

# World Journal of *Gastroenterology*

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## Retrospective Study

Current status of *Helicobacter pylori* eradication and risk factors for eradication failure

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## Abstract

## BACKGROUND

The *Helicobacter pylori* (*H. pylori*) eradication rate is decreasing in the general population of China.

## AIM

To evaluate the *H. pylori* eradication status in real-world clinical practice and to explore factors related to eradication failure.

## METHODS

Patients with *H. pylori* infection who were treated with standard 14-d quadruple therapy and received a test of cure at a provincial medical institution between June 2018 and May 2019 were enrolled. Demographic and clinical data were recorded. Eradication rates were calculated and compared between regimens and subgroups. Multivariate analysis was performed to identify predictors of eradication failure.

## RESULTS

Of 2610 patients enrolled, eradication was successful in 1999 (76.6%) patients. Amoxicillin-containing quadruple regimens showed a higher eradication rate than other quadruple therapy regimens (83.0% vs 69.0%,  $P < 0.001$ ). The quadruple therapy containing amoxicillin plus clarithromycin achieved the highest eradication rate (83.5%). Primary therapy had a higher eradication rate than rescue therapy (78.3% vs 66.5%,  $P < 0.001$ ). In rescue therapy, the amoxicillin- and furazolidone-containing regimens achieved the highest eradication rate (80.8%). Esomeprazole-containing regimens showed a higher eradication rate than those containing other proton pump inhibitors (81.8% vs 74.9%,  $P = 0.001$ ). Multivariate regression analysis found that older age, prior therapy, and use of omeprazole or pantoprazole were associated with an increased risk of eradication failure.

of the authors declare that they have no conflicts of interest to disclose.

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## CONCLUSION

The total eradication rate is 76.6%. Amoxicillin-containing regimens are superior to other regimens. Age, prior therapy, and use of omeprazole or pantoprazole are independent risk factors for eradication failure.

**Key words:** *Helicobacter pylori*; Eradication; Quadruple therapy; Proton pump inhibitor; Retrospective study

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**Core tip:** The *Helicobacter pylori* eradication rate is decreasing worldwide, and there is a lack of recent data from China. The current study of 14-d quadruple regimens in Eastern China revealed an eradication rate of 76.6%. Amoxicillin-containing regimens had the highest eradication rate in primary therapy, and amoxicillin- and furazolidone-containing regimens showed superiority in rescue therapy. Age, prior therapy, and use of omeprazole or pantoprazole were independent risk factors for eradication failure. This study can improve the choice of antibiotics and proton pump inhibitors and indicates that in clinical practice, attention should be paid to elderly patients and rescue therapy.

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## INTRODUCTION

*Helicobacter pylori* (*H. pylori*) is a widespread bacterium that typically infects the human gastric mucosa. The infection may induce numerous gastrointestinal diseases, including gastritis, peptic ulcer, gastric carcinoma, and gastric lymphoma<sup>[1-3]</sup>, and it is also associated with significant extragastric diseases, such as idiopathic thrombocytopenic purpura, idiopathic iron deficiency anemia, and vitamin B12 deficiency<sup>[4]</sup>. Epidemical studies reported that *H. pylori* affects 24%-50% of people in industrialized nations and up to 79% of those in less-developed countries. *H. pylori* infection is a worldwide threat to public health<sup>[5]</sup>.

Currently, *H. pylori* infection is considered the most important (yet controllable) risk factor for intestinal gastric cancer, as it accounts for the vast majority of cases of gastric cancer, which generally develops from a normal gastric mucosa to superficial gastritis and pre-neoplastic lesions<sup>[6]</sup>. A large number of studies have confirmed that *H. pylori* screening and treatment strategies could prevent gastric cancer in a cost-effective way, especially before the appearance of pre-neoplastic lesions and in high-risk areas<sup>[7-9]</sup>. In recent decades, the urea breath test has been widely used to detect *H. pylori* infection not only in specialized hospitals but also in physical examination centers and community hospitals in China. This has led to large numbers of asymptomatic patients being referred to specialized clinics for treatment<sup>[10]</sup>.

However, *H. pylori* eradication therapies are facing decreasing eradication rates, mainly owing to antimicrobial resistance, and are partially influenced by the efficacy of acid-suppressive drugs<sup>[11]</sup>. Recent guidelines recommend 14-d combination therapies with two types of antibiotics, a proton pump inhibitor (PPI) and bismuth<sup>[12,13]</sup>. Studies using susceptibility tests based on *H. pylori* strains cultured *in vitro* and prospective studies with relatively small sample sizes reported increasing resistance rates to clarithromycin, metronidazole, and levofloxacin, while resistance rates to amoxicillin, tetracycline, and furazolidone were low<sup>[14,15]</sup>. However, there is a scarcity of eradication data from large-sample size studies of real-world practice, which are important for formulating future guidelines and conducting clinical work in China. Moreover, it remains uncertain whether the acidic environment in the stomach during therapy, prior therapy, and demographic characteristics are related to eradication failure.

In this study, we reviewed the medical records of a large series of *H. pylori*-positive patients from the First Affiliated Hospital, Zhejiang University School of Medicine. We

evaluated the *H. pylori* eradication status in the local population of Eastern China in real clinical practice and explored factors related to therapy failure.

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## MATERIALS AND METHODS

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### **Study design and research subjects**

All of the patients diagnosed with *H. pylori* infection in the electronic medical records obtained from the First Affiliated Hospital, Zhejiang University School of Medicine (Hangzhou, China) between June 2018 and May 2019 were included. In addition, separate databases of laboratory test, endoscopy, and pathology results were searched. Anonymized information of each patient was linked to a unique identification number. Two clinicians checked the therapy regimens independently.

