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Short-term outcomes and intermediate-term follow-up of *Helicobacter pylori* infection treatment for naïve patients: a retrospective observational study

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ABSTRACT

Objectives To explore the outcomes of *Helicobacter pylori* infection treatments for naïve patients in the real-world settings.

Design A retrospective observational study.

Setting Single tertiary level academic hospital in China.

Participants We identified patients initially receiving quadruple therapy for *H. pylori* infection from 2017 to 2020 in whom eradication was confirmed (n=23 470).

Primary outcome Efficacy of different initial *H. pylori* infection treatments.

Secondary outcome Results of urea breath test (UBT) after *H. pylori* eradication.

Results Among 23 470 patients who received initial *H. pylori* treatment, 21 285 (90.7%) were treated with amoxicillin-based regimens. The median age of the patients decreased from 2017 to 2020 (45.0 vs 39.0, p<0.0001). The main treatments were therapies containing amoxicillin and furazolidone, which had an eradication rate of 87.6% (14 707/16 784); those containing amoxicillin and clarithromycin had an eradication rate of 85.5% (3577/4182). The date of treatment, age, antibiotic regimen and duration of treatment showed correlations with the failure of *H. pylori* eradication in a multivariable logistic regression analysis. Finally, positive UBT results after eradication clustered around the cut-off value, in both the ^{13}C-UBT and ^{14}C-UBT.

Conclusions The major *H. pylori* infection treatments for naïve patients were those containing amoxicillin and furazolidone, which offered the highest eradication rate. The date of treatment, age, antibiotic regimen and duration of treatment were risk factors for the failure of *H. pylori* eradication. Additionally, positive UBT results after eradication clustered around the cut-off value.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This observational retrospective study is based on a large clinical dataset, to avoid bias and ensure comprehensiveness.
⇒ All data were extracted from an electronic medical record system, to ensure authenticity and relatively high completeness.
⇒ The findings lack generalisability due to limitations of the data source; this was a single-centre study.
⇒ Some data were inevitably missing, as the treatment protocol could not be strictly enforced.

INTRODUCTION

Helicobacter pylori is a gram-negative bacterium with prevalence varying from 24.4% to 70.1% worldwide; it accounts for over a third of global infection-attributable cancer cases.[1 2] *H. pylori* infection results in gastric diseases like chronic active gastritis and peptic ulcer disease, as well as extragastric diseases including heart diseases.[3] As *H. pylori* infection remains a major public health issue, the antibiotic resistance of *H. pylori* has increased alarmingly.[4] Fortunately, the reinfection rate remains relatively low.[5] Therefore, the effectiveness of initial *H. pylori* therapy *is crucial* because the rate of eradication failure increases with two or more rounds of treatment.[6]

Although the prevalence of *H. pylori* infection in mainland China exhibited a slow decline of around 0.9% per year in the past decades, it is still widespread.[1 7] Successful treatment is defined as a ≥90% eradication rate.[8] The preferred empirical therapy for *H. pylori* infection in China,[9] that is, bismuth-containing quadruple therapy, achieved an eradication rate of 87.3% in East Asia in a recent meta-analysis.[10] Meanwhile, resistance of *H. pylori* has been increasing in recent years, and resistance to clarithromycin is considered a major cause of the failure of clarithromycin-based therapy.[4 11 12] However, the eradication rate for susceptibility-guided therapy with clarithromycin is promising, at >95%.[13] The outcome of clarithromycin-containing therapy in real-world practice remains uncertain.

