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Effects of *Helicobacter pylori* Infection and Its Eradication on Lipid Profiles and Cardiovascular Diseases

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Abstract

Background: We aimed to examine the relationship of current *Helicobacter pylori* infection with lipid profile and cardiovascular disease and its eradication effect.

Methods: Healthy subjects, who underwent routine checkup between October 2003 and December 2007, were followed up until June 2009. *Helicobacter pylori* and lipid profiles were measured both baseline and follow-up. Multiple logistic regression models for odds ratios (ORs) and 95% confidence intervals (CIs) were used to estimate the effects of *H. pylori* infection and its eradication, on lipids and cardiovascular disease.

Results: Current infection with *H. pylori* with 50.5% (6759/13383) at baseline increased low-density lipoprotein (LDL) and decreased high-density lipoprotein (HDL) than *H. pylori*-negative group. Successful eradication of *H. pylori* decreased the risk of high LDL compared with the persistent infection (OR 0.76, 95% CI 0.59–96), which was comparable to that of the persistent negative group (OR 0.82, 95% CI 0.70–0.97), and decreased the risk of low HDL (OR 0.68, 95% CI 0.49–0.96). Current infection of *H. pylori* increased the risk of cardiovascular disease (OR 3.27, 95% CI 1.31–8.14) at baseline, but its eradication failed to decrease the risk at a 2-year follow-up. However, persistent negative infection decreased the risk (OR 0.57, 95% CI 0.35–0.94) comparing to persistent positive infection at follow-up.

Conclusions: Current infection with *H. pylori* had a positive association with high LDL, low HDL, and cardiovascular disease. Successful *H. pylori* eradication decreased the risk of high LDL and low HDL, but did not reduce the risk of cardiovascular disease.

Helicobacter pylori (H. pylori) is well known to be associated with gastritis, peptic ulcer disease, mucosa-associated lymphoid tissue lymphoma [1], and gastric cancer [2]. Possible relationships between *H. pylori* infection and extra-digestive diseases, such as idiopathic thrombocytopenic purpura and iron deficiency anemia, have also been suggested [3,4]. Many studies have demonstrated that the seropositivity for *H. pylori* is associated with lipid abnormalities and cardiovascular disease, suggesting a causal relationship that remains controversial [5–8]. In contrast, reports of a relationship between a current *H. pylori* infection, lipids [9], and cardiovascular disease [10] are rare. Furthermore, although the effects of *H. pylori* eradication on lipid levels are reported [11,12], those on cardiovascular disease are not known. To explore these unanswered relationships, we evaluated the effects of both *H. pylori* infection and eradication on lipid profiles and cardiovascular disease in a large cohort of self-motivated individuals participating in a health screening program.

Methods

Study Population and Questionnaire Assessment

This is a prospective cohort study of participants in a self-motivated health screening program at the Center for Cancer Prevention and Detection, National Cancer Center, Korea [13,14]. Subjects who underwent comprehensive health screening examination from October

2003 to December 2007 were enrolled at baseline. Subjects who had previously undergone gastric surgery, who did not undergo endoscopy or *H. pylori* evaluation, who were previously cured of *H. pylori*, who are current users of lipid lowering drug, or did not complete the questionnaires were excluded (Fig. 1).

Repeat endoscopy was performed after 1–3 years (mean [SD] = 2.02 [0.018]). Enrolled subjects were racially homogeneous Koreans. Personal data (age, sex, alcohol consumption, smoking status, medical history, and medication history) were collected before the endoscopy. Smoking and alcohol consumption were classified as current (daily or occasionally) or noncurrent. Serum levels of total cholesterol, triglyceride (TG), low-density lipoprotein (LDL), high-density lipoprotein (HDL), and fasting glucose were measured and categorized as follows: TG ≥150 mg/dL, LDL ≥130 mg/dL, and fasting glucose ≥110 mg/dL for both sexes; HDL <40 mg/dL for men; HDL <50 mg/dL for women. Weight and height were measured (In Body; Biospace Co., Ltd, Seoul, Korea), and body mass index (BMI) was calculated as weight/height^2 (kg/m^2). High blood pressure was defined as systolic pressure of >140 mmHg or diastolic pressure of >90 mmHg. Cardiovascular disease included angina and previous myocardial infarction. Education duration representing social status was classified into two groups (<16 and ≥16 years).

