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ARTICLE

Association of *Helicobacter pylori* Infection With Lipid Metabolism, Inflammatory Markers, and Modified Framingham Stroke Risk Score in Patients at High-Risk of Ischemic Stroke: A Retrospective Study

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Abstract

Aims/Background *Helicobacter pylori* (*H. pylori*) infection is prevalent in 42–64% of the Chinese population, with emerging evidence linking it to extragastrointestinal diseases, including stroke. This study aimed to investigate the association between *H. pylori* infection and lipid metabolism, inflammatory markers, and the modified Framingham stroke risk score in patients at high risk of ischemic stroke, and to further analyze the relationship between the Framingham risk score and related clinical variables.

Methods A retrospective analysis was performed on 320 patients at high risk of ischemic stroke (10-year stroke risk $\geq$10% by modified Framingham scale) admitted to Jinhua People's Hospital from January 2020 to December 2022. Patients were divided into a *H. pylori*-positive group (n = 180) and a *H. pylori*-negative group (n = 140) based on ^{14}C urea breath test ($\geq$100 dpm/mmol vs. $<$100 dpm/mmol). Clinical data, lipid profiles (total cholesterol [TC], triglycerides [TG], low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [HDL-C]), inflammatory markers (high-sensitivity C-reactive protein [hs-CRP], homocysteine [Hcy], fibrinogen [FIB]), and modified Framingham stroke risk scores were compared between groups. Correlation and multivariate regression analyses were used to explore the relationships between variables.

Results Compared with the *H. pylori*-negative group, the *H. pylori*-positive group had significantly higher levels of TC, TG, LDL-C, hs-CRP, Hcy, FIB, and modified Framingham scores (all $p < 0.05$), and lower HDL-C ($p < 0.05$). *H. pylori* infection correlated positively with the modified Framingham stroke risk score (point-biserial $r = 0.33$, $p < 0.001$). Multivariate regression showed that *H. pylori* infection was an independent predictor of elevated modified Framingham stroke risk scores ($\beta = 0.21$, $p < 0.001$).

Conclusion *H. pylori* infection is associated with abnormal lipid metabolism, enhanced inflammatory response, and increased ischemic stroke risk in high-risk patients, suggesting its potential role in stroke pathogenesis.

Key words: *Helicobacter pylori*; ischemic stroke; lipid metabolism; inflammatory markers; risk assessment

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Introduction

Ischemic stroke remains one of the most pressing global health challenges, accounting for approximately 70% of all stroke cases and causing over 6 million deaths annually worldwide (GBD 2021 Stroke Risk Factor Collaborators, 2024).

In China, the burden is particularly severe: recent epidemiological data indicate an annual incidence of 270 per 100,000 population, with nearly 2 million new cases each year (Tu et al., 2023). Alarmingly, stroke survivors often face long-term disabilities—millions of individuals in China live with stroke-related sequelae, which place immense physical, emotional, and economic strain on families and healthcare systems (Ji et al., 2025). As such, identifying modifiable risk factors and refining risk stratification tools are critical for improving primary prevention strategies.

Current clinical management of ischemic stroke relies on neuroimaging (computed tomography/magnetic resonance imaging) for diagnosis and thrombolysis/thrombectomy for acute treatment (Libby, 2021; Jabbour et al, 2023). However, primary prevention remains the cornerstone of reducing stroke burden. While antihypertensives, statins, and antiplatelet agents are guideline-recommended for high-risk individuals (Pothineni et al., 2017), approximately 30% of ischemic strokes occur in those deemed having "low-intermediate risk" based on conventional scales (Zhou et al., 2023). This residual risk suggests that traditional models may not fully account for non-classical contributors—particularly chronic inflammation and infection—which are increasingly recognized as important drivers of stroke. Consequently, several critical gaps remain: (1) existing risk models underestimate inflammatory/infectious drivers of atherosclerosis; (2) biomarkers linking chronic infections to stroke pathogenesis are underexplored; (3) no trials have assessed whether targeting *Helicobacter pylori* (*H. pylori*) infection modifies stroke risk in primary prevention settings.