The urea breath test (UBT) is the preferred non-invasive method to detect *H. pylori* infection for initial diagnosis and assessment after treatment.[14] The principle of UBT is based on the highly active urease enzymes produced

by *H. pylori*, which catalyse the reaction of a labelled urea molecule into labelled carbon dioxide that can be detected in breath samples.[15] ^{13}C-UBT and ^{14}C-UBT have shown similar sensitivity and specificity.[16] ^{13}C-UBT can be used in children and pregnant women, while ^{14}C-UBT is contraindicated for these populations because of its radioactivity.[17] It is widely acknowledged that results close to cut-off values are not reliable.[9] Setting a low cut-off value improves sensitivity while specificity remains high.[18] It is suggested that the cut-off value should also be set according to the timing of UBT, that is, before or after the eradication treatment. In most studies, UBT results in the 'grey zone' were not common,[19] which differs from clinical practice. Thus, the cut-off value for UBT after *H. pylori* eradication should still be set in light of new evidence.

In this study, we aimed to provide an overview of the management of *H. pylori* infection based on a large clinical dataset. The aim was to elucidate the ongoing changes in the diagnosis, treatment and outcomes of *H. pylori* infection, to offer fresh insight into management strategies.

MATERIALS AND METHODS

Study design and population

Patients diagnosed with *H. pylori* infection who received initial proton pump inhibitor (PPI)-bismuth-containing quadruple treatment between 1 January 2017 and 31 December 2020 were identified by searching the electronic medical records of the Second Affiliated Hospital, Zhejiang University School of Medicine (Hangzhou, China). Patients with a positive biopsy for *H. pylori* or UBT were diagnosed with *H. pylori* infection. Patients were excluded if they had previously undergone *H. pylori* eradication treatment, experienced a change in regimen during therapy, did not have their *H. pylori* infection status confirmed after eradication or had incomplete clinical data. We retrospectively collected data from the patients' medical records, including age, sex and treatment-related variables (date of treatment, regimen, treatment duration and *H. pylori* eradication outcome). Data extraction was performed in September 2021. Patients' data were deidentified and two researchers checked the data independently. Online supplemental file 1 shows the detailed study protocol.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans for this research.

Exposure

Gastroenterologists inquired about treatment-naïve patients' history of antibiotic exposure before prescribing treatment, and determined the treatment based on their clinical experience. The prescription was recorded in the electronic medical record system. We focused on bismuth-containing quadruple therapies (PPI+bismuth+two antibiotics), which were recommended as the main empirical therapy for *H. pylori* eradication in China.[9] Different first-line treatments were classified into seven categories, and PPIs into six categories, according to the fifth Chinese National Consensus Report on the management of *H. pylori* infection (online supplemental file 2).

Follow-up and outcomes

Follow-up was performed through outpatient clinical visits. Patients were asked to visit the outpatient clinics over a period of at least 4 weeks after completion of *H. pylori* therapy. Eradication of *H. pylori* infection was confirmed by ^{13}C-UBT or ^{14}C-UBT at least 4 weeks after therapy. ^{14}C-UBT was contraindicated in children and pregnant women because of its radioactivity. Patients were informed about the similar sensitivity and specificity of ^{13}C-UBT or ^{14}C-UBT and the different costs and contraindications due to radioactivity. The patients chose the treatments themselves. The cut-off value for ^{13}C-UBT was 4.0‰ (delta over baseline, DOB), and that of ^{14}C-UBT was 100 (disintegrations per minute). Patients were not permitted to take any PPIs 2 weeks prior to the UBT, or any antibiotics 4 weeks before the UBT.

Univariate and multivariable logistic analyses

A binary logistic regression analysis was performed to examine the relationship between the failure of *H. pylori* eradication and various factors. Patients who did not receive regimens with amoxicillin plus furazolidone, amoxicillin plus clarithromycin or furazolidone plus clarithromycin were not included in the analyses. Patients who received 12-day treatment were also excluded from the analyses. Covariates were included in the multivariable model when their p values were <0.1 in univariate analysis, when adding the covariate to the model changed the OR by >10%, or on the basis of previous findings. After verifying the stability of the results among different models, we derived the final model using the forward stepwise method (likelihood ratio; criterion for model inclusion and removal=0.05 and 0.10, respectively).