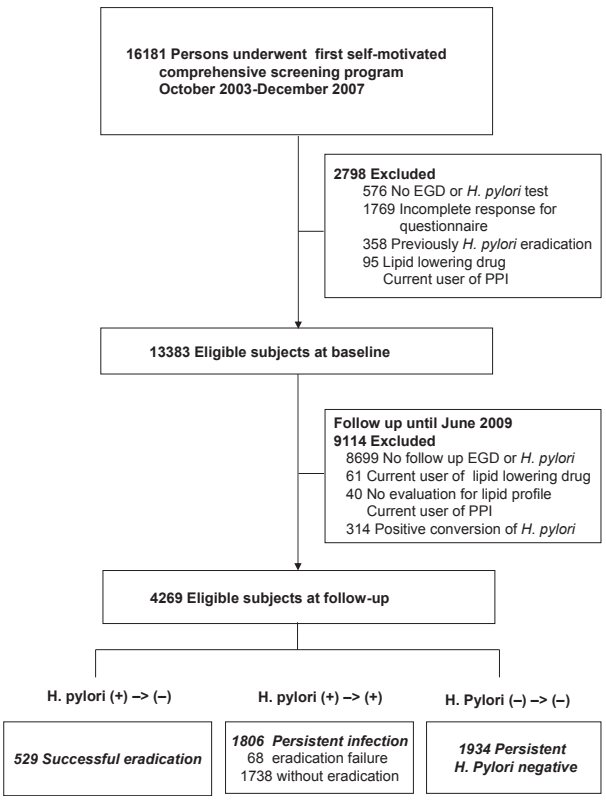

Figure 1 Flowchart of the study. EGD, esophagogastroduodenoscopy; PPI, proton-pump inhibitor

Endoscopy and Follow-up

A gastroenterologist specializing in endoscopy, who was blinded to the questionnaire results, performed the endoscopies with a flexible endoscope (Q260 and Q240; Olympus Optical Co., Ltd., Tokyo, Japan). Subjects had fasted overnight and were under conscious sedation. Biopsy specimens were tested for current infection with *H. pylori* using a rapid urease test with a sensitivity of 98.1% and specificity of 100% (Pronto Dry, Medical Instruments Corporation, Solothurn, Switzerland) [15].

Helicobacter pylori eradication therapy (omeprazole 20 mg, clarithromycin 500 mg, and amoxicillin 1000 mg, twice daily for 7 days) was provided according to clinical indications (duodenal or benign gastric ulcer) or participant's wish (in cases of nonulcer dyspepsia or asymptomatic subjects). Four to eight weeks after completion of the eradication treatment, *H. pylori* eradication was confirmed by a C13 urea breath test, a rapid urease test, or histologic examination. Follow-up endoscopy was performed 1–3 years after *H. pylori* eradication therapy, at which time *H. pylori* status was assessed by a rapid urease test or histologic examination (Fig. 1). At follow-up, subjects were classified into three groups: successful eradication, persistent infection, and persistent *H. pylori* negative. The persistent infection group was used as the reference group for comparisons. The group with spontaneous positive conversion of *H. pylori* was excluded because of a possibility of false negativity at baseline.

The study was approved by the National Cancer Center Institutional Review Board [protocol number NCCNCS-13781]. Written informed consent for sedated endoscopy and use of personal data for research purposes was obtained from subjects before endoscopy.

