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Original Article

The multicenter real-world report of the efficacies of 14-day esomeprazole-based and rabeprazole-based high-dose dual therapy in first-line *Helicobacter pylori* eradication in Taiwan

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High dose dual therapy;
Antibiotic susceptibility

Abstract *Background:* High-dose dual therapy (HDDT) using proton-pump inhibitors (PPI) and amoxicillin attracted attention for its simplicity and lower adverse event profile. Besides, vonoprazan is not available worldwide. This real-world study aims to compare the efficacy of esomeprazole-based and rabeprazole-based HDDT regimens and to identify clinical factors influencing outcomes.
Methods: A retrospective study enrolled 346 *Helicobacter pylori*-infected naïve patients from January 2016 to August 2023. Patients were assigned to either a 14-day esomeprazole-based HDDT (EA-14; esomeprazole 40 mg t.i.d. and amoxicillin 750 mg q.i.d. for 14 days, n = 173) or a 14-day rabeprazole-based HDDT (RA-14; rabeprazole 20 mg and amoxicillin 750 mg q.i.d. for 14 days, n = 173).
Results: Five patients from the EA-14 group and 10 from the RA-14 group were lost to follow-up, resulting in 168 and 163 patients for the per-protocol (PP) analysis, respectively. Eradication rates for the EA-14 and RA-14 groups were 90.2% and 80.9% (P = 0.014) in intention-to-treat (ITT) analysis; and 92.9% and 85.9% (P = 0.039) in PP analysis. Adverse event rates were

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similar between the two groups (11.9% vs 11.7%, P = 0.944). In multiple logistic regression analysis, age≧60 was associated with eradication failure (P = 0.046) and a trend of significance for smoking (P = 0.060) in the EA-14 group but not in the RA-14 group. A trend of significance was also observed for eradication regimens (EA-14 vs RA-14) (P = 0.071).

The antibiotic resistance rates were amoxicillin (2.3%), clarithromycin (14.7%), metronidazole (40.3%), and dual resistance to clarithromycin and metronidazole (7.0%).

Conclusions: Esomeprazole-based HDDT achieved over 90% eradication rates but rabeprazole-based HDDT, which failed.

Introduction

Helicobacter pylori (H. pylori) is a gram-negative bacterium associated with various gastrointestinal diseases such as peptic ulcers, gastritis, and even gastric cancer.[1] The pathogen affects approximately half of the global population, making its management a crucial public health concern.[2]

One of the significant challenges in eradicating *H. pylori* has been the rising rates of antibiotic resistances, notably to clarithromycin and metronidazole.[3] This issue is also a challenging issue in Taiwan, where regions report high clarithromycin resistance rates (>15%), compounding the problem of drug-resistant *H. pylori* strains.[4] Given the growing resistance, traditional triple therapy involving a proton-pump inhibitor (PPI), clarithromycin, and amoxicillin, has seen decreasing efficacy.[5] The Maastricht VI/Florence Consensus recommends bismuth quadruple therapy or concomitant therapy in regions with high clarithromycin resistance.[6]

High-Dose Dual Therapy (HDDT) offers a promising alternative to conventional therapies, particularly in the context of antibiotic resistance. HDDT employs high doses of a single antibiotic—usually amoxicillin—alongside a PPI to create an environment in which the antibiotic can function optimally.[7] One of the key optimistic advantages of this regimen is its ability to avoid multiple drug-resistances. Recent studies have shown that the resistance rate for amoxicillin remains relatively below 1%, making it a viable candidate for first-line treatment in *H. pylori* eradication.[4,8]