The inclusion criteria were the following: (1) The general and clinical information and the prescription records were complete and available; (2) The *H. pylori* infection status before treatment was directly determined by one or more of the standard detection methods (urea breath test, histologic staining, and/or bacterial culture); (3) Patients received quadruple therapy for *H. pylori* infection according to the standard antibiotic combinations and dosages of the “Fifth Chinese National Consensus Report on the management of *H. pylori* infection,” which highlights bismuth-containing quadruple therapy (PPI, bismuth, and two antibiotics) as the main empirical therapy for *H. pylori* eradication<sup>[12]</sup>; (4) The treatment lasted 14 d; and (5) Test of cure: The *H. pylori* status was confirmed by urea breath test 4-8 wk after the end of treatment.

The exclusion criteria were the following: (1) Patients who were lost to follow-up or changed the therapy regimen; and (2) Therapies that included other drugs, such as probiotics and/or Chinese traditional medicines.

The study protocol was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital, Zhejiang University School of Medicine.

### **Statistical analysis**

Statistical analyses were performed using SPSS version 22.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, USA). Categorical variables are displayed as frequencies and proportions (%). Continuous variables are presented as the mean and standard deviation (SD) unless otherwise stated. Continuous variables were compared by Student's *t*-test or one-way ANOVA. Categorical variables were compared using the  $\chi^2$  test. The Cochran-Armitage trend test was used to analyze *H. pylori* eradication rates in the different age groups. A stepwise logistic regression analysis was performed to examine the relationship between *H. pylori* eradication failure and risk factors (probability to enter = 0.05 and probability to remove = 0.10). Two-tailed *P* values < 0.05 were considered to indicate statistical significance.

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## RESULTS

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### **Patient selection and clinical characteristics**

A total of 2652 *H. pylori*-positive patients received 14-d quadruple therapy between June 2018 and May 2019 and took the urea breath test 4-8 wk later. We excluded 34 patients because the therapy regimens were changed due to drug intolerance. We also excluded another five patients who received amoxicillin plus metronidazole-based therapy and three patients who received levofloxacin plus metronidazole-based therapy owing to the small sample sizes. Finally, 2610 patients (1088 men and 1522 women) with a mean age of  $44.53 \pm 14.43$  years were included in the analyses (Figure 1).

Of the 2610 patients, 373 (14.3%) had a prior history of *H. pylori* treatment, and 2237 (85.7%) did not (Table 1). One or more symptoms were observed in 1301 (49.8%) patients, including upper abdominal pain (15.6%), abdominal distension (24.6%), nausea (5.3%), acid regurgitation or heartburn (9.6%), bitter taste in the mouth (6.0%), belching (8.6%), increased stool frequency (5.5%), and others (5.8%). A total of 1390 (53.3%) patients underwent gastroscopy before or after therapy, 244 had at least one peptic ulcer, 416 had atrophy, intestinal metaplasia, or dysplasia, as determined by biopsy histology, and 17 were diagnosed with MALT lymphoma or gastric cancer (Table 1).

Table 1 Demographic and clinical characteristics of patients with *Helicobacter pylori* infection

Variable	Cases (n)	Percentage
Overall cases	2610	
Gender		
Male	1088	41.70%
Female	1522	58.30%
Age, range (yr)		
< 30	582	22.30%
30-40	576	22.10%
40-50	478	18.30%
50-60	528	20.20%
> 60	446	17.10%
Chief complaint		
Upper abdominal pain	406	15.60%
Abdominal distension	643	24.60%
Nausea	138	5.30%
Acid regurgitation or heartburn	250	9.60%
Bitter taste in mouth	157	6.00%
Belching	224	8.60%
Increased stool frequency	143	5.50%
Others	152	5.80%
No symptoms	1309	50.20%
Received gastroscopy	1390	53.30%
Endoscopic and pathological findings		
Peptic ulcer	244	9.30%
Pre-neoplastic lesions	416	15.90%
MALT lymphoma or gastric cancer	17	0.70%
Eradication attempts		
Primary	2237	85.70%
Rescue	373	14.30%