Atherosclerosis, the pathological cornerstone of ischemic stroke, is increasingly recognized as a dynamic inflammatory process rather than a simple lipid-deposition disorder (Libby, 2021). This paradigm shift highlights the role of chronic infections in driving vascular inflammation and accelerating atherosclerotic progression (Pothineni et al., 2017). Among various pathogens, *H. pylori*, a gram-negative bacterium colonizing the gastric mucosa in 42–64% of the Chinese population, has emerged as a particularly intriguing candidate (Zhou et al., 2023; Tan and Goh, 2012). Beyond its well-established role in peptic ulcer disease and gastric cancer, *H. pylori* has been linked to extragastrointestinal conditions, including coronary artery disease, cerebrovascular disorders, and even neurodegenerative diseases (Doheim et al., 2021; Du et al., 2025). The mechanisms underlying *H. pylori*'s systemic effects are multifaceted. First, *H. pylori*-induced gastric inflammation triggers a cascade of pro-inflammatory cytokines, such as tumor necrosis factor alpha (TNF-α) and interleukin-6 (IL-6), that enter the systemic circulation, promoting endothelial dysfunction and vascular smooth muscle cell proliferation—key steps in atherogenesis. Second, *H. pylori* infection disrupts lipid metabolism: studies have consistently shown associations of *H. pylori* infection with elevated total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), alongside reduced high-density lipoprotein cholesterol (HDL-C) (Xie et al., 2023; Chen et al., 2024). Third, *H. pylori* may impair homocysteine metabolism by interfering with vitamin B12 and folate absorption, leading to hyperhomocysteinemia—a known risk factor for thrombosis and endothelial damage (Chen et al., 2021). Ad-

ditionally, *H. pylori*-derived virulence factors such as cytotoxin-associated gene A (*CagA*) can directly activate platelets and coagulation pathways, increasing thrombotic risk (Sundqvist et al., 2023).

Against this backdrop, risk assessment tools like the modified Framingham stroke risk score play a pivotal role in identifying high-risk individuals. This validated scale integrates traditional risk factors—including age, hypertension, diabetes, smoking, and cardiovascular history—to estimate 10-year ischemic stroke risk (Zhou et al., 2017; Wang et al., 2003). However, its utility could be enhanced by incorporating novel biomarkers or infectious factors, as current iterations do not account for chronic inflammatory or infectious contributors. Notably, previous studies exploring *H. pylori*'s association with ischemic stroke have yielded conflicting results: while some report a significant link (Shindler-Itskovitch et al., 2019), others find no association (Keikha and Karbalaei, 2022), likely due to variations in study design, sample size, and population characteristics.

Crucially, most existing research focuses on acute stroke patients, with limited data on high-risk populations before the onset of clinical events. This gap is significant, as primary prevention in high-risk individuals offers the greatest potential for reducing stroke burden. Furthermore, the interplay between *H. pylori* infection, metabolic perturbations (e.g., dyslipidemia), inflammatory markers (e.g., high-sensitivity C-reactive protein [hs-CRP], homocysteine [Hcy]), and validated risk scores like the Framingham scale remains underexplored. Understanding these relationships could shed light on *H. pylori*'s role in amplifying traditional risk factors and inform targeted prevention strategies.

In this context, our retrospective study aimed to address these gaps by investigating: (1) the association between *H. pylori* infection and lipid metabolism indices in high-risk individuals; (2) the relationship between *H. pylori* infection and systemic inflammatory markers; (3) whether *H. pylori* status correlates with modified Framingham stroke risk scores; and (4) whether *H. pylori* independently predicts stroke risk after controlling for confounders including lipid-lowering medications. This study on a cohort with a 10-year risk of ischemic stroke $\geq$10% provides insights into *H. pylori*'s potential as a modifiable target for primary prevention in those most vulnerable to stroke.

Methods

Study Population

We retrospectively enrolled 320 patients at high risk of ischemic stroke (10-year risk $\geq$10% by modified Framingham scale) from January 2020 to December 2022. The inclusion criteria of this study are as follows: (1) 10-year ischemic stroke risk $\geq$10% according to the modified Framingham stroke risk score; (2) age $\geq$18 years; (3) availability of complete clinical and laboratory data; (4) ^{14}C urea breath test (^{14}C-UBT) performed within 1 week of admission.

