○ |
| I9 | 64 | F | \*1/\*2 | IM | 3.2 | - | 5.4 | - | 0.1 | ○ |
| I10 | 34 | M | \*1/\*2 | IM | 3.1 | - | 6.9 | - | 0.3 | ○ |
| I11 | 52 | M | \*1/\*2 | IM | 3.7 | - | 4.9 | - | 0.8 | ○ |
| I12 | 64 | M | \*1/\*2 | IM | 3.6 | - | 4.5 | - | 0.2 | ○ |
| I13 | 55 | M | \*1/\*3 | IM | 2 | - | 4.7 | - | 1.1 | ○ |
| I14 | 58 | M | \*1/\*2 | IM | 3.8 | - | 9.4 | - | 0.6 | ○ |
| I15 | 66 | F | \*1/\*3 | IM | 1.4 | - | 3.7 | - | 1 | ○ |
| I16 | 47 | M | \*1/\*2 | IM | 4 | - | 5.4 | - | 0 | ○ |
| I17 | 42 | M | \*1/\*3 | IM | 2.8 | 1+ | 5.3 | - | 0.4 | ○ |
| I18 | 53 | M | \*1/\*2 | IM | 2.3 | 1+ | 3.7 | - | 0.8 | ○ |
| I19 | 56 | M | \*1/\*3 | IM | 2 | 1+ | 4 | - | 2.4 | ○ |
| I20 | 51 | F | \*1/\*2 | IM | 1.1 | 1+ | 3.3 | - | 0 | ○ |
| I21 | 62 | F | \*1/\*2 | IM | 2.3 | 1+ | 4.1 | - | 0.3 | ○ |
| I22 | 39 | F | \*1/\*2 | IM | 2.7 | 2+ | 6 | - | 0.4 | ○ |
| I23 | 63 | F | \*1/\*3 | IM | 2.1 | 2+ | 4 | - | 0.1 | ○ |
| I24 | 53 | F | \*1/\*2 | IM | 2.3 | 2+ | 4.1 | - | 0.3 | ○ |
| I25 | 45 | M | \*1/\*2 | IM | 2.4 | 2+ | 4.9 | - | 0.6 | ○ |
| I26 | 55 | M | \*1/\*2 | IM | 2.6 | 2+ | 4.2 | - | 0.5 | ○ |
| I27 | 50 | M | \*1/\*2 | IM | 1.8 | 2+ | 3.9 | - | 0.6 | ○ |
| I28 | 55 | M | \*1/\*2 | IM | 1.3 | 3+ | 3.6 | - | 0 | ○ |
| I29 | 53 | F | \*1/\*2 | IM | 1.7 | 2+ | 2.9 | 2+ | 0.4 | ○ |
| I30 | 64 | M | \*1/\*2 | IM | 1.2 | 3+ | 2.5 | 2+ | 1.5 | ○ |
| I31 | 66 | F | \*1/\*2 | IM | 0.8 | 3+ | 0.8 | 3+ | 1.4 | ○ |
| I32 | 53 | M | \*1/\*3 | IM | 4.1 | - | 4.5 | - | 49.8 | × |
| I33 | 61 | M | \*1/\*2 | IM | 4.2 | - | 3.2 | - | 24.8 | × |
| I34 | 44 | F | \*1/\*2 | IM | 3.2 | - | 3.2 | - | 44.5 | × |
| I35 | 51 | F | \*1/\*2 | IM | 2.4 | 2+ | 3.1 | - | 21.7 | × |
| I36 | 28 | F | \*1/\*3 | IM | 2.2 | - | 2.2 | 1+ | 43.6 | × |
| I37 | 70 | M | \*1/\*3 | IM | 2.7 | 1+ | 2.7 | 1+ | 9.3 | × |
| I38 | 70 | F | \*1/\*2 | IM | 2.5 | 1+ | 2 | 1+ | 39.2 | × |
| I39 | 65 | M | \*1/\*3 | IM | 3.1 | - | 3 | 2+ | 28 | × |
| I40 | 45 | F | \*1/\*3 | IM | 2.8 | - | 2.5 | 2+ | 13 | × |
| I41 | 78 | F | \*1/\*2 | IM | 0.8 | 3+ | 1.4 | 3+ | 4.1 | × |
| I42 | 45 | F | \*1/\*2 | IM | 1.5 | 3+ | 1.6 | 3+ | 17 | × |
| I43 | 70 | M | \*1/\*3 | IM | 1.1 | 3+ | 1.1 | 3+ | 37.4 | × |