### *Helicobacter pylori* eradication rates

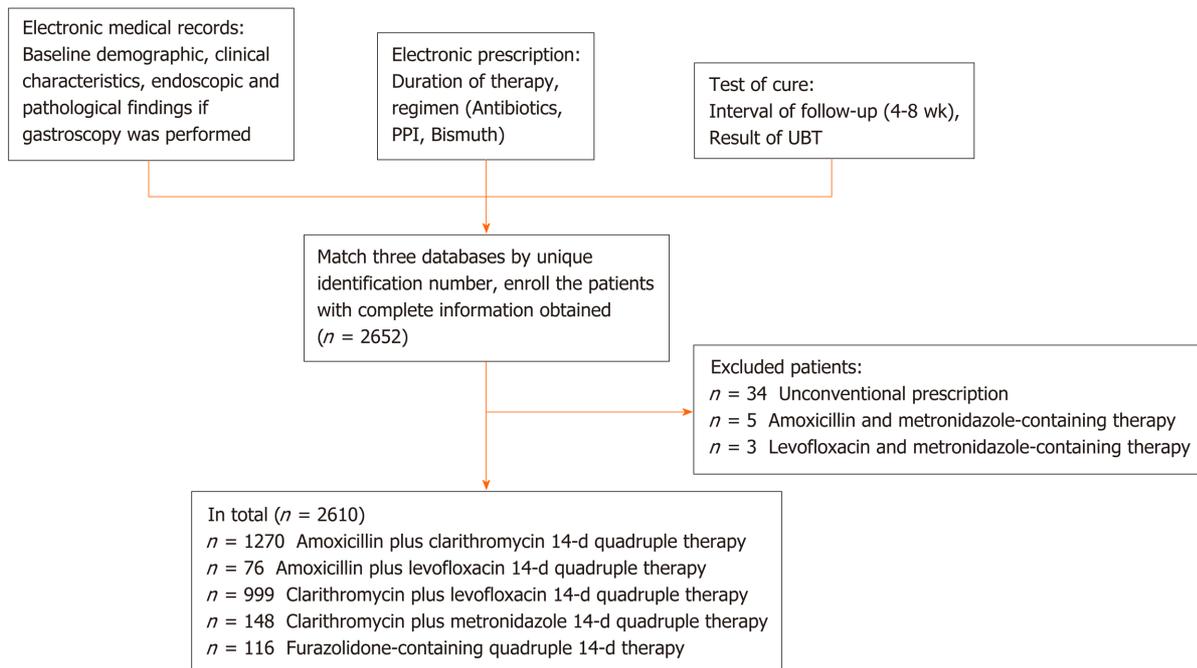
Of the 2610 patients, eradication was successful in 1999 (76.6%) patients. The eradication rate of each antibiotic combination is illustrated in Figure 2. Amoxicillin-based therapy showed a significantly higher eradication rate than other regimens (83.0% vs 69.0%,  $P < 0.001$ ). Therapy consisting of amoxicillin plus clarithromycin achieved the highest eradication rate (83.5%; 95%CI: 81.4%-85.5%), followed by therapy that consisted of amoxicillin plus furazolidone (79.4%; 95%CI: 69.4%-89.4%), amoxicillin plus levofloxacin (78.9%; 95%CI: 69.8%-88.1%), clarithromycin plus levofloxacin (72.1%; 95%CI: 69.3%-74.9%), levofloxacin plus furazolidone (63.2%; 95%CI: 41.5%-84.8%), clarithromycin plus metronidazole (54.7%; 95%CI: 46.7%-62.7%), and clarithromycin plus furazolidone (44.1%; 95%CI: 27.4%-60.8%). The eradication rate was not significantly different among the three different amoxicillin-based therapies (Figure 2).

We also found that the choice of PPI is a factor that influenced the eradication rate (Table 2). Therapy with esomeprazole achieved the highest eradication rate (81.8%; 95%CI: 78.2%-84.0%), followed by therapies with rabeprazole (78.6%; 95%CI: 75.8%-81.4%), lansoprazole (78.2%; 95%CI: 67.3%-89.1%), pantoprazole (74.0%; 95%CI: 70.5%-77.5%), and omeprazole (68.6%; 95%CI: 64.1%-73.1%). Eradication rates of therapies

**Table 2** Eradication rates of specific *Helicobacter pylori* regimens classified by proton pump inhibitor

PPI	Successful eradication (n)	Total (n)	Eradication rate (%)	95%CI (%)
Esomeprazole	566	698	81.1	78.2-84.0
Non-esomeprazole PPIs	1433	1912	74.9	73.0-76.8
Rabeprazole	657	836	78.6	75.8-81.4
Lansoprazole	43	55	78.2	67.3-89.1
Pantoprazole	449	607	74.0	70.5-77.5
Omeprazole	284	414	68.6	64.1-73.1

The following PPI dosages were prescribed: Esomeprazole, 20 mg bid; rabeprazole, 20 mg bid; omeprazole, 20 mg bid; lansoprazole, 30 mg bid; pantoprazole, 40 mg bid. PPI: Proton pump inhibitor.



**Figure 1** Study flowchart.

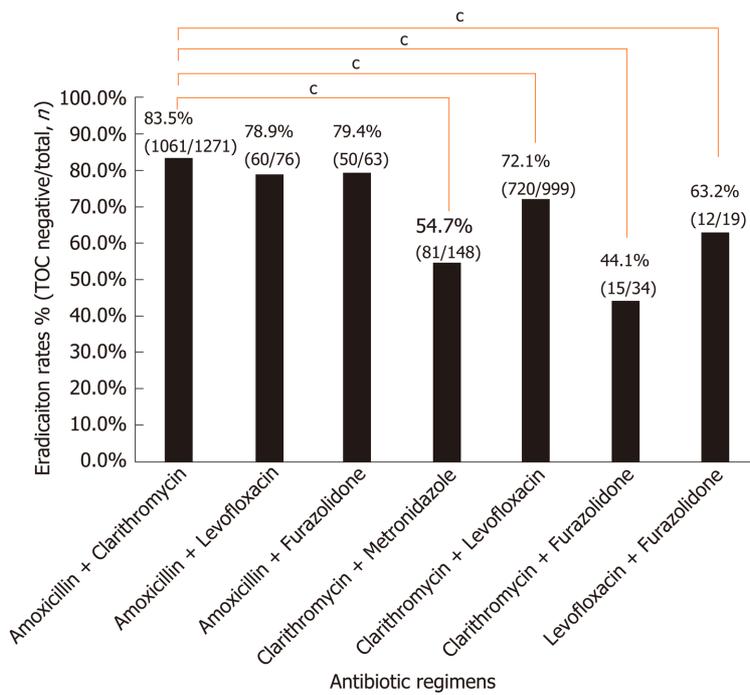
with omeprazole and pantoprazole were significantly lower than that of therapy with esomeprazole ( $P < 0.005$ ). Eradication rates of therapies with rabeprazole and lansoprazole were lower than that of therapy with esomeprazole, but the difference was not statistically significant. Therapies with esomeprazole showed a significantly higher overall eradication rate than those with other PPIs (81.8% vs 74.9%,  $\chi^2 = 10.755$ ,  $P = 0.001$ ).