One systematic review with meta-analysis included 15 trials with a total of 3818 patients and concluded that HDDT's eradication rate was neither significantly inferior nor superior to other recommended treatment regimens such as triple therapy, bismuth quadruple therapy, or non-bismuth quadruple therapy. The relative risk (RR) of eradication was 1.00, with a 95% confidence interval (CI) of 0.96—1.05, p = 0.870. Additionally, the HDDT group exhibited significantly fewer adverse events with an RR of 0.48, 95% CI of 0.37—0.64, p < 0.001.[9] However, an important limitation of this systematic review was the heterogeneity in the types and dosage of PPIs used across the included studies. This heterogeneity has been implicated in the variable eradication outcomes reported, ranging from 52.0 % to 95.7%.[10—14] The choice of a strong acid suppression which can provide and maintain consistent optimal intra-gastric acid pH such as PPI or a novel potassium competitive acid blocker like vonoprazan given at the right dose and interval plays a critical role in influencing treatment outcomes. Realistically, vonoprazan is not available worldwide. In Taiwan, the Taiwan National Health Insurance System will pay for the prescription of vonoprazan in patients with gastroesophageal reflux disease only.

Given these considerations and challenges of *H. pylori* eradication in Taiwan, this real world report aims to offer a head-to-head comparison of the real-world efficacies of esomeprazole-based and rabeprazole-based HDDT in first-line *H. pylori* eradication.

Materials and methods

Patients

We conducted this multicenter study on a cohort of 346 *H. pylori*-infected naïve patients, aged 20 or older, who were identified from a prospectively-maintained patient registry at outpatient clinics of Kaohsiung Chang Gung Memorial Hospital and An Nan Hospital, China Medical University, in Tainan, Taiwan between January 2016 and August 2023. The naïve *H. pylori* infected patients were administered with 14-day high-dose dual therapy (HDDT) regimens: either an esomeprazole-based HDDT (EA-14; esomeprazole 40 mg t.i.d. and amoxicillin 750 mg q.i.d., n = 173) or a rabeprazole-based HDDT (RA-14; rabeprazole 20 mg and amoxicillin 750 mg q.i.d., n = 173). All enrolled patients had undergone endoscopic examination, revealing either peptic ulcers or gastritis. The diagnosis of *H. pylori* infection was confirmed through histological analysis of endoscopic biopsy specimens or gastric mucosa, or via a rapid urease test. Exclusion criteria encompassed: (a) prior *H. pylori* eradication therapy, (b) intake of antibiotics, bismuth compounds, or PPIs within the preceding 4 weeks, (c) known allergies to the medications employed in the study, (d) history of gastric surgical procedures, (e) concurrent severe systemic illnesses, such as decompensated liver cirrhosis or uremia, and (f) pregnancy. Patients were scheduled for a follow-up visit at the second week post-treatment to evaluate drug compliance and record any adverse events. The status of *H. pylori* eradication was subsequently assessed using a urea breath test eight weeks' post-treatment with eradication being defined as a negative test result.

This protocol was approved by the institutional review board and the Ethics Committee of Chang Gung Memorial Hospital (IRB-202300557B0) and An Nan Hospital (IRB-TMANH109-REC002). This protocol was approved by the institutional review board and the Ethics Committee of both hospitals. The Ethics Committee waived the requirement for informed consent for this retrospective study and all the data were analyzed anonymously. None of our patients were minors or children. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

Follow-up after treatment

Evaluation of adverse events is carried out in a prospective manner 14 days after they finish the medications. Medication compliance is assessed at the conclusion of the treatment phase by enumerating the number of unused medication units. Suboptimal compliance is explicitly characterized as the consumption of less than 80% of the prescribed medication regimen.[15] The urea breath test is executed 8 weeks after they completed the 14-day treatment.