Statistical Analysis

Data are presented as mean [standard deviation (SD)] or number (percent). A Pearson chi-square test or independent t-test was employed to assess the difference in lipids and confounding factors between the two groups (presence vs absence of *H. pylori*). Risk factors for each lipid and cardiovascular disease were estimated with odds ratios (OR) and 95% confidence intervals (CI) using logistic regression analysis. Changes in lipid levels and prevalence of cardiovascular disease in both the *H. pylori* eradication group and noneradication group

Table 1 Baseline characteristics in 4269 persons by *Helicobacter pylori* status

Variable	Presence of *H. pylori* (n = 2335)	Absence of *H. pylori* (n = 1934)	*p* value[a]
Male sex, No. (%)	1422 (60.9)	1128 (58.3)	.09
Age, mean (SD), year	48.7 (8.6)	48.7 (9.2)	.94
Body mass index, mean (SD), kg/m^2	23.9 (3.2)	23.7 (3.6)	.06
Current smoker, No. (%)	693 (29.7)	578 (29.9)	.85
Current drinker, No. (%)	1557 (66.7)	1291 (66.8)	.96
Education ≥16 year, No. (%)	1182 (50.6)	972 (50.3)	.81
LDL-C, mean (SD), mg/dL	127.2 (31.7)	124.3 (31.6)	.004
HDL-C, mean (SD), mg/dL	53.0 (13.9)	54.9 (14.9)	<.001
Glucose, mean (SD), mg/dL	89.0 (18.5)	89.5 (18.7)	.40
TG, mean (SD), mg/dL	118.2 (84.2)	114.8 (82.0)	.19
Blood pressure, mean (SD), mmHg			
Systolic	119.9 (19.3)	118.8 (19.0)	.07
Diastolic	73.9 (13.2)	73.2 (13.2)	.06
Cardiovascular disease, No (%)	22 (0.9)	6 (0.3)	.01

LDL, low-density lipoprotein; HDL high-density lipoprotein; TG, triglyceride.
[a]*p* values were derived from chi-square test or t-test.

were compared at follow-up. We used STATA software (version 11; College Station, TX, USA) for our analyses. All statistical tests were two-sided, and $p < .05$ was considered statistically significant.

Results

Baseline Characteristics

The prevalence of *H. pylori* was 50.5% (6759/13383) at baseline. A total of 4269 persons were followed up. The only difference between follow-up and non-follow-up subjects was sex ratio (data not shown). Men followed up more than women (32.9% vs 30.5%). Current infection with *H. pylori* was associated with high LDL, low HDL, and cardiovascular disease at baseline subjects, but had no association with age, smoking status, drinking status, education duration, triglyceride, or glucose level (Table 1).

Effect of *Helicobacter pylori* on Lipid and Cardiovascular Disease at Baseline

Current infection of *H. pylori* increased the risk of high LDL and low HDL in adjusted analysis (Table 2). Male sex, increasing age, increasing BMI, and current smoker status increased the risk of high LDL. Multivariate analysis showed no association of *H. pylori* with categorical TG level (Table 2). Male sex, increasing BMI, and current smoker status increased the risk of high TG. Female sex, increasing BMI, and current smoker status increased the risk of low HDL, whereas current drinker status decreased the risk of low HDL (Table 2).

Male sex, increasing age, increasing BMI, and current smoker status increased the risk of high blood pressure (Table 3). Current infection of *H. pylori* increased the risk of cardiovascular disease 3.28-fold in adjusted analysis for age, sex, BMI, smoking status, and drinking status and 3.44-fold in adjusted analysis for these factors plus lipid profile, hypertension, and diabetes (Table 3).

Changes of Lipids and Cardiovascular Disease after *Helicobacter pylori* Eradication

The mean reduction of LDL cholesterol (LDL-C) is prominent in the *H. pylori* eradication group (−6.4 mg/dL) comparing to noneradication group (−4.3 mg/dL) at follow-up (Table S1, $p = .05$).