In addition, we found that the eradication rate showed a significant decreasing trend with increase in age (Figure 3). The eradication rates were 84.0%, 79.3%, 74.5%, 70.8%, and 72.4% in patients aged < 30, 30-39, 40-49, 50-59, and  $\geq 60$  years, respectively ( $P$  for trend < 0.001).

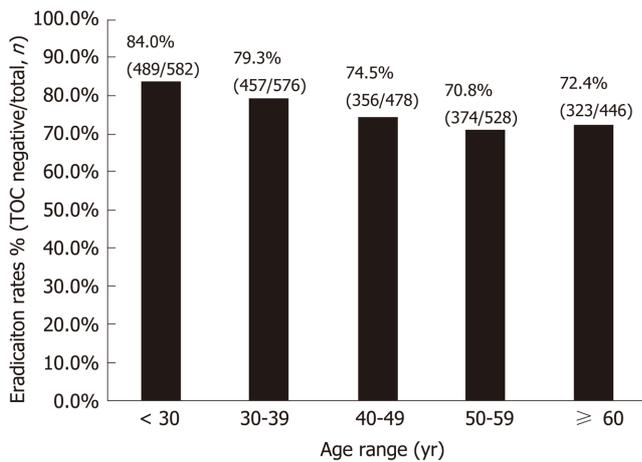
**Subgroup analysis**

The eradication rates for primary and rescue therapies were 78.3% (95%CI: 76.6%-80.0%) and 66.5% (95%CI: 61.7%-71.3%), respectively. Primary therapy showed a higher eradication rate than rescue therapy ( $P < 0.001$ ). The amoxicillin-containing regimens showed superiority in primary therapy, and amoxicillin- and furazolidone-containing regimens achieved the highest eradication rate (80.8%; 95%CI: 70.1%-91.5%) in rescue therapy, followed by amoxicillin- and clarithromycin-containing regimens (77.1%; 95%CI: 69.1%-85.2%).

The regimens containing amoxicillin plus levofloxacin, clarithromycin plus



**Figure 2 Eradication rates of *Helicobacter pylori* treatment regimens classified by antibiotic combination.** <sup>c</sup>*P* < 0.001 compared with the regimen containing amoxicillin plus clarithromycin.



**Figure 3 Eradication rates in specific patient age ranges.**

levofloxacin, and clarithromycin plus metronidazole showed lower eradication rates in rescue therapy than in primary therapy (*P* < 0.05). The regimens containing amoxicillin plus clarithromycin, amoxicillin plus furazolidone, clarithromycin plus furazolidone, and levofloxacin plus furazolidone showed no significant difference in eradication rates between primary and rescue therapy (Table 3).

**Risk factors for eradication failure**

We performed stepwise logistic regression analyses to explore factors associated with eradication failure. The univariate analysis showed that age, prior therapy, antibiotic regimen, and choice of PPI were significantly associated with the risk of eradication failure, while gender and chief complaint were not. The multivariate logistic regression analysis confirmed that older age and prior therapy were significantly associated with an increased risk of eradication failure (*P* < 0.001). Setting the regimen containing amoxicillin plus clarithromycin as the reference group, regimens containing clarithromycin plus levofloxacin, clarithromycin plus metronidazole, and clarithromycin plus furazolidone all showed a higher odds of eradication failure (*P* <

Table 3 Subgroup comparison of eradication rates

	Antibiotic regimen	Successful eradication (n)	Total (n)	Eradication rate (%)	95%CI (%)
Primary	Total	1751	2237	78.3	76.6-80.0
	Amoxicillin plus clarithromycin	980	1166	84.0	81.9-86.1
	Amoxicillin plus levofloxacin	47	54	87.0	78.1-96.0
	Amoxicillin plus furazolidone	8	11	72.7	46.4-99.0
	Clarithromycin plus metronidazole	61	112	54.5	45.2-63.7
	Clarithromycin plus levofloxacin	647	871	74.3	71.4-77.2
	Clarithromycin plus furazolidone	7	20	35.0	14.1-55.9
	Levofloxacin plus furazolidone	1	3	33.3	0.0-86.7
Rescue	Total	248	373	66.5	61.7-71.3
	Amoxicillin plus clarithromycin	81	105	77.1	69.1-85.2
	Amoxicillin plus levofloxacin	13	22	59.1	38.5-79.6
	Amoxicillin plus furazolidone	42	52	80.8	70.1-91.5
	Clarithromycin plus metronidazole	20	36	55.6	39.3-71.8
	Clarithromycin plus levofloxacin	73	128	57.0	48.5-65.6
	Clarithromycin plus furazolidone	8	14	57.1	31.2-83.1
	Levofloxacin plus furazolidone	11	16	68.8	46.0-91.5

The following antibiotic dosages were prescribed: Amoxicillin, 1000 mg bid; clarithromycin, 500 mg bid; levofloxacin, 500 mg qd or 200 mg bid; furazolidone, 100 mg bid; metronidazole, 200 mg bid, 400 mg bid, or 200 mg tid.

0.001). Other regimens were not significantly associated with eradication failure. Setting regimens containing esomeprazole as the reference group, the regimens containing omeprazole and pantoprazole showed a significantly higher risk of eradication failure ( $P < 0.05$ ), whereas rabeprazole and lansoprazole were not significantly associated with eradication failure (Table 4).