1(-), PG I ≥ 70 ng/mL and PG I/PG II ratio ≥ 3.0; (1+), PG I < 70 ng/mL and PG I/PG II ratio < 3.0; (2+), PG I < 50 ng/mL and PG I/PG II ratio < 3.0; (3+), PG I < 30 ng/mL and PG I/PG II ratio < 2.0. Eradication rate = 31/43 (72.1%). PG: pepsinogen; IM: intermediate metabolizer; UBT: 13C-urea breath test.

**Table 3** **CYP2C19 genotype, serum pepsinogen level, and *Helicobacter pylori* eradication in the poor metabolizer group (genotype: \*2/\*2, \*2/\*3, \*3/\*3)**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Case** | **Age** | **Sex** | **CYP2C19** | | **PG I/II1** | | | | **UBT** | **Eradication** |
| **Before eradication** | | **After eradication** | |
| P1 | 64 | F | \*2/\*2 | PM | 3.6 | - | 5.8 | - | 0.2 | ○ |
| P2 | 46 | M | \*2/\*2 | PM | 4 | - | 5.5 | - | 1.2 | ○ |
| P3 | 64 | F | \*2/\*2 | PM | 2.2 | 1+ | 3.8 | - | 1.1 | ○ |
| P4 | 63 | F | \*2/\*2 | PM | 2.1 | 2+ | 3.9 | - | 0 | ○ |
| P5 | 62 | F | \*2/\*3 | PM | 2.3 | 2+ | 4.2 | - | 0.2 | ○ |
| P6 | 64 | M | \*2/\*3 | PM | 2.2 | 2+ | 5 | - | 0 | ○ |
| P7 | 63 | M | \*2/\*2 | PM | 2.7 | 2+ | 4.9 | - | 1.2 | ○ |
| P8 | 77 | F | \*3/\*3 | PM | 1.7 | 3+ | 2.9 | 2+ | 0.1 | ○ |
| P9 | 68 | M | \*2/\*2 | PM | 1.3 | 2+ | 1.9 | 3+ | 1.2 | ○ |
| P10 | 60 | M | \*2/\*2 | PM | 0.6 | 3+ | 1.4 | 3+ | 0.8 | ○ |
| P11 | 57 | M | \*2/\*2 | PM | 4.1 | - | ND | ND | 0.2 | ○ |
| P12 | 65 | F | \*2/\*2 | PM | 2 | 1+ | 2 | 1+ | 30.2 | × |
| P13 | 38 | F | \*2/\*2 | PM | 2.3 | 2+ | 2.5 | 1+ | 63.8 | × |

1(-), PG I ≥ 70 ng/mL and PG I/PG II ratio ≥ 3.0; (1+), PG I < 70 ng/mL and PG I/PG II ratio < 3.0; (2+), PG I < 50 ng/mL and PG I/PG II ratio < 3.0; (3+), PG I < 30 ng/mL and PG I/PG II ratio < 2.0. Eradication rate = 11/13 (84.6%). ND: not detected; PG: pepsinogen; PM: poor metabolizer; UBT: 13C-urea breath test.

**Table 4 Correlation between pepsinogen I/II ratio and *Helicobacter pylori* eradication**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | **PG I/II ratio** | | | **Total** |
| **Increase** | **No change** | **Decrease** |
| Eradication success | 26 | 26 | 1 | 53 |
| Eradication failure | 4 | 18 | 3 | 25 |
| Total | 30 | 44 | 4 | 78 |

Serum PG I level and PG I/II ratio were significantly increased after eradication of *Helicobacter pylori* (*p* < 0.01). PG: pepsinogen.

**Table 5 Multiple logistic regression analysis to identify independent predictors associated with *Helicobacter pylori* eradication**

|  |  |
| --- | --- |
|  | ***p* value** |
| CYP2C19 genotype (EM *vs* non-EM) | 0.048 |
| Age | 0.603 |
| Sex | 0.637 |
| Pepsinogen I/II before eradication | 0.809 |

EM: extensive metabolizer.