Individuals fulfilling the following criteria were excluded: (1) recent use of lipid-lowering drugs (statins, ezetimibe, proprotein convertase subtilisin/kexin type 9 [PCSK9] inhibitors, fibrates) within 3 months; (2) pregnancy or lactation; (3)

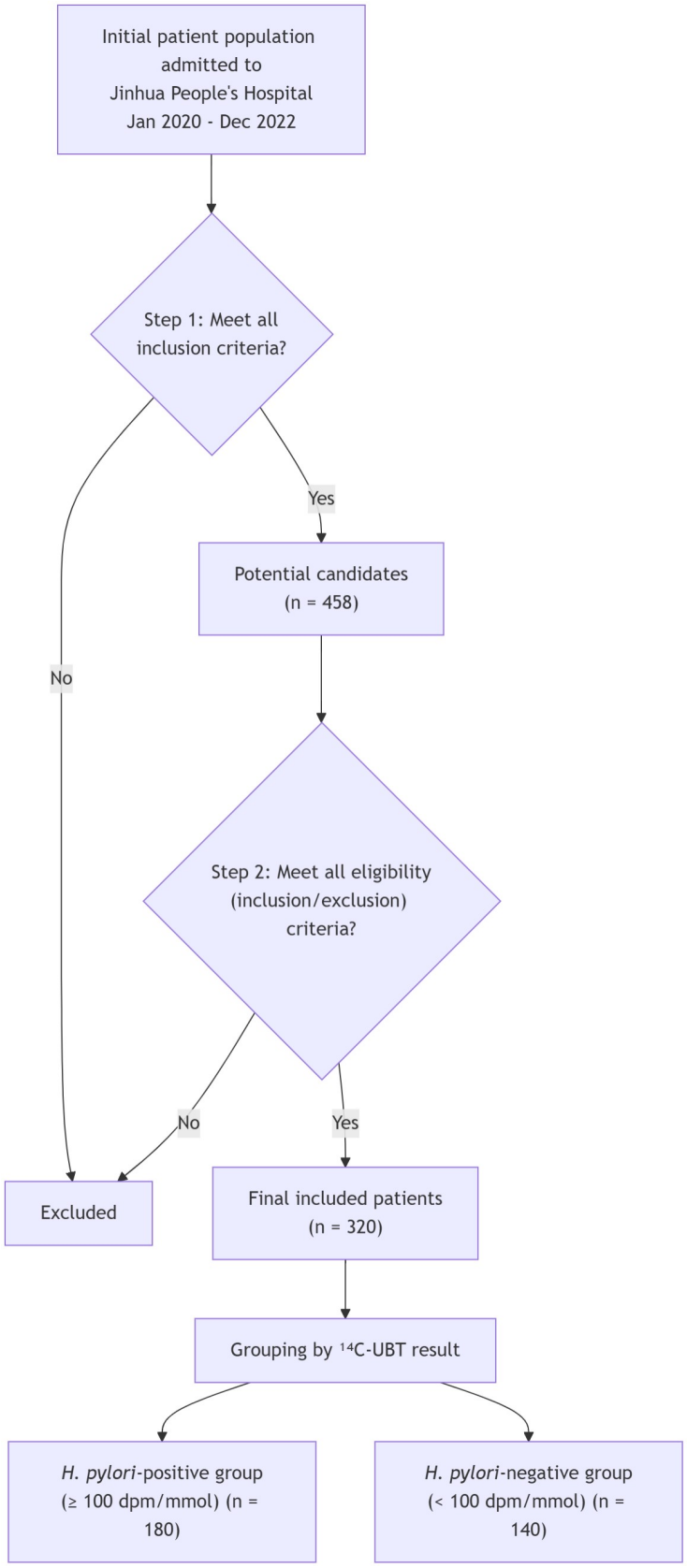

Fig. 1. Flowchart of patient screening, enrollment, and grouping process. Abbreviations: *H. pylori*, *Helicobacter pylori*; ^{14}C-UBT, ^{14}C urea breath test.

other active bacterial infections; (4) systemic corticosteroid/immunosuppressant use; (5) medication washout: antibiotics/bismuth ≥4 weeks; proton pump inhibitors (PPIs) ≥2 weeks before ^{14}C-UBT. It is important to note that the exclusion criterion 'recent use of lipid-lowering drugs' refers to continuous use within 3 months prior to enrollment. Patients who had discontinued lipid-lowering therapy for ≥3 months before enrollment were not excluded. Patients were divided into a *H. pylori*-positive group (^{14}C-UBT ≥100 dpm/mmol) and a *H. pylori*-negative group (<100 dpm/mmol). The flowchart summarizing the patient screening, enrollment, and grouping process is presented in Fig. 1 (initial screening: n = 458; final analyzed: n = 320).