The susceptibility of *H. pylori* strains to antibiotics including amoxicillin, clarithromycin, levofloxacin, tetracycline, and metronidazole was assessed utilizing the Epsilometer test (E-test) methodology (AB Biodisk, Solna, Sweden). According to the European Committee on Antimicrobial Susceptibility Testing (EUCAST), resistance breakpoints were established with MIC values set at $\geq$0.5 mg/L for amoxicillin, $\geq$1 mg/L for clarithromycin and levofloxacin, $\geq$4 mg/L for tetracycline, and $\geq$8 mg/L for metronidazole.[16]

Statistical analysis

The principal outcome measures encompassed eradication efficacy, incidence of adverse events, and patient compliance. To compare these outcomes between treatment groups, statistical analyses were performed employing the Chi-square test, with or without Yates' continuity correction, and Fisher's exact test as appropriate. A p-value of less than 0.05 was deemed statistically significant. A univariate analysis by way of logistic regression modeling was performed to investigate the factors affecting the eradication rates. Multivariate analysis was performed unless none of the p-value in the univariate analysis cannot be determined. Eradication rates were appraised through both intention-to-treat (ITT) and per-protocol (PP) analytical methodologies. All statistical analyses were executed utilizing SPSS software (version 22.0 for Windows, IBM Corp., Armonk, NY, USA).

Results

As depicted in Fig. 1, a total of 346 patients were included in the ITT analysis, with each treatment group (EA-14 and RA-14) comprising 173 participants. In the PP analysis, five patients from the EA-14 group and 10 from the RA-14 group were lost to follow-up, leaving 168 and 163 patients in their respective groups. Eradication rates in the ITT analysis were 90.2% (95% confidence interval [CI]: 84.8—94.2%) for the EA-14 group and 80.9% (95% CI: 74.2—86.5%) for the RA-14 group (p = 0.014). In the PP analysis, the rates were 92.9% (95% CI: 87.9—96.3%) and 85.9% (95% CI: 79.6—90.9%) for EA-14 and RA-14 groups respectively (p = 0.039). Demographic characteristics are summarized in Table 1. No significant differences were observed between the groups in any of the variables, with the exception of alcohol consumption. A higher percentage of alcohol consumption was noted in the EA-14 group compared to the RA-14 group (17.9% vs. 8.6%, p = 0.013) (Table 1).

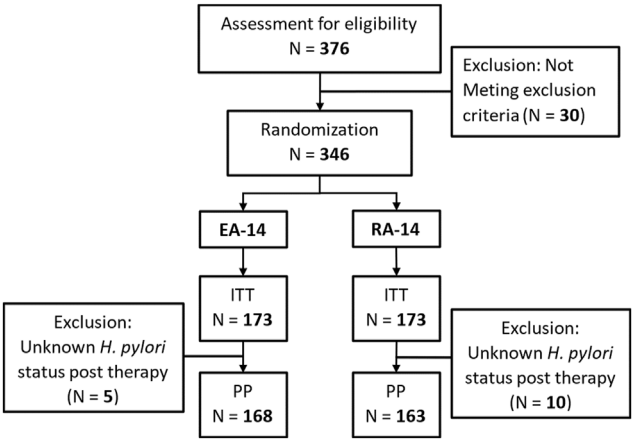

Figure 1. Patients' deposition.
Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; RA-14: rabeprazole based high dose dual therapy for 14 days; ITT: intention-to-treat; PP: per-protocol.

Adverse events and compliances

The incidence of adverse effects was identical across both study groups, with rates of 11.9% and 11.7%, respectively (p = 0.944) as shown in Table 2. The observed adverse events encompassed symptoms, such as abdominal pain, constipation, diarrhea, dizziness, headache, nausea/vomiting, and skin rash (see Table 3). Importantly, the severity of these events was generally mild, posing minimal disruption to the patients' routine activities. Consequently, medication compliance remained high in both cohorts, registering at 100%.

The clinical factors influencing the efficacy of *H. pylori* eradication therapy

Table 4 presents a univariate analysis of *H. pylori* eradication rates among patients undergoing an EA-14 or RA-14. The efficacy of the treatment varied across different patient demographics and behaviors. In EA-14 group, eradication rates were higher among patients younger than 60 years old compared to those 60 and above (96.1% vs. 87.7%, p = 0.039). Men and women showed similar eradication rates (90.4% and 94.7%, respectively, p = 0.281). A statistically significant difference is observed based on smoking habits; non-smokers achieve a much higher eradication rate

Table 1 Demographic data and endoscopic appearance of two patient groups.