Statistical analyses

Non-normally distributed continuous variables are presented as median (IQR) and categorical variables as absolute frequencies (proportions). The primary outcome was the *H. pylori* infection eradication rate. Continuous variables were compared using the non-parametric Kruskal-Wallis test. Categorical variables were compared using the χ^2 test. Statistical significance was defined as p<0.05. Statistical analyses were performed using SPSS (V.26.0) and GraphPad PRISM software (V.9.0; GraphPad Software, Inc., San Diego, California, USA).

RESULTS

From January 2017 to December 2020, 25 796 naïve patients diagnosed with *H. pylori* infection received PPI-bismuth-containing quadruple therapy and took a UBT for at least 4 weeks after the treatment. Among those

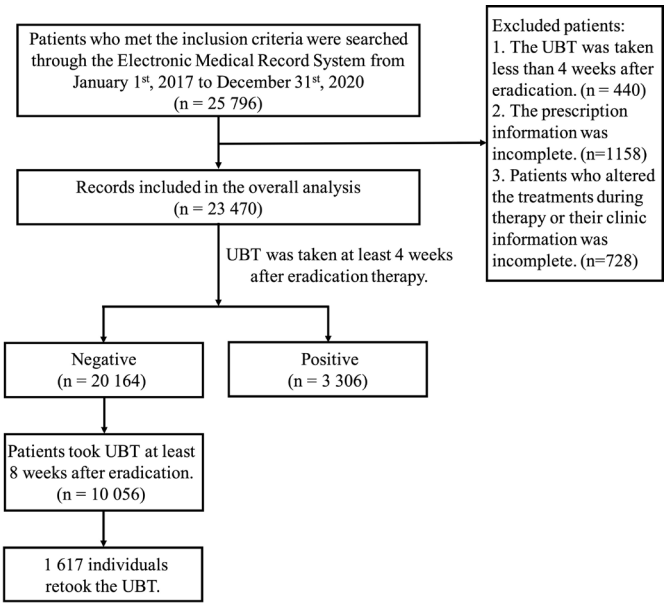

Figure 1 Study flow chart. UBT, urea breath test.

patients, 23 470 (91%) were included in the analysis (figure 1). Most of the patients (90.7%, 21 285/23 470) were treated with amoxicillin-based regimens.

Baseline characteristics

The patients' baseline demographic and clinical characteristics are presented in table 1.

Time-trend analysis

Online supplemental figure 1A depicts the age distribution among people who received *H. pylori* eradication treatment from 2017 to 2020. Bimodal distributions existed for all groups, with an increase in the number of young patients occurring over time. The median age was 45.0 (33.0–54.0) in 2017, 40.0 (31.0–54.0) in 2018, 39.0 (30.0–53.0) in 2019 and 39.0 (30.0–54.0) in 2020. Online supplemental figure 1B shows relative proportions of different UBTs used; an increase in the use of ^{14}C-UBT over time can be seen, from 42.2% in 2017 to 59.6% in 2020 (p<0.05).

Efficacy results

The overall *H. pylori* infection eradication rate rose considerably from 83.8% in 2017 to 86.8% in 2020 (online supplemental table 1). Figure 2A shows that amoxicillin-based therapies achieved a higher cure rate than amoxicillin-free therapies every year during the time frame (85.5% vs 70.1%, p<0.001 in 2017; 88.3% vs 70.8%, p<0.001 in 2018; 86.7% vs 77.4%, p<0.001 in 2019 and 87.7% vs 75.8%, p<0.001 in 2020). Figure 2B depicts the eradication rate of three dominant regimens by date of treatment. The eradication rate of therapies containing amoxicillin and furazolidone was higher than that of therapies containing amoxicillin and clarithromycin in 2017 (87.0% vs 78.9%, p<0.001). However, there was no significant difference between these two therapies in later years (88.5% vs 86.9%, p=0.178 in 2018; 86.7% vs 86.9%, p=0.814 in 2019 and 88.1% vs 86.1%, p=0.112 in 2020). During the 4-year period, therapies containing furazolidone and clarithromycin had the lowest cure rate (63.1% in 2017, 66.3% in 2018, 75.4% in 2019 and 75.1% in 2020). The high eradication rates of the other therapies might be inconsistent with real-world practice due to the small sample size (online supplemental table 2).