Data Collection

Demographic and clinical data included: age, body mass index (BMI), gender, history of hypertension, diabetes mellitus, smoking status, alcohol consumption, family history of cardiovascular disease, and medication use. Fasting venous blood was collected to detect TC, TG, LDL-C, HDL-C (Hitachi 7180 analyzer, Hitachi High-Tech Corporation, Tokyo, Japan), hs-CRP (by means of immunoturbidimetry, using kit CSB-E08617h-IS, CUSABIO Bioengineering Co., Ltd., Wuhan, China), Hcy (by means of chemiluminescence, using ARCHITECT i2000SR, Abbott Laboratories, Chicago, IL, USA), and fibrinogen (FIB; commercial clotting assay, Sysmex CS-2500, SYSMEX, Kobe, Japan). Modified Framingham stroke risk score was calculated using a method reported previously (D'Agostino et al., 2013), which incorporates weighted scores for: age (60–64 years = 1 point; 65–69 years = 2 points; 70–74 years = 3 points; 75–79 years = 4 points), systolic blood pressure (120–139 mmHg = 1 point; 140–159 mmHg = 2 points; ≥160 mmHg = 3 points), anti-hypertensive medication use (+1 point), diabetes (+2 points), current smoking (+3 points), cardiovascular disease (+3 points), atrial fibrillation (+6 points), and left ventricular hypertrophy (+4 points). Total score ranges from 0 to 26 points. The raw score was then converted into a predicted 10-year risk of ischemic stroke using the algorithm derived from the Framingham cohort. For clinical risk stratification, patients were categorized as follows: 10–15% (Lowest high-risk), 15–20% (Moderate high-risk), and ≥20% (Highest high-risk).

Statistical Analysis

Statistical analysis was performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Normality of continuous variables was evaluated using the Shapiro-Wilk test. Student's t-test was used to compare normally distributed continuous variables, which are expressed as mean ± standard deviation (SD). Variables with a skewed distribution were log-transformed prior to analysis. The chi-square test or chi-square correction test was used to compare categorical variables, which are expressed as frequencies (percentages). Correlation analysis was performed using point-biserial correlation. The variable selection process for regression analysis followed a two-step approach: First, univariate linear regression was conducted, including all demographic, clinical, laboratory, and inflammatory variables (listed in Tables 1,2,3). Second, variables demonstrating statistical significance ($p < 0.05$)

Table 1. Baseline characteristics of the *H. pylori*-positive and *H. pylori*-negative groups.

Characteristic	*H. pylori*-positive group (n = 180)	*H. pylori*-negative group (n = 140)	χ^2/t	p
Age (years)	65.2 ± 8.7	64.5 ± 9.1	0.696	0.487
BMI (kg/m^2)	26.4 ± 3.1	25.8 ± 2.9	1.781	0.076
Male, *n* (%)	102 (56.7)	75 (53.6)	0.193	0.661
Hypertension, *n* (%)	126 (70.0)	91 (65.0)	0.687	0.407
Diabetes, *n* (%)	63 (36.1)	45 (32.1)	0.174	0.677
Current smoking, *n* (%)	98 (54.4)	105 (75.0)	13.473	0.000
Alcohol use, *n* (%)	58 (32.2)	38 (27.1)	0.741	0.389
Family stroke history, *n* (%)	44 (24.4)	30 (21.4)	0.251	0.616
Statin use, *n* (%)	85 (47.2)	62 (44.3)	0.168	0.682

Abbreviations: BMI, body mass index; *H. pylori*, *Helicobacter pylori*.
Note: Statin use in this table refers to a history of lipid-lowering medication use (including statins) at any point prior to enrollment, excluding continuous use within 3 months before enrollment (which was an exclusion criterion). Patients who had discontinued statin therapy for ≥3 months were included in the analysis.

in univariate analysis were entered into the multivariate linear regression model to identify independent predictors while controlling for potential confounders. Multicollinearity was assessed using the variance inflation factor (VIF) and tolerance, with VIF <5 and tolerance >0.2 indicating no significant multicollinearity. The $p < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