Characteristics	EA-14 n = 168	RA-14 n = 163	*P*-value
Age (year) (mean ± SD)	55.8 ± 12.3	56.3 ± 14.4	0.737
Gender (male/female)	73/95 (43.5/56.5)	81/82 (49.7/50.3)	0.255
Smoking, n (%)	11 (6.5)	21 (12.9)	0.051
Alcohol consumption, n (%)	30 (17.9)	14 (8.6)	0.013
Endoscopic findings, n (%)			
Gastritis	86 (51.2)	91 (55.8)	0.209
Gastric ulcer	56 (33.3)	40 (24.5)	
Duodenal ulcer	19 (11.3)	19 (11.7)	
Gastric and duodenal ulcer	7 (4.2)	13 (8.0)	

Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; RA-14: rabeprazole based high dose dual therapy for 14 days; SD: Standard deviation.

(94.3% vs. 72.7%, p = 0.007). No statistically significance was observed for the eradication rate between alcohol consumers compared to non-consumers in EA group (86.7% vs. 94.2%, p = 0.146). In RA-14 group, eradication rates were generally consistent across different age groups, genders, and lifestyle factors like smoking and alcohol consumption. None of these subgroups showed a statistically significant difference in eradication rates. Multivariate logistic regression analysis of the clinical factors influencing the efficacy of *H. pylori* eradication therapy in EA-14 group showed that age≧60 was associated with eradication failure (P = 0.046) and a trend of significance for smoking (P = 0.060) in the EA-14 group but not in the RA-14 group (Table 5). A trend of significance was also observed for eradication regimens (EA-14 vs RA-14) (P = 0.071) (Table 6).

Antibiotic resistance

A total of 141 patient samples were cultured for the identification of *H. pylori*, yielding a positivity rate of 91.5% (n = 129/141). Table 4 delineates the antibiotic resistance profiles, indicating resistance rates for amoxicillin (2.3%), clarithromycin (14.7%), and metronidazole (40.3%), as well as dual resistance to both clarithromycin and metronidazole (7.0%). The table also elucidates the influence of bacterial susceptibility on eradication outcomes across two treatment cohorts, EA-14 and RA-14. For patients harboring amoxicillin-susceptible *H. pylori* strains, comparable eradication rates were observed: 91.3% in EA-14 and 88.8% in RA-14. Although the RA-14 group exhibited a 66.7% eradication rate for amoxicillin-resistant cases, it is crucial to note that the sample size for this subgroup was notably small (n = 3). As for clarithromycin (Cla) susceptibility(S) and metronidazole (Met) susceptibility(S) or resistance(R) (ClaS MetS & ClaS MetR), the patients where *H. pylori* was susceptible to clarithromycin and either susceptible or resistant to metronidazole, the eradication rates were again relatively similar between both groups (EA-14: 88.9%—92.3%, RA-14: 87.5%—93.3%). None of these comparisons showed a statistically significant difference (p = 0.736 and p = 0.376, respectively). As for the ClaR MetS & ClaR MetR, both groups showed high eradication rates when *H. pylori* was resistant to clarithromycin and either susceptible or resistant to metronidazole. The *H. pylori* eradication rates for the dual resistant to both clarithromycin and metronidazole were 100% (4/4) in the EA-14, and 60% (3/5) in the RA-14. However, the sample sizes are small, and these findings are not statistically significant.

Discussion

Our study responds to the present globally rising antibiotic resistances in *H. pylori* strains, specifically focusing on resistance to clarithromycin and metronidazole. This trend has led to an increase in eradication failure rates and has prompted the development of novel therapeutic strategies, such as sequential therapy, non-bismuth quadruple therapy, and hybrid therapy. Importantly, we showed that amoxicillin resistance rates were at 2.3%, corroborating the low resistance rates observed globally and also in Taiwan,

Table 2 The major outcomes of the two groups of patients.