The eradication rates were 89.5%, 87.2%, 85.6%, 83.3% and 80.4% in patients aged ≤30, 31–40, 41–50, 51–60 and >60 years, respectively (p<0.001, figure 2C), indicating a higher eradication rate among younger patients. The same age trend was also observed for therapies containing

Table 1 Baseline characteristics

Characteristics	
Overall cases	23 470
Age, median (IQR)	40 (30–54)
Sex, N (%)	
Male	11 008 (46.9)
Female	12 462 (53.1)
Date of treatment, N (%)	
2017	3957 (16.9)
2018	6486 (27.6)
2019	7568 (32.2)
2020	5459 (23.3)
Season, N (%)	
Spring	4473 (19.1)
Summer	5942 (25.3)
Autumn	6322 (26.9)
Winter	6733 (28.7)
Antibiotic regimens, N (%)	
Amoxicillin+furazolidone	16 784 (71.5)
Amoxicillin+clarithromycin	4182 (17.8)
Amoxicillin+levofloxacin	309 (1.3)
Furazolidone+clarithromycin	1669 (7.1)
Furazolidone+levofloxacin	358 (1.5)
Clarithromycin+levofloxacin	95 (0.4)
Others	73 (0.3)
Duration, N (%)	
10	5641 (24.0)
12	1060 (4.5)
14	16 769 (71.4)
Proton pump inhibitor, N (%)	
Rabeprazole10mg	9654 (41.1)
Rabeprazole20mg	21 (0.1)
Pantoprazole	5815 (24.8)
Esomeprazole	4811 (20.5)
Omeprazole	2236 (9.5)
Lansoprazole	933 (4.0)

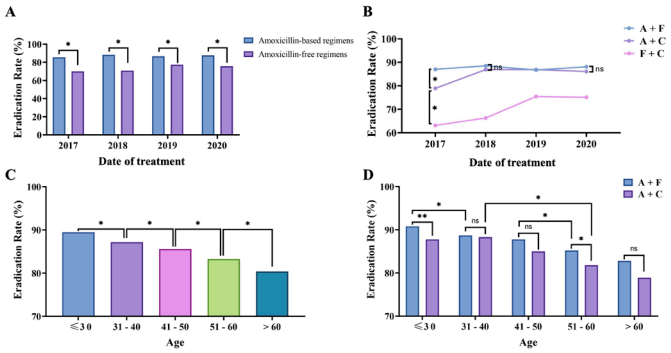

Figure 2 Efficacy results. (A) The eradication rate of amoxicillin-based regimens and amoxicillin-free regimens. (B) The eradication rate of three dominant therapies by date of treatment. (C) The eradication rate by age. (D) The eradication rate of two dominant therapies by age. A, amoxicillin; C, clarithromycin; F, furazolidone.

amoxicillin and furazolidone, and for those containing amoxicillin and clarithromycin (figure 2D). In patients aged ≤30 and 51–60 years, therapies containing amoxicillin and furazolidone had better outcomes than therapies containing amoxicillin and clarithromycin (90.8% vs 87.8%, p=0.002 and 85.2% vs 81.8%, p=0.020). Patients aged >60 years old had the lowest cure rate with both kinds of therapies (82.8% vs 78.9%, p=0.052).