Table 2 Adjusted analysis for the effect of *Helicobacter pylori* on lipid profile at baseline

	LDL ≥130 mg/dL		TG ≥150 mg/dL		Low HDL	
Variable	OR (95% CI)	*p* value[a]	OR (95% CI)	*p* value[a]	OR (95% CI)	*p* value[a]
H. pylori	1.19 (1.05–1.35)	.006	0.99 (0.85–1.15)	.88	1.19 (1.01–1.38)	.03
Male sex	1.12 (0.95–1.31)	.17	3.23 (2.58–4.04)	<.001	0.65 (0.53–0.79)	<.001
Age	1.03 (1.02–1.04)	<.001	1.00 (0.99–1.01)	.94	1.01 (1.00–1.01)	.22
Body mass index	1.09 (1.07–1.11)	<.001	1.19 (1.15–1.22)	<.001	1.16 (1.13–1.20)	<.001
Current smoker	1.18 (1.02–1.38)	.03	1.99 (1.68–2.35)	<.001	1.53 (1.27–1.85)	<.001
Current drinker	0.93 (0.80–1.08)	.36	1.11 (0.90–1.35)	.30	0.71 (0.59–0.85)	<.001
Education ≥16 year	1.13 (0.98–1.28)	.08	0.84 (0.67–2.27)	.11	0.83 (0.68–1.02)	.08

LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglyceride; DM, diabetes mellitus.
[a]Adjusted for age, sex, body mass index, smoking, drinking, and education duration.

Table 3 Adjusted analysis for the effect of *Helicobacter pylori* on cardiovascular disease at baseline

	High BP or hypertension[a]		Cardiovascular disease		Cardiovascular disease	
Variable	OR (95% CI)	*p* value[b]	OR (95% CI)	*p* value[b]	OR (95% CI)	*p* value[c]
H. pylori	0.99 (0.85–1.16)	.92	3.27 (1.31–8.14)	.01	3.42 (1.36–8.61)	.009
Male sex	1.41 (1.16–1.72)	.001	1.26 (0.48–3.25)	.64	1.16 (0.43–3.07)	.77
Age	1.06 (1.05–1.07)	<.001	1.13 (1.08–1.18)	<.001	1.13 (1.08–1.18)	<.001
Body mass index	1.20 (1.16–1.23)	<.001	1.00 (0.88–1.13)	.97	0.97 (0.85–1.12)	.70
Current smoker	0.78 (0.65–0.94)	.01	1.02 (0.92–1.13)	.76	1.11 (0.40–3.11)	.84
Current drinker	0.99 (0.83–1.19)	.94	1.99 (0.79–5.00)	.14	2.03 (0.81–5.11)	.13
Education ≥16 year	0.89 (0.73–1.09)	.30	0.69 (0.31–1.53)	.37	0.74 (0.33–1.64)	.46

[a]Systolic blood pressure (BP) ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or hypertension.
[b]Adjusted for age, sex, body mass index, smoking, drinking, and education duration.
[c]Adjusted for age, sex, body mass index, smoking, drinking, diabetes, hypertension, low-density lipoprotein, high-density lipoprotein, triglyceride, and education duration.

Increases of both systolic and diastolic blood pressure were greater in the noneradication group than the eradication group and reached statistical significance for diastolic blood pressure in the noneradication group (1.5 mmHg) compared with the eradication group (0.04 mmHg, $p = .01$).

High blood pressure had no association with *H. pylori* status both at baseline and follow-up (Table 3 and Table S2). Even if cardiovascular disease was lower in *H. pylori*-negative persons comparing to *H. pylori* positive group at baseline (Table 3), it had no difference between the persistent *H. pylori* positive and successful eradication group at follow-up (Table S2). However, persistent negative group continued to be low prevalence of cardiovascular disease compared to persistent *H. pylori* positive group (1.5% vs 2.3%, Table S2).

Effect of *Helicobacter pylori* Eradication on Lipid and Cardiovascular Disease at Follow-up

Helicobacter pylori eradication decreased the risk of high LDL (adjusted OR, 0.76; 95% CI, 0.59–0.96) at follow-up to a level close to that of the *H. pylori*-negative group (adjusted OR, 0.82; 95% CI, 0.70–0.97, Table 4).