Table 1 summarizes baseline characteristics of the included patients. Notably, both *H. pylori*-positive and *H. pylori*-negative groups were comparable in terms of statin usage (*H. pylori*-positive: 47.2% vs. *H. pylori*-negative: 44.3%, $p = 0.682$) and family stroke history (*H. pylori*-positive: 24.4% vs. *H. pylori*-negative: 21.4%, $p = 0.616$). BMI values were comparable between groups (*H. pylori*-positive: 26.4 ± 3.1 kg/m^2 vs. *H. pylori*-negative: 25.8 ± 2.9 kg/m^2, $p = 0.076$). The prevalence of hypertension was also similar between the two groups (*H. pylori*-positive: 70.0% vs. *H. pylori*-negative: 65.0%, $p = 0.407$). The prevalence of current smoking was significantly higher in the *H. pylori*-negative group than in the *H. pylori*-positive group ($p < 0.001$). All other baseline characteristics showed no statistically significant differences between the *H. pylori*-positive and *H. pylori*-negative groups ($p > 0.05$).

Lipid Metabolism Indices

Compared with the *H. pylori*-negative group, the *H. pylori*-positive group had significantly higher TC, TG, LDL-C, and lower HDL-C levels (all $p < 0.05$) (Table 2).

Table 2. Comparisons of lipid metabolism indices between the *H. pylori*-positive and *H. pylori*-negative groups (mean ± SD).

Index	*H. pylori*-positive group (n = 180)	*H. pylori*-negative group (n = 140)	t	p
TC (mmol/L)	5.8 ± 1.2	5.2 ± 1.0	4.77	<0.001
TG (mmol/L)	2.2 ± 0.8	1.8 ± 0.7	4.68	<0.001
LDL-C (mmol/L)	3.5 ± 0.6	3.0 ± 0.6	7.40	<0.001
HDL-C (mmol/L)	1.0 ± 0.3	1.2 ± 0.3	5.92	<0.001

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides; SD, standard deviation.

Table 3. Comparisons of inflammatory markers between the *H. pylori*-positive and *H. pylori*-negative groups (mean ± SD).

Marker	*H. pylori*-positive group (n = 180)	*H. pylori*-negative group (n = 140)	t	p
hs-CRP (mg/L)	4.3 ± 1.8	3.2 ± 1.3	6.34	<0.001
Hcy (μmol/L)	17.8 ± 6.3	13.8 ± 4.9	6.40	<0.001
FIB (g/L)	3.6 ± 0.7	3.2 ± 0.6	5.50	<0.001

Abbreviations: FIB, fibrinogen; Hcy, homocysteine; hs-CRP, high-sensitivity C-reactive protein.

Inflammatory Markers

Levels of hs-CRP, Hcy, and FIB were significantly higher in the *H. pylori*-positive group than in the *H. pylori*-negative group (all $p < 0.05$) (Table 3).

Modified Framingham Stroke Risk Scores

The *H. pylori*-positive group had significantly higher modified Framingham risk scores compared to the *H. pylori*-negative group ($p < 0.001$). Risk category distribution also differed significantly between the two groups ($\chi^2 = 11.03$, $p = 0.004$) (Table 4).

Table 4. Modified Framingham risk scores in the *H. pylori*-positive and *H. pylori*-negative groups.

Index	*H. pylori*-positive group (n = 180)	*H. pylori*-negative group (n = 140)	Statistics	p
Total score	18.6 ± 4.2	15.2 ± 3.8	$t = 7.58$	<0.001
10-year stroke risk (%)			$\chi^2 = 11.03$	0.004
Lowest high-risk (10–15%)	15 (8.3%)	25 (17.9%)		
Moderate high-risk (15–29%)	62 (34.4%)	58 (41.4%)		
Highest high-risk (≥20%)	103 (57.2%)	57 (40.7%)		

Correlation Analysis

H. pylori infection was positively correlated with TC ($r = 0.28$), TG ($r = 0.24$), LDL-C ($r = 0.31$), hs-CRP ($r = 0.35$), Hcy ($r = 0.29$), FIB ($r = 0.27$), and mod-

ified Framingham risk scores (r = 0.33) (all $p < 0.05$) (Table 5). Critically, *H. pylori* infection showed a significant negative correlation with HDL-C (r = –0.19, p = 0.018), indicating diminished reverse cholesterol transport capacity in infected individuals.