We also analysed how the treatment duration and UBT result before treatment impacted the *H. pylori* eradication (online supplemental figure 2). Generally, there is little significant difference between 10-day and 14-day therapies with amoxicillin and furazolidone. For therapies including amoxicillin and clarithromycin, 14-day treatment provided a better result than 10-day treatment in 2019 (88.8% vs 82.8%, p=0.002), but no significant difference was observed in 2020 (84.6% vs 88.4%, p=0.233). The UBT value before treatment was approximately the same regardless of whether the eradication succeeded (p>0.05, online supplemental figure 3).

Multivariable logistic regression analysis of the failure of *H. pylori* eradication

We used a logistic regression model to identify factors predicting the failure of *H. pylori* eradication (table 2). We derived the final model using the forward stepwise method (likelihood ratio; criterion for model inclusion and removal =0.05 and 0.10, respectively; Hosmer and Lemeshow test statistic, p=0.652). The multivariable analysis showed that age, date of treatment, antibiotic regimen and treatment duration were associated with the poor outcomes, while sex, season and PPI use were not.

Specificity of UBT after *H. pylori* eradication

Figure 3 shows the data of positive ^{13}C-UBT and ^{14}C-UBT for naïve patients before and after eradication treatment. The median UBT value for patients positive before eradication treatment was much higher than that after treatment (23.40 (14.30–34.90) vs 12.30 (6.50–24.60) for ^{13}C-UBT, p<0.0001; 1118.0 (636.0–1702.0) vs 303.0 (146.0–930.0) for ^{14}C-UBT, p<0.0001). The results for positive UBT patients after eradication clustered around the cut-off value, but this is not seen for those with negative results (online supplemental figure 4).

Recurrence after confirmation of *H. pylori* eradication with stricter criteria

Successful *H. pylori* eradication with stricter criteria was determined based on the UBT performed at least 8 weeks after the end of the initial *H. pylori* eradication treatment.[5] Recurrence was determined based on a UBT result >2.5 times higher than the cut-off value after successful eradication. Among 10 056 patients for whom *H. pylori* eradication was successful, 1617 retook the UBT (23 had qualitative but not quantitative data). The ^{13}C-UBT result for 16 of 843 individuals was >10‰, and the ^{13}C-UBT results for 16 of 751 individuals was >250 (online supplemental table 3). The overall recurrence rate was 2.2%. For patients who received the amoxicillin-furazolidone and amoxicillin-clarithromycin regimens, the recurrence rates were 1.8% and 2.1%, respectively; there was no significant difference between these rates.

DISCUSSION

In this large-scale retrospective study, we present the outcomes and follow-up data of initial *H. pylori* treatments performed over a 4-year period in patients seen at a single centre in East China.

The recommendation that *H. pylori*-positive individuals receive early eradication treatment, to benefit both themselves and society, led to a shift in practice.[20] The indication for *H. pylori* eradication were also expanded in China, where eradication is recommended for confirmed *H. pylori* infection cases.[9] We observed that the age of patients decreased over time. There were two main age clusters, that is, young and middle-aged. The risk profiles of these two groups differed, such that they were treated via two different strategies.

From 2017 to 2020, *H. pylori* treatments included 21 285 amoxicillin-based regimens and 2185 amoxicillin-free regimens. The eradication rate of amoxicillin-free treatments was much lower than that of amoxicillin-based treatments. Amoxicillin is considered as a major component of *H. pylori* treatment in case of low resistance.[4] Doctors should carefully investigate documented patient allergies to penicillin. Previous reports indicate that most patients who claim to be allergic to penicillin ultimately have a negative skin test.[21–23] Moreover, *H. pylori* might correlate with the occurrence and persistence of chronic spontaneous urticaria,[24] which could result in false positive skin tests. In addition, some patients mistook adverse reactions, such as nausea, for allergy. Detailed information should be recorded to help us identify the truly allergic patients. Furthermore, only one fatal case of anaphylaxis in the UK between 1972 and 2007 was potentially associated with oral amoxicillin.[25] Delabelling penicillin allergy is currently of great concern, and direct challenge might