## DISCUSSION

In this large-sized retrospective study, we evaluated the efficiency of various standard 14-d quadruple regimens recommended for *H. pylori* treatment. We found that amoxicillin-based quadruple therapy was superior, and amoxicillin- and furazolidone-based therapy showed a high eradication rate in rescue therapy. Our multivariate analysis showed that older age, prior therapy, and application of omeprazole or pantoprazole increased the risk of eradication failure.

This study reports an unsatisfactory eradication rate of 76.6%, even though prescription was in strict accordance with guidelines. In a single-center retrospective study performed by another hospital in Eastern China, 992 patients received 10 to 14 d of quadruple therapy for *H. pylori* infection based on furazolidone and amoxicillin between January and December 2015. The eradication rate of rescue therapy was 91.3%<sup>[16]</sup>. However, in our study, the eradication rate of 14-d quadruple rescue therapy based on amoxicillin and furazolidone was only 80.8%. One possible reason for this discrepancy is that *H. pylori* resistance rates to antibiotics have increased during the past years. However, antibiotic resistance of *H. pylori* cultures was not investigated for all of the enrolled patients. Because of its cost and relatively low sensitivity, *H. pylori* culture is not recommended for routine diagnosis of *H. pylori* infection<sup>[17]</sup>. Another reason might be the lack of tetracycline-containing regimens and the low proportion of furazolidone-containing regimens, the resistance rates of which are relatively low in China<sup>[18]</sup>. Unfortunately, most hospitals in China are facing shortages of tetracycline, which yielded effective anti-*H. pylori* results in the USA<sup>[19]</sup>. Moreover, the potentially severe side effects of furazolidone limit its widespread application in initial empiric

Table 4 Univariate and multivariate analyses of risk factors for eradication failure

Variable		Univariate analysis			Multivariate analysis		
		OR	95%CI	P value	OR	95%CI	P value
Gender	Male	1 (Reference)					
	Female	1.202	0.998-1.447	0.052			
Age		1.018	1.011-1.024	< 0.001	1.014	1.008-1.021	< 0.001
Eradication attempts	Primary	1 (Reference)			1 (Reference)		
	Rescue	1.816	1.432-2.302	< 0.001	1.538	1.179-2.007	0.002
Antibiotic regimens	Amoxicillin plus clarithromycin	1 (Reference)			1 (Reference)		
	Amoxicillin plus levofloxacin	1.347	0.761-2.385	0.306	1.167	0.654-2.084	0.601
	Amoxicillin plus furazolidone	1.314	0.701-2.461	0.394	0.982	0.505-1.911	0.958
	Clarithromycin plus metronidazole	4.179	2.928-5.966	< 0.001	3.139	2.125-4.637	< 0.001
	Clarithromycin plus levofloxacin	1.958	1.599-2.397	< 0.001	1.863	1.517-2.287	< 0.001
	Clarithromycin plus furazolidone	6.4	3.200-12.797	< 0.001	5.748	2.834-11.655	< 0.001
	Levofloxacin plus furazolidone	2.947	1.147-7.574	0.025	2.115	0.798-5.605	0.132
PPIs	Esomeprazole	1 (Reference)			1 (Reference)		
	Rabeprazole	1.168	0.909-1.502	0.225	1.138	0.879-1.473	0.327
	Lansoprazole	1.197	0.614-2.332	0.598	1.262	0.638-2.496	0.504
	Pantoprazole	1.509	1.161-1.961	0.002	1.398	1.067-1.831	0.015
	Omeprazole	1.963	1.482-2.600	< 0.001	1.513	1.113-2.056	0.008

therapy. Therefore, furazolidone-containing regimens are more frequently used for patients with refractory *H. pylori* infection<sup>[20]</sup>.

In this study, we also observed that only half of the patients had symptoms, and the other half were asymptomatic. As more asymptomatic patients are referred to the hospital for *H. pylori* therapy, we predict that antibiotic resistance of *H. pylori* will increase in the near future. It is, therefore, worthwhile to explore methods to improve the eradication rate. A previous study reported that patient compliance is an indispensable factor influencing treatment results<sup>[21]</sup>. In addition, high-dose PPI and amoxicillin dual therapy could decrease the use of unnecessary antibiotics, which is a promising alternative approach<sup>[22,23]</sup>. Adjuvant therapy, including specific probiotics or vitamins, also showed good results, although more evidence will be needed<sup>[24]</sup>.

Consistent with previous studies, our results also suggest that acid-suppressive drugs play an important role in eradication therapy. A previous meta-analysis reported that regimens containing new-generation PPIs (esomeprazole or rabeprazole) showed a significantly higher eradication rate than those containing first-generation PPIs (omeprazole, lansoprazole, or pantoprazole)<sup>[25]</sup>. In this study, we also found a significantly lower eradication rate for omeprazole- or pantoprazole-containing regimens than for those containing new-generation PPIs. However, the difference in eradication rates between regimens containing lansoprazole and new-generation PPIs was not significant. Due to the relatively small size of the lansoprazole group, this result needs to be confirmed in future studies. The main role of PPIs in the treatment of *H. pylori* infections is to elevate the gastric pH, leading to an increase in the population of dividing *H. pylori*. Subsequently, the bacteria become more susceptible to antibiotics, such as amoxicillin and clarithromycin<sup>[26]</sup>. Selecting a PPI with a stable effect and high efficacy that is weakly influenced by CYP2C19 genotypes can improve the eradication rate<sup>[12]</sup>. In addition to the modification of dual therapy by high-dose PPI mentioned above, vonoprazan, a first-in-class potassium-competitive acid blocker, was recently reported to be an independent factor for successful *H. pylori* eradication in both primary and rescue therapy<sup>[27]</sup>.