	Eradication rate		
	EA-14 (n = 168)	RA-14 (n = 163)	*P*-value
Intention to treat	90.2% (156/173)	80.9% (140/173)	0.014
Per-protocol	92.9% (156/168)	85.9% (140/164)	0.039
Adverse effect	11.9% (20/168)	11.7% (19/164)	0.944
Compliance	100% (168/168)	100% (164/164)	—

Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; RA-14: rabeprazole based high dose dual therapy for 14 days.

Table 3 Adverse events of the two groups of patients.

	EA-14 n = 168	RA-14 n = 163	*P*-value
Abdominal pain, n (%)	6 (3.6)	4 (2.5)	0.553
Constipation, n (%)	2 (1.2)	2 (1.2)	0.976
Diarrhea, n (%)	1 (0.6)	2 (1.2)	0.544
Dizziness, n (%)	3 (1.8)	3 (1.8)	0.970
Headache, n (%)	3 (1.8)	1 (0.6)	0.329
Nausea/vomiting, n (%)	4 (2.4)	8 (4.9)	0.219
Skin rash, n (%)	1 (0.6)	0 (0)	0.324

Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; RA-14: rabeprazole based high dose dual therapy for 14 days.

which makes amoxicillin a potent weapon in the fight against *H. pylori*.

During our analysis process for the demographic data of two patient groups, we observed a higher rate of alcohol consumption in the EA-14 group compared to the RA-14 group by chance (17.9% vs. 8.6%, p = 0.013) (Table 1). However, twenty-six of the 30 patients with social drinking history were eradicated by prescribing EA-14 comparing to the success rate of those without drinking (130/138, 94.2%, p = 0.146) (Table 4). A recent meta-analysis conducted by Jing Yu et al. found no significant association between alcohol consumption and the risk of *H. pylori* eradication failure (OR = 1.09, 95% CI, 0.94—1.26) except for Asian population with alcohol intake >40 g/day (OR = 3.17, 95% CI, 1.56—6.41).[17] Since these 30 patients were social drinking habit, it could explain the eradication rates of these 30 patients. Moreover, our results showed that no statistically significance was observed for the eradication rate between alcohol consumers compared to non-consumers in the univariate analysis of EA group (86.7% vs. 94.2%, p = 0.146) and in RA-14 group (85.9% vs. 85.7%, p = 0.984). In addition, alcohol consumption was not the clinical factor influencing the efficacy of *H. pylori* eradication therapy in multivariate analysis.

Our study reveals a key factor for the success of HDDT is the ability to maintain intra-gastric pH above 6 to optimize amoxicillin sensitivity.[18,19] This builds upon early attempts at dual therapies that failed largely due to inadequate acid suppression. In our case, the use of PPI at high doses was crucial. The role of PPI in maintaining intra-gastric pH cannot be overstated, especially when it comes to the success rates of *H. pylori* eradication therapies. This aspect becomes even more relevant given the increasing prevalence of antibiotic-resistant strains of *H. pylori*. Amidst the milieu of eradication therapies, the significance of PPI dosing, specifically the use of esomeprazole, has gained attention for its superiority to control intra-gastric pH as compared to other PPIs.

According to a study by Clive H Wilder-Smith et al., esomeprazole at a 40 mg dose was shown to provide more

Table 4 Univariate analysis of the clinical factors influencing the efficacy of *H. pylori* eradication therapy.