Table 2 Univariate and multivariable analyses of risk factors for *H. pylori* eradication failure

		Univariate analysis		Multivariable analysis	
Characteristics	**N**	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Age					
≤ 30	5400	1.00	–	1.00	–
30–40	5634	1.25 (1.12 to 1.41)	<0.001	1.25 (1.11 to 1.41)	<0.001
40–50	3774	1.43 (1.26 to 1.62)	<0.001	1.43 (1.26 to 1.62)	<0.001
50–60	4310	1.68 (1.49 to 1.89)	<0.001	1.70 (1.51 to 1.91)	<0.001
> 60	2586	2.04 (1.79 to 2.32)	< 0.001	2.01 (1.76 to 2.29)	< 0.001
Sex					
Male	10 257	1.00	–		
Female	11 447	0.98 (0.91 to 1.06)	0.646		
Date of treatment					
2017	3695	1.00	–	1.00	–
2018	6123	0.82 (0.73 to 0.91)	<0.001	0.85 (0.75 to 0.95)	0.005
2019	6740	0.86 (0.77 to 0.96)	0.007	0.90 (0.80 to 1.01)	0.071
2020	5146	0.80 (0.71 to 0.90)	<0.001	0.86 (0.76 to 0.97)	0.017
Season					
Spring	4008	1.00	–		
Summer	5489	0.86 (0.77 to 0.96)	0.009		
Autumn	5828	0.88 (0.78 to 0.98)	0.021		
Winter	6379	0.88 (0.79 to 0.98)	0.024		
Antibiotic regimens					
Amoxicillin+furazolidone	16 230	1.00	–	1.00	–
Amoxicillin+clarithromycin	3885	1.19 (1.08 to 1.32)	0.001	1.21 (1.09 to 1.34)	<0.001
Furazolidone+clarithromycin	1589	2.99 (2.66 to 3.36)	<0.001	2.97 (2.64 to 3.34)	<0.001
Duration					
10	5348	1.00	–	1.00	–
14	16 356	0.81 (0.75 to 0.89)	<0.001	0.89 (0.82 to 0.97)	0.011
Proton pump inhibitor					
Rabeprazole10mg	8826	1.00	–		
Rabeprazole20mg	21	1.05 (0.31 to 3.55)	0.944		
Pantoprazole	5455	1.11 (1.01 to 1.22)	0.029		
Esomeprazole	4530	1.11 (1.00 to 1.23)	0.049		
Omeprazole	2010	0.83 (0.72 to 0.96)	0.014		
Lansoprazole	862	1.02 (0.84 to 1.25)	0.818		

be a safe and effective approach.[26] Based on the existing evidence, physicians should have more confidence in the safety of oral amoxicillin.

Amoxicillin treatment schemes involving furazolidone or clarithromycin are the most widely used, and are both generally prescribed as 14-day regimens. We could discern an effect of an updated guideline not recommending levofloxacin for initial treatment (ie, few prescriptions thereof).[9] *H. pylori* remains highly sensitive to amoxicillin, furazolidone and tetracycline in China, especially East China.[12] Antibiotic regimens with amoxicillin and furazolidone dominated in the past few years, as tetracycline was not available in our hospital pharmacy. However, furazolidone is not used in some countries despite its low resistance. The Federal Drug Agency warns that furazolidone may reduce fertility or injure unborn children.[27] Nevertheless, the International Agency for Research on Cancer classified furazolidone into group 3, that is, not carcinogenic in humans.[28] The Shire company stopped marketing furazolidone, and eventually withdrew it because of poor sales.[29] According to a meta-analysis, a 14-day furazolidone-containing regimen with a low daily dose of 200 mg was well-tolerated and should be used as first-line treatment.[30] No serious adverse events were