In this study, a significant trend of decreasing eradication rates was observed with increasing age, which is consistent with previous reports<sup>[27,28]</sup>. Possible reasons include lower tolerance to and compliance with therapy, more potential complications, increased risks of drug side effects, and increased antibiotic resistance because of higher accumulated antibiotic consumption<sup>[29]</sup>. In contrast, no significant difference in

the eradication rate or frequency of adverse effects between the elderly group and the younger group was found in other studies<sup>[30,31]</sup>.

Several limitations should be considered when explaining the results of this study. First, because of its retrospective nature, the classification of primary or rescue therapy was completely dependent on the electronic medical records. The percentage of rescue therapy might be underestimated if the patients' medical histories were not fully recorded, and some rescue therapy cases might be misclassified as primary therapy, resulting in a relatively low eradication rate in the primary therapy group. Second, patient compliance was not analyzed in this study. However, all of the patients enrolled in this study completed the urea breath test 4-8 wk after finishing treatment, indicating a relatively high compliance. Third, similar to previous reports of *H. pylori* eradication, the data used in this study were extracted from a single center. The results may not be extrapolated to other areas, especially if resistance rates vary geographically. In addition, the small sample sizes of some regimens, such as the furazolidone-containing regimens in subgroup analysis of primary therapy and lansoprazole-containing regimens, limit the reliability of the corresponding results.

In conclusion, this study revealed an unsatisfactory *H. pylori* eradication rate of 76.6% in Eastern China. Amoxicillin-containing 14-d quadruple regimens have the highest eradication rate in primary therapy, and amoxicillin- and furazolidone-containing regimens show superiority in rescue therapy. An inferiority of omeprazole and pantoprazole is also observed. These findings may be helpful to improve the eradication rate of anti-*H. pylori* therapy.

## ARTICLE HIGHLIGHTS

### Research background

*Helicobacter pylori* (*H. pylori*) is a widespread bacterium that affects approximately 50% of the world's population and induces numerous gastrointestinal and extragastric diseases. Currently, *H. pylori* infection is considered the most important (yet controllable) risk factor for gastric cancer. To date, there are limited data in clinical practice regarding eradication rate and factors related to therapy failure.

### Research motivation

In recent years, *H. pylori* eradication therapies are facing decreasing eradication rates. However, risk factors related to therapy failure are still uncertain. In addition, there is a lack of recent eradication rate from China. Study in this aspect will certainly be helpful to improve the effectiveness of anti-*H. pylori* therapy in the future.

### Research objectives

This study aimed to evaluate the *H. pylori* eradication status in the local population of Eastern China and to explore factors related to eradication failure.

### Research methods

Medical records for patients with *H. pylori* infection who underwent standard 14-d quadruple therapy and received urea breath test after treatment were retrospectively reviewed. Eradication rates were calculated and compared between regimens and subgroups. Multivariate analysis was performed to identify predictors of eradication failure.

### Research results

Of 2610 patients enrolled, eradication was successful in 1999 (76.6%) patients. Amoxicillin-containing quadruple regimens showed a higher eradication rate than other quadruple therapy regimens (83.0% vs 69.0%,  $P < 0.001$ ). The quadruple therapy containing amoxicillin plus clarithromycin achieved the highest eradication rate (83.5%). Primary therapy had a higher eradication rate than rescue therapy (78.3% vs 66.5%,  $P < 0.001$ ). In rescue therapy, amoxicillin- and furazolidone-containing regimens achieved the highest eradication rate (80.8%). Esomeprazole-containing regimens showed a higher eradication rate than those containing other proton pump inhibitors (81.8% vs 74.9%,  $P = 0.001$ ). Multivariate regression analysis found that older age, prior therapy, and use of omeprazole or pantoprazole were associated with an increased risk of eradication failure.

### Research conclusions

This study confirmed that the total eradication rate is 76.6% in eastern China. Amoxicillin-containing regimens are superior to other regimens. Age, prior therapy, and use of omeprazole or pantoprazole are independent risk factors for eradication failure.

### Research perspectives

This study can improve the choice of antibiotics and proton pump inhibitors and indicates that in clinical practice, attention should be paid to elderly patients and rescue therapy. Further prospective research focusing on optimizing the treatment strategies considering these factors is required.