Table 5. Point-biserial correlation between *H. pylori* infection and clinical parameters.

Parameter	Point-biserial r	p
TC	0.28	<0.001
TG	0.24	0.003
LDL-C	0.31	<0.001
HDL-C	–0.19	0.018
hs-CRP	0.35	<0.001
Hcy	0.29	<0.001
FIB	0.27	<0.001
Modified Framingham risk score	0.33	<0.001

Univariate Analysis

Univariate linear regression analysis was performed, including all variables from Tables 1,2,3 to assess their relationship with the modified Framingham risk scores. The analysis identified several significant predictors: *H. pylori* infection status, lipid parameters (TC, TG, LDL-C, HDL-C), and inflammatory markers (hs-CRP, Hcy, FIB) all showed significant associations with the Framingham risk scores (all $p < 0.05$). The complete univariate regression results for all analyzed variables, including *H. pylori* infection, Hcy, and FIB, are presented in Table 6.

Multivariate Regression Analysis

Variables demonstrating statistical significance ($p < 0.05$) in the univariate analysis were entered into a multivariate linear regression model to identify independent predictors of the modified Framingham risk score. Based on multicollinearity diagnostics, predictors with a tolerance >0.2 and VIF <5 (mean VIF = 2.7) were included in the multivariate linear regression analysis. *H. pylori* infection, LDL-C, hs-CRP, and Hcy were identified as independent predictors of the elevated modified Framingham risk scores (Table 7).

The final regression model demonstrated significant explanatory power, with adjusted R^2 = 0.36 (36% of Framingham risk score variance was accounted for), Akaike Information Criterion (AIC) score = 482.3, and a significant overall model fit, F (4, 315) = 21.7 ($p < 0.001$).

Discussion

This retrospective study demonstrated that *H. pylori* infection in patients at high risk of ischemic stroke is associated with abnormal lipid metabolism, elevated levels of inflammatory markers, and higher modified Framingham stroke risk

Table 6. Univariate linear regression analysis of Framingham risk score predictors.

Variable	β	95% CI	p
H. pylori infection	0.83	0.58–1.08	<0.001
TC	0.21	0.08–0.34	0.002
TG	0.06	0.01–0.11	0.015
LDL-C	0.23	0.10–0.36	0.001
HDL-C	–0.30	–0.46– –0.14	<0.001
hs-CRP	0.33	0.19–0.47	<0.001
Hcy	0.76	0.51–1.01	<0.001
FIB	0.37	0.21–0.53	<0.001
BMI	0.03	–0.02–0.08	0.285
Gender (Male vs. Female)	0.13	–0.08–0.34	0.232
Alcohol use (Yes vs. No)	0.07	–0.17–0.31	0.570
Family stroke history (Yes vs. No)	0.11	–0.14–0.36	0.387
Statin use (Yes vs. No)	–0.09	–0.31–0.13	0.389

Abbreviation: CI, confidence interval.

Table 7. Multivariate regression analysis of the modified Framingham risk scores.

Variable	β	SE	t	p	95% CI
H. pylori infection	0.21	0.04	5.25	<0.001	0.13–0.29
LDL-C	0.18	0.06	3.00	0.002	0.06–0.30
hs-CRP	0.23	0.05	4.60	<0.001	0.13–0.33
Hcy	0.15	0.13	1.15	<0.001	0.09–0.21

Abbreviation: SE, standard error.

scores. These findings provide new insights into the potential role of *H. pylori* in stroke pathogenesis and risk stratification.

Our results showed that *H. pylori*-positive patients had significantly higher levels of TC, TG, and LDL-C, accompanied by lower HDL-C levels, compared to *H. pylori*-negative patients. This aligns with previous meta-analyses reporting that *H. pylori* infection is linked to adverse lipid profiles (Li et al., 2021). The underlying mechanisms may involve multiple pathways: First, *H. pylori*-derived lipopolysaccharides (LPS) can upregulate hepatic cholesterol synthesis by activating sterol regulatory element-binding proteins (SREBPs), a key transcription factor for cholesterol metabolism (Graugnard et al., 2013). Second, *H. pylori* infection may impair reverse cholesterol transport by reducing ATP-binding cassette transporter A1 (ABCA1) expression in macrophages, thereby lowering HDL-C levels (de la Llera Moya et al., 2012). Third, chronic gastric inflammation induced by *H. pylori* could disrupt bile acid metabolism, leading to increased intestinal cholesterol absorption (Ye et al., 2023). Notably, LDL-C emerged as an independent predictor of elevated modified Framingham risk scores in our multivariate analysis. LDL-C is a well-established driver of atherosclerosis, and its accumulation in the arterial intima triggers foam cell formation and plaque progression (Waksman et al., 2024). The positive correlation between *H. pylori* infection and LDL-C suggests that *H.*