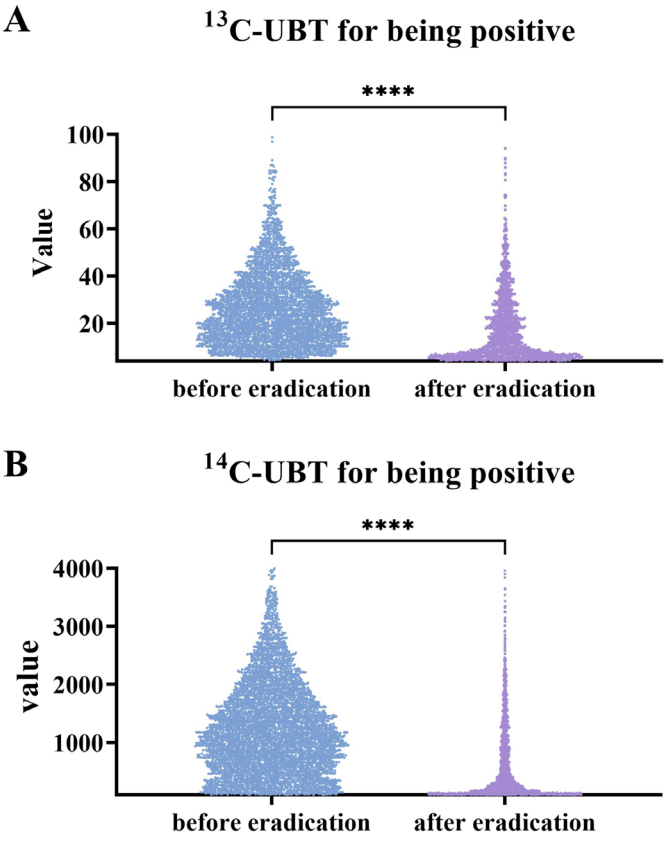

Figure 3 Results of UBT for being positive before and after *H. pylori* eradication. (A) The scatter plot of positive ^{13}C-UBT results before and after *H. pylori* eradication. (B) The scatter plot of positive ^{14}C-UBT results before and after *H. pylori* eradication. The cut-off value of ^{13}C-UBT was 4.0‰ (delta over baseline), and that of ^{14}C-UBT was 100 (disintegrations per minute). UBT, urea breath test. **** represents P < 0.0001.

reported among the cases in our study. Furazolidone-containing therapies with a high eradication rate should be re-evaluated in other countries.

Clarithromycin resistance has increased in the Asia-Pacific region in the past few decades, presumably due to the increasing consumption of macrolides.[31–33] Clarithromycin-containing regimens are not recommended in areas where clarithromycin resistance exceeds 20%.[32] However, the effectiveness of regimens with amoxicillin and clarithromycin was similar to that of regimens with amoxicillin and furazolidone from 2018 to 2020. According to updated guidelines, the gastroenterologists in our hospital were instructed to inquire about the patients' history of antibiotic exposure before prescription, which might explain the contradictory results. This suggests that we should further investigate regimens involving clarithromycin for *H. pylori* eradication, and focus on patient populations for whom they may be effective. In a population with high resistance to clarithromycin, metronidazole and levofloxacin, susceptibility-guided therapies and a highly effective empiric regimen both achieved eradication levels >95%.[13] The latter treatment should be preferred, considering its simplicity. Given the controversy over the empiric regimen of choice in our region, further prospective studies are warranted for this scenario.