Principle parameter		EA-14			RA-14		
		Case no.	Eradication Rate (%)	*P*-value	Case no.	Eradication Rate (%)	*P*-value
Age	<60 years	99/103	96.1	0.039	73/84	86.9	0.701
	≥60 years	57/65	87.7		67/79	84.8	
Sex	Male	66/73	90.4	0.281	67/81	82.7	0.247
	Female	90/95	94.7		73/82	89.0	
Smoking	(−)	148/157	94.3	0.007	121/142	85.2	0.518
	(+)	8/11	72.7		19/21	90.5	
Alcohol consumption	(−)	130/138	94.2	0.146	128/149	85.9	0.984
	(+)	26/30	86.7		12/14	85.7	
Compliance	Good	156/168	92.9	—	140/163	85.9	—
	Poor	0	0		0	0	
Culture (n = 129)		(n = 46)			(n = 83)		
Amoxicillin	Susceptible	42/46	91.3	—	71/80	88.8	0.249
	Resistant	0	0		2/3	66.7	
ClaS	MetS	24/27	88.9	0.736	35/40	87.5	0.376
	MetR	12/13	92.3		28/30	93.3	
ClaR	MetS	2/2	100.0	—	7/8	87.5	0.510
	MetR	4/4	100.0		3/5	60.0	

Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; RA-14: rabeprazole based high dose dual therapy for 14 days; ClaS: clarithromycin-susceptible; ClaR: clarithromycin-resistant; MetS; metronidazole-susceptible; MetR: metronidazole-resistant.

Table 5 Multivariate analysis of the clinical factors influencing the efficacy of *H. pylori* eradication therapy in EA-14 group.

Principle parameter		Eradication Rate (%)	Univariate p-value	Multivariate O.R. (95%CI)	p-value
Age	<60 years	96.1	0.039	3.728 (1.026−13.547)	0.046
	≥60 years	87.7			
Smoking	(−)	94.3	0.007	6.024 (0.925−39.230)	0.060
	(+)	72.7			

Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; O.R.: Odds ratio.

effective and sustained control of intra-gastric pH than lansoprazole 30 mg or rabeprazole 20 mg.[20] The study reveals that the intra-gastric pH was maintained at >4 for 65% of the 24-h period with esomeprazole compared to 53% for lansoprazole and 45% for rabeprazole. This finding supports our study's results showing >90% eradication rates achieved with a high dose of esomeprazole 40 mg, administered three times daily. The ability of esomeprazole to maintain an intra-gastric pH above 6 appears to be a pivotal factor in its superior eradication capabilities, thereby enabling a more effective antibiotic sensitivity of amoxicillin against *H. pylori*. Although direct comparisons of esomeprazole 40 mg administered three times daily with other PPI regimens regarding intragastric pH control are lacking in the literature, evidence supports the superiority of esomeprazole over other PPIs in achieving sustained intragastric pH elevation. A study by Miehlke S et al. demonstrated that esomeprazole 40 mg twice daily significantly outperformed pantoprazole 40 mg twice daily in maintaining higher median intragastric pH levels over a 24-h period (pH 6.4 vs. 5.1, $P < 0.00005$), with a greater duration of pH > 4 (21.1 h vs. 16.8 h, $P < 0.0001$).[21]

The review studies also shed light on the considerable differences in the acid-suppressive effects between different PPIs. It affirms that esomeprazole provided a significantly higher percentage of patients with an intragastric pH greater than 4.0 for more than 12 h relative to the other proton pump inhibitors ($p < 0.05$).[22,23] Furthermore, Taiwanese also benefited from the influence of the CYP2C19 metabolizer genotype on eradication rates. Asians have a higher prevalence of the poor metabolizer genotype for PPIs, which could result in prolonged drug action and possibly contribute to better outcomes.[24,25]

In our study, we observed that the clinical factors influencing the efficacy of *H. pylori* eradication therapy in EA-14 group showed that age≧60 was associated with eradication failure ($P = 0.046$) and a trend of significance for smoking ($P = 0.060$) in the EA-14 group but not in the RA-14 group. While eradication outcomes in elderly patients across various regimens may show variability due to factors such as overall health status and antibiotic resistance, it is important to note that these patients still stand to gain from eradication therapy to prevent the progression of gastric mucosal lesions and reduce the risk of developing gastric cancer.[26] The impact of smoking on eradication success is supported by a meta-analysis,[27] which reported summary odds ratio (OR) for eradication failure among smokers relative to nonsmokers of 1.95 (95% CI: 1.55−2.45; $p < 0.01$). However, the literature directly comparing the influence of host factors such as age and smoking on the differential efficacy between esomeprazole and rabeprazole is scarce. It is plausible that rabeprazole's pharmacokinetics exhibit reduced sensitivity to variations in the cytochrome P450 (CYP) enzyme system,[28] which is known to be affected by age, smoking, and genetic polymorphisms. This characteristic may contribute to the observed differences in how these host factors impact the eradication success rates between the two treatment groups.