## REFERENCES

- Boltin D**, Niv Y, Schütte K, Schulz C. Review: Helicobacter pylori and non-malignant upper gastrointestinal diseases. *Helicobacter* 2019; **24** Suppl 1: e12637 [PMID: 31486237 DOI: 10.1111/hel.12637]
- Sugano K**. Effect of Helicobacter pylori eradication on the incidence of gastric cancer: a systematic review and meta-analysis. *Gastric Cancer* 2019; **22**: 435-445 [PMID: 30206731 DOI: 10.1007/s10120-018-0876-0]
- Venerito M**, Vasapolli R, Rokkas T, Delchier JC, Malfertheiner P. Helicobacter pylori, gastric cancer and other gastrointestinal malignancies. *Helicobacter* 2017; **22** Suppl 1 [PMID: 28891127 DOI: 10.1111/hel.12413]
- Franceschi F**, Covino M, Roubaud Baudron C. Review: Helicobacter pylori and extragastric diseases. *Helicobacter* 2019; **24** Suppl 1: e12636 [PMID: 31486239 DOI: 10.1111/hel.12636]
- Sjomina O**, Pavlova J, Niv Y, Leja M. Epidemiology of Helicobacter pylori infection. *Helicobacter* 2018; **23** Suppl 1: e12514 [PMID: 30203587 DOI: 10.1111/hel.12514]
- Rugge M**, Genta RM, Di Mario F, El-Omar EM, El-Serag HB, Fassan M, Hunt RH, Kuipers EJ, Malfertheiner P, Sugano K, Graham DY. Gastric Cancer as Preventable Disease. *Clin Gastroenterol Hepatol* 2017; **15**: 1833-1843 [PMID: 28532700 DOI: 10.1016/j.cgh.2017.05.023]
- Lansdorp-Vogelaar I**, Sharp L. Cost-effectiveness of screening and treating Helicobacter pylori for gastric cancer prevention. *Best Pract Res Clin Gastroenterol* 2013; **27**: 933-947 [PMID: 24182612 DOI: 10.1016/j.bpg.2013.09.005]
- Han Y**, Yan T, Ma H, Yao X, Lu C, Li Y, Li L. Cost-Effectiveness Analysis of Helicobacter pylori Eradication Therapy for Prevention of Gastric Cancer: A Markov Model. *Dig Dis Sci* 2020; **65**: 1679-1688 [PMID: 31673902 DOI: 10.1007/s10620-019-05910-1]
- Bae SE**, Choi KD, Choe J, Kim SO, Na HK, Choi JY, Ahn JY, Jung KW, Lee J, Kim DH, Chang HS, Song HJ, Lee GH, Jung HY. The effect of eradication of Helicobacter pylori on gastric cancer prevention in healthy asymptomatic populations. *Helicobacter* 2018; **23**: e12464 [PMID: 29345408 DOI: 10.1111/hel.12464]
- Du Y**, Zhu H, Liu J, Li J, Chang X, Zhou L, Chen M, Lu N, Li Z. Consensus on eradication of Helicobacter pylori and prevention and control of gastric cancer in China (2019, Shanghai). *J Gastroenterol Hepatol* 2020; **35**: 624-629 [PMID: 31788864 DOI: 10.1111/jgh.14947]
- Suzuki S**, Gotoda T, Kusano C, Ikehara H, Ichijima R, Ohyauchi M, Ito H, Kawamura M, Ogata Y, Ohtaka M, Nakahara M, Kawabe K. Seven-day vonoprazan and low-dose amoxicillin dual therapy as first-line Helicobacter pylori treatment: a multicentre randomised trial in Japan. *Gut* 2020; **69**: 1019-1026 [PMID: 31915235 DOI: 10.1136/gutjnl-2019-319954]
- Liu WZ**, Xie Y, Lu H, Cheng H, Zeng ZR, Zhou LY, Chen Y, Wang JB, Du YQ, Lu NH; Chinese Society of Gastroenterology, Chinese Study Group on Helicobacter pylori and Peptic Ulcer. Fifth Chinese National Consensus Report on the management of Helicobacter pylori infection. *Helicobacter* 2018; **23**: e12475 [PMID: 29512258 DOI: 10.1111/hel.12475]
- Malfertheiner P**, Megraud F, O'Morain CA, Gisbert JP, Kuipers EJ, Axon AT, Bazzoli F, Gasbarrini A, Atherton J, Graham DY, Hunt R, Moayyedi P, Rokkas T, Rugge M, Selgrad M, Suerbaum S, Sugano K, El-Omar EM; European Helicobacter and Microbiota Study Group and Consensus panel. Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report. *Gut* 2017; **66**: 6-30 [PMID: 27707777 DOI: 10.1136/gutjnl-2016-312288]
- Hu Y**, Zhu Y, Lu NH. Primary Antibiotic Resistance of Helicobacter pylori in China. *Dig Dis Sci* 2017; **62**: 1146-1154 [PMID: 28315035 DOI: 10.1007/s10620-017-4536-8]
- Zhang W**, Chen Q, Liang X, Liu W, Xiao S, Graham DY, Lu H. Bismuth, lansoprazole, amoxicillin and metronidazole or clarithromycin as first-line Helicobacter pylori therapy. *Gut* 2015; **64**: 1715-1720 [PMID: 26338726 DOI: 10.1136/gutjnl-2015-309900]
- Zhang YW**, Hu WL, Cai Y, Zheng WF, Du Q, Kim JJ, Kao JY, Dai N, Si JM. Outcomes of furazolidone- and amoxicillin-based quadruple therapy for Helicobacter pylori infection and predictors of failed eradication. *World J Gastroenterol* 2018; **24**: 4596-4605 [PMID: 30386109 DOI: 10.3748/wjg.v24.i40.4596]
- Atkinson NS**, Braden B. Helicobacter Pylori Infection: Diagnostic Strategies in Primary Diagnosis and After Therapy. *Dig Dis Sci* 2016; **61**: 19-24 [PMID: 26391269 DOI: 10.1007/s10620-015-3877-4]
- Zhang YX**, Zhou LY, Song ZQ, Zhang JZ, He LH, Ding Y. Primary antibiotic resistance of Helicobacter pylori strains isolated from patients with dyspeptic symptoms in Beijing: a prospective serial study. *World J Gastroenterol* 2015; **21**: 2786-2792 [PMID: 25759550 DOI: 10.3748/wjg.v21.i9.2786]
- Alsamman MA**, Vecchio EC, Shawwa K, Acosta-Gonzales G, Resnick MB, Moss SF. Retrospective Analysis Confirms Tetracycline Quadruple as Best Helicobacter pylori Regimen in the USA. *Dig Dis Sci* 2019; **64**: 2893-2898 [PMID: 31187323 DOI: 10.1007/s10620-019-05694-4]