pylori may accelerate atherogenesis by exacerbating dyslipidemia, which in turn contributes to higher stroke risk as reflected by the Framingham risk score. This highlights the potential of *H. pylori* eradication as a complementary strategy to lipid-lowering therapy in high-risk populations, although further randomized controlled trials are needed to confirm this.

Inflammation is a central driver of atherosclerotic progression (Gonzalez et al., 2025), and our data revealed that *H. pylori*-positive patients had significantly higher levels of hs-CRP, Hcy, and FIB compared to *H. pylori*-negative patients. While Hcy primarily reflects endothelial dysfunction and FIB is a coagulation marker, both are elevated in systemic inflammation and contribute to thrombotic risk. Hs-CRP, a sensitive marker of systemic inflammation, showed a moderate positive correlation with *H. pylori* infection ($r = 0.35$) and remained an independent predictor of higher Framingham risk scores in multivariate analysis. These findings support the hypothesis that *H. pylori*-induced chronic inflammation contributes to vascular damage and elevated risk of long-term stroke (Chen et al., 2024). *H. pylori* infection triggers inflammatory responses through multiple mechanisms: (1) *H. pylori*-derived virulence factors such as cytotoxin-associated gene A (*CagA*) and vacuolating cytotoxin A (VacA) activate nuclear factor kappa B (NF-κB) signaling in gastric epithelial cells, promoting the release of pro-inflammatory cytokines (e.g., TNF-α, IL-6) (Frauenlob et al., 2023); (2) systemic dissemination of *H. pylori* antigens or LPS can induce a low-grade inflammatory state, activating circulating monocytes and endothelial cells (Pachathundikandi et al., 2023); (3) *H. pylori* infection impairs gastric absorption of vitamin B12 and folate, leading to hyperhomocysteinemia (as observed in our *H. pylori*-positive group, Hcy = 17.8 $\pm$ 6.3 μmol/L). Hcy promotes oxidative stress and endothelial dysfunction by generating reactive oxygen species and inhibiting nitric oxide synthesis, thereby accelerating atherothrombosis (Kaplan et al., 2020).

Fibrinogen promotes platelet aggregation via glycoprotein IIb/IIIa (GPIIb/IIIa) activation (Tran et al., 2022). This, combined with endothelial damage from inflammation and dyslipidemia, creates a "pro-thrombotic" state that may contribute to the higher 10-year stroke risk observed in the *H. pylori*-positive patients. The modified Framingham risk score integrates traditional risk factors (e.g., hypertension, diabetes, smoking) to estimate 10-year risk of ischemic stroke (Zhou et al., 2023; Du et al., 2025). Our study found that *H. pylori*-positive patients had significantly higher total scores and 10-year risk, and *H. pylori* infection remained an independent predictor after adjustment of confounding factors. This suggests that *H. pylori* may act as a "risk amplifier" by exacerbating existing metabolic and inflammatory abnormalities, thereby increasing the cumulative stroke risk captured by the Framingham model. Several lines of evidence support this hypothesis: First, *H. pylori* infection is more prevalent in smokers (40.0% vs. 30.0% in our study) (Ferro et al., 2019), and smoking itself is a major contributor to the Framingham risk score (Jin et al., 2023). The synergistic effect of *H. pylori* and smoking on inflammation and oxidative stress may further elevate the risk (Lahner et al., 2018). Second, *H. pylori* infection has been linked to hypertension, a key component of the Framingham score, via mechanisms such as endothelial dysfunction and increased

renin-angiotensin system activity (Sugimoto et al., 2012). Although hypertension prevalence did not differ significantly between groups in our study, subclinical vascular damage arising from *H. pylori* infection may still enhance the impact of existing hypertension on stroke risk.