Since adequate acid suppression is one of the most important key points to successfully eradicate *H. pylori* infection, the emergence of vonoprazan, a novel potassium-competitive acid blocker merits to the improvement of treatment success. Distinct from traditional PPI, vonoprazan has demonstrated superior capabilities in maintaining the intragastric pH above 6 for more extended periods.[29] In contrast to conventional PPIs, vonoprazan-amoxicillin (VA) dual therapy has shown promising results as a first-line treatment for *H. pylori* infection in Japanese studies. Notably, the regimen achieved an impressive eradication rate of 87.5% and 89.6% by ITT and PP analysis, respectively.[30] However, the application of VA dual therapy extends beyond the Japanese population, necessitating further investigation.

Table 6 Multivariate analysis of the clinical factors influencing the efficacy of *H. pylori* eradication therapy in overall study cohort.

Principle parameter		Eradication Rate (%)	Multivariate O.R. (95%CI)	p-value
Age	<60 years	92.0	1.718 (0.839−3.519)	0.139
	≥60 years	81.6		
Eradication agent	**EA-14**	92.9	1.979 (0.942−4.155)	0.071
	RA-14	85.9		

Abbreviations: EA-14: esomeprazole based high dose dual therapy for 14 days; RA-14: rabeprazole based high dose dual therapy for 14 days; O.R.: Odds ratio.

One recent study on Chinese patients revealed less-than-optimal eradication rates (<90%) with either 7- or 10-day VA dual therapy regimens, underscoring the need for protocol optimization.[31] A subsequent study examining 14-day low-dose (1000 mg b.i.d.) or high-dose (1000 mg t.i.d) amoxicillin -vonoprazan (20 mg b.i.d.) regimens produced satisfactory eradication rates of 89.1% and 87.3% by ITT analysis, respectively, and 94.1% and 95.9% by per-protocol analysis, respectively.[32] These findings point out a potential avenue for expanding the duration to 14 days of VA dual therapy as a robust first-line treatment option for *H. pylori* infection in China and possibly other regions.

The strength of this study lies in the real-world data analysis and the reported the updated antibiotic resistance rates, offering critical information for optimizing treatment strategies, particularly in regions with prevalent antibiotic resistance. The main limitation of our study was the inability to conduct CYP2C19 genotyping. The study used a retrospective design to analyze data, which may introduce selection bias or data inconsistencies. The study was conducted in specific hospitals in Taiwan, limiting the generalizability of the findings to other geographical areas or healthcare settings. While the study did collect information on lifestyle factors such as coffee and tea consumption, it did not explore how these factors might interact with or impact the efficacy of treatment. While the study does an admirable job of breaking down eradication rates among different subgroups (e.g., based on antibiotic resistance), the sample sizes for some of these subgroups are quite small, affecting the statistical power of these findings.

In conclusions, the study offers valuable insights into the comparative efficacies of EA-14 and RA-14 regimens in many real-world settings without vonoprazan or limited the use of vonoprazan for treating gastroesophageal disease such as in Taiwan. Esomeprazole containing HDDT attained >90% eradication rates but rabeprazole-based HDDT failed. The findings of this study were crucial in guiding the PPI selection of first-line HDDT *H. pylori* eradication therapies.

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Data availability

All data extracted from included studies.

Declaration of competing interest

All authors declared there was no conflict of interests.

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