Factors associated with eradication failure in this study included the date of treatment and duration, patient age and antibiotic regimen. Patients who received therapies during the period 2018–2020 were less likely to experience eradication failure than those in 2017, when the new expert consensus report was published. There might be a relationship between eradication outcomes and clinicians' knowledge of clinical practice guidelines. Moreover, failure of *H. pylori* eradication was more likely in older patients. However, the 'test and treat' strategy is not recommended for young children; it is considered unnecessary until middle-school age Japan, and in those aged ≤14 years in China.[9 14 34] However, screening among high-school students and undergraduates might be an important measure to improve the eradication rate, reduce the risk of gastric cancer and prevent transmission, although a lower eradication rate has also been reported in younger patients, especially those with gastric ulcers.[35] Symptoms and endoscopic and pathological findings suggest varying pathological mechanisms of *H. pylori* infection. Thus, these factors should be assessed in future studies to determine the relationship between age and eradication outcomes. Consistent with the recommendation of the Maastricht V/Florence Consensus Report that the treatment duration of bismuth quadruple therapy be extended to 14 days,[17] our work showed a slight positive correlation between the treatment duration and outcome. However, the difference between the two major therapies was not significant; this should be further investigated.

In agreement with a prospective study, we observed no association between the UBT value before treatment and *H. pylori* eradication status.[36] Also, patient outcomes were not significantly different according to the PPI used. However, a meta-analysis reported higher cure rates with new-generation PPIs (esomeprazole and rabeprazole) than first-generation PPIs (omeprazole, lansoprazole and pantoprazole), especially in CYP2C19 extensive metabolisers.[37] Other factors such as adherence to treatment, cigarette smoking and genetic factors, also played a role.[38 39] These factors should be further explored in future investigations.

UBT is recommended after *H. pylori* eradication, with the monoclonal feacal antigen test serving as an alternative.[9] However, the monoclonal feacal antigen test was not available in our hospital until November 2021. After radioactive drugs containing 1 µCi of carbon-14 urea were approved,[40] the use of ^{14}C-UBT increased over time, although less than predicted considering its economic benefits. Unexpectedly, after eradication treatment, UBT results close to the cut-off value were not uncommon in our cohort. Long-term follow-up of ^{13}C-UBT results after *H. pylori* eradication suggested that a lower cut-off value may improve diagnostic accuracy, based on the changes seen in the gastric density of microorganisms.[18] Negative UBT results were not clustered around the cut-off, in

contrast to the positive ones. This might lead to misclassification of the eradication failure and underestimation of the eradication rate. However, the stool antigen test is even less accurate for patients after *H. pylori* eradication, and thus has lower positive predictive value than the UBT.[41 42] Further studies are needed to address this important but overlooked issue.

This study had several limitations. First, retrospective studies do not permit definite conclusions to be drawn, and some bias is inevitable. Furthermore, the follow-up schedule was not as strict as would have been the case in a prospective study. Second, patient information was incomplete. Factors such as prior antibiotic exposure, resistance to antibiotics, treatment compliance/adherence, smoking history, the *H. pylori* infection status of family members, socioeconomic status and hygiene status were not analysed. Third, although there are other first-line treatment regimens for *H. pylori* infection,[10] we only focused on therapies containing PPI and bismuth, especially amoxicillin-based therapies including furazolidone or clarithromycin. Vonoprazan, as a potent new acid inhibitor, has not yet been approved for *H. pylori* infection in China.[43] Vonoprazan-based therapies achieved eradication rates >90%, indicating promise for *H. pylori* infection treatment.

With improved understanding and greater public attention, the treatment options for *H. pylori* infection, especially for young people, might increase. Amoxicillin-free regimens accounted for 9.3% of the treatments in our cohort. Doctors should be aware of the importance of amoxicillin and correct concept of penicillin allergy. Regimens involving amoxicillin and furazolidone were the most widely used among our cohort, presumably due to the generally acknowledged increasing resistance of *H. pylori* to clarithromycin and levofloxacin. However, the observed effectiveness of quadruple therapy containing amoxicillin-clarithromycin contradicts this. Notably, ^{13}C-UBT and ^{14}C-UBT results after *H. pylori* eradication clustered around the cut-off value, which suggests the need to review current mainstream diagnostic methods. Further studies to confirm the effectiveness of different regimens, and the specificity of UBT for *H. pylori* diagnosis, are needed.

Correction notice This article has been corrected since it first published. The affiliation of the second author, Yu Xiang has been updated.

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