Notably, the Framingham risk score does not currently include infectious markers, but our findings suggest that *H. pylori* status could improve its predictive accuracy in high-risk populations. For example, among patients with similar Framingham risk scores, those with *H. pylori* infection may have a higher actual stroke risk due to underlying inflammation and dyslipidemia. Future studies could explore whether integrating *H. pylori* status into risk assessment models enhances their clinical utility.

Our findings have potential clinical implications: First, screening for *H. pylori* infection in patients at an increased risk for ischemic stroke (e.g., those with elevated Framingham risk scores) may help identify individuals who could benefit from eradication therapy. Pilot studies have shown that *H. pylori* eradication reduces hs-CRP and LDL-C levels (Zhang et al., 2024; Yu et al., 2018), and a recent meta-analysis suggested a trend toward lower cardiovascular events after eradication (Sun et al., 2023). Second, *H. pylori* eradication could serve as an adjunct to primary prevention strategies (e.g., statins, antiplatelet therapy) in high-risk patients, particularly those with persistent inflammation despite optimal risk factor control.

However, our study has several limitations. Firstly, the patients in this study were primarily high-risk individuals with a substantial smoking burden; therefore, the conclusions of this study should be interpreted with caution and may not be directly extrapolated to the general population. Secondly, its retrospective design cannot establish causality, and residual confounding (e.g., dietary factors, socioeconomic status) may influence the results. Thirdly, we did not assess *H. pylori* virulence factors (e.g., CagA status), which may modify its effects on lipid and inflammatory markers (Capitani et al., 2019). In addition, because long-term follow-up data on stroke events were not available, a direct association between *H. pylori* infection and incident ischemic stroke could not be determined. Finally, the single-center design may limit results generalizability, as *H. pylori* prevalence and strain distribution vary by region (Xue et al., 2021). Future prospective studies should address these limitations by: (1) investigating whether *H. pylori* eradication improves lipid profiles, reduces inflammation, and lowers stroke risk; (2) exploring interactions between *H. pylori* virulence factors and host genetics in modulating stroke risk; and (3) validating the utility of *H. pylori* status in enhancing risk prediction models such as the Framingham risk score.

Conclusion

H. pylori infection independently predicts higher modified Framingham stroke risk scores in high-risk patients, correlating with dyslipidemia marked by increased LDL-C and reduced HDL-C, accompanied by elevated levels of inflammatory and thrombotic markers such as hs-CRP, Hcy, and FIB. While causality cannot be in-

ferred from retrospective data, our findings support *H. pylori* screening in stroke prevention programs. Future studies should assess whether *H. pylori* eradication reduces stroke incidence.

Key Points

- Patients infected with *Helicobacter pylori* (*H. pylori*) exhibited significantly higher low-density lipoprotein cholesterol (LDL-C) and lower high-density lipoprotein cholesterol (HDL-C) than the *H. pylori*-negative controls ($p < 0.05$).
- High-sensitivity C-reactive protein (hs-CRP) and homocysteine (Hcy) levels were 34% and 29%, respectively, higher in the *H. pylori*-positive group ($p < 0.001$).
- Point-biserial correlation revealed an association between *H. pylori* infection and Framingham risk score ($r = 0.33$, $p < 0.001$).
- Multivariate regression analysis demonstrated that *H. pylori* infection was an independent predictor of elevated Framingham risk score ($\beta = 0.21$, $p < 0.001$).

Availability of Data and Materials

All data included in this study are available from the corresponding author upon reasonable request.

Author Contributions

DX and RQZ designed the research study. JRZ and RJD performed the research. DX drafted the manuscript. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Jinhua People's Hospital (IBR-20220021-R) and complied with the Declaration of Helsinki and China's Regulations of Ethical Reviews of Biomedical Research Involving Human Subjects (2016). Retrospective data usage was qualified for exemption under Article 39 (informed consent waiver) of the Regulations. In this study, only de-identified medical records were used, with no new biological samples collected. Patients admitted during 2020–2022 were not contactable because their contact details were not retained per hospital data policy. The protocol involved no patient intervention or additional testing. Waiver would not adversely affect subjects' rights (Article 39.1 and 39.2).

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Conflict of Interest

The authors declare no conflict of interest.

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