- 20 **Nijevitch AA**, Shcherbakov PL, Sataev VU, Khasanov RSh, Al Khashash R, Tuygunov MM. Helicobacter pylori eradication in childhood after failure of initial treatment: advantage of quadruple therapy with nifuratel to furazolidone. *Aliment Pharmacol Ther* 2005; **22**: 881-887 [PMID: 16225499 DOI: 10.1111/j.1365-2036.2005.02656.x]
- 21 **Wang T**, Yang X, Li Y, Li L, Liu J, Ji C, Sun Y, Li Y, Zuo X. Twice daily short-message-based re-education could improve Helicobacter pylori eradication rate in young population: A prospective randomized controlled study. *Helicobacter* 2019; **24**: e12569 [PMID: 30848868 DOI: 10.1111/hel.12569]
- 22 **Yang J**, Zhang Y, Fan L, Zhu YJ, Wang TY, Wang XW, Chen DF, Lan CH. Eradication Efficacy of Modified Dual Therapy Compared with Bismuth-Containing Quadruple Therapy as a First-Line Treatment of Helicobacter pylori. *Am J Gastroenterol* 2019; **114**: 437-445 [PMID: 30807294 DOI: 10.14309/ajg.000000000000132]
- 23 **Tai WC**, Liang CM, Kuo CM, Huang PY, Wu CK, Yang SC, Kuo YH, Lin MT, Lee CH, Hsu CN, Wu KL, Hu TH, Chuah SK. A 14 day esomeprazole- and amoxicillin-containing high-dose dual therapy regimen achieves a high eradication rate as first-line anti-Helicobacter pylori treatment in Taiwan: a prospective randomized trial. *J Antimicrob Chemother* 2019; **74**: 1718-1724 [PMID: 30768161 DOI: 10.1093/jac/dkz046]
- 24 **Hu Y**, Zhu Y, Lu NH. Recent progress in Helicobacter pylori treatment. *Chin Med J (Engl)* 2020; **133**: 335-343 [PMID: 31929363 DOI: 10.1097/CM9.0000000000000618]
- 25 **McNicholl AG**, Linares PM, Nyssen OP, Calvet X, Gisbert JP. Meta-analysis: esomeprazole or rabeprazole vs. first-generation pump inhibitors in the treatment of Helicobacter pylori infection. *Aliment Pharmacol Ther* 2012; **36**: 414-425 [PMID: 22803691 DOI: 10.1111/j.1365-2036.2012.05211.x]
- 26 **Hu Y**, Zhu Y, Lu NH. Novel and Effective Therapeutic Regimens for *Helicobacter pylori* in an Era of Increasing Antibiotic Resistance. *Front Cell Infect Microbiol* 2017; **7**: 168 [PMID: 28529929 DOI: 10.3389/fcimb.2017.00168]
- 27 **Mori H**, Suzuki H, Omata F, Masaoka T, Asaoka D, Kawakami K, Mizuno S, Kurihara N, Nagahara A, Sakaki N, Ito M, Kawamura Y, Suzuki M, Shimada Y, Sasaki H, Matsuhisa T, Torii A, Nishizawa T, Mine T, Ohkusa T, Kawai T, Tokunaga K, Takahashi S. Current status of first- and second-line *Helicobacter pylori* eradication therapy in the metropolitan area: a multicenter study with a large number of patients. *Therap Adv Gastroenterol* 2019; **12**: 1756284819858511 [PMID: 31320930 DOI: 10.1177/1756284819858511]
- 28 **Kim BJ**, Yang CH, Song HJ, Jeon SW, Kim GH, Kim HS, Kim TH, Shim KN, Chung IK, Park MI, Choi IJ, Kim JH, Kim BW, Baik GH, Han SW, Seo HE, Jung WT, Hwan Oh J, Kim SG, Lee JH, Park SK, Park BJ, Yang BR, Lee J, Kim JG. Online registry for nationwide database of Helicobacter pylori eradication in Korea: Correlation of antibiotic use density with eradication success. *Helicobacter* 2019; **24**: e12646 [PMID: 31368629 DOI: 10.1111/hel.12646]
- 29 **Boyanova L**, Gergova G, Markovska R, Kandilarov N, Davidkov L, Spassova Z, Mitov I. Primary Helicobacter pylori resistance in elderly patients over 20 years: A Bulgarian study. *Diagn Microbiol Infect Dis* 2017; **88**: 264-267 [PMID: 28506722 DOI: 10.1016/j.diagmicrobio.2017.05.001]
- 30 **Kobayashi S**, Joshita S, Yamamoto C, Yanagisawa T, Miyazawa T, Miyazawa M, Kubota D, Sato J, Umemura T, Tanaka E. Efficacy and safety of eradication therapy for elderly patients with helicobacter pylori infection. *Medicine (Baltimore)* 2019; **98**: e16619 [PMID: 31348311 DOI: 10.1097/MD.00000000000016619]
- 31 **Nishizawa T**, Suzuki H, Fujimoto A, Kinoshita H, Yoshida S, Isomura Y, Toyoshima A, Kanai T, Yahagi N, Toyoshima O. Effects of patient age and choice of antisecretory agent on success of eradication therapy for *Helicobacter pylori* infection. *J Clin Biochem Nutr* 2017; **60**: 208-210 [PMID: 28584402 DOI: 10.3164/jcbs.16-86]



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