Table 4 Effect of *Helicobacter pylori* eradication on lipid profile at follow-up

	LDL ≥130 mg/dL		TG ≥150 mg/dL		Low HDL	
Variable	OR (95% CI)	*p* value[a]	OR (95% CI)	*p* value[a]	OR (95% CI)	*p* value[a]
Change of *H. pylori* status						
Persistent *H. pylori* infection	1 (Reference)		1 (Reference)		1 (Reference)	
Successful eradication	0.76 (0.59–0.96)	.02	1.08 (0.84–1.39)	.56	0.68 (0.49–0.96)	.03
Persistent *H. pylori* negative	0.82 (0.70–0.97)	.02	0.97 (0.82–1.16)	.77	0.88 (0.71–1.01)	.26
Male sex	0.86 (0.72–1.02)	.09	1.73 (1.41–2.13)	<.001	0.50 (0.39–0.65)	.001
Age at follow-up (year)	1.03 (1.02–1.03)	<.001	0.99 (0.98–1.00)	.04	1.01 (0.99–1.02)	.29
Current smoker at follow-up	1.05 (0.87–1.26)	.63	1.29 (1.07–1.56)	.008	1.15 (0.96–1.01)	.37
Current drinker at follow-up	1.01 (0.99–1.29)	.47	1.00 (0.98–1.02)	.94	0.99 (0.96–1.02)	.38
BMI at follow-up (kg/m^2)	1.10 (1.07–1.13)	<.001	1.17 (1.14–1.21)	<.001	1.10 (1.06–1.14)	<.001
Change of BMI (kg/m^2)	1.11 (1.04–1.18)	.001	1.09 (1.02–1.17)	.01	1.05 (1.00–1.11)	.12
Time to follow-up (year)	0.98 (0.93–1.05)	.61	1.06 (0.99–1.14)	.07	0.85 (0.78–0.93)	.001
Education ≥16 year	0.95 (0.77–1.16)	.60	1.00 (0.84–1.19)	1.00	0.90 (0.73–1.11)	.32
LDL ≥130 mg/dL at baseline	8.71 (7.48–10.16)	<.001	–	–	–	–
TG ≥150 mg/dL at baseline	–	–	7.12 (5.95–8.51)	<.001	–	–
Low HDL at baseline	–	–	–	–	12.82 (10.42–15.67)	<.001

LDL, low-density lipoprotein; HDL high-density lipoprotein; TG, triglyceride.
[a]*p* values were derived from multivariate logistic regression.

Table 5 Effect of *Helicobacter pylori* eradication on blood pressure and cardiovascular disease at follow-up

Variable	High BP or hypertension		Cardiovascular disease	
	Adjusted OR (95% CI)	*p* value[a]	Adjusted OR (95% CI)	*p* value[a]
Change of *H. pylori* status				
Persistent *H. pylori* infection	1		1	
Successful eradication	0.93 (0.73–1.20)	.60	1.21 (0.67–2.19)	.51
Persistent *H. pylori* negative	1.03 (0.88–1.21)	.74	0.57 (0.35–0.94)	.03
Male sex	1.40 (1.17–1.68)	<.001	1.40 (0.80–2.43)	.24
Age at follow-up (year)	1.05 (1.04–1.06)	<.001	1.08 (1.05–1.11)	<.001
Current smoker at follow-up	1.25 (1.04–1.45)	.02	1.01 (0.55–1.83)	.99
Current drinker at follow-up	1.00 (0.99–1.02)	.55	0.98 (0.86–1.12)	.78
BMI at follow-up (kg/m^2)	1.18 (1.15–1.22)	<.001	1.01 (0.96–1.01)	.84
Change of BMI (kg/m^2)	1.00 (0.98–1.01)	.64	0.98 (0.94–1.01)	.19
Time to follow-up (year)	1.00 (0.94–1.06)	.91	1.11 (0.94–1.31)	.21
LDL ≥130 mg/dL at follow-up	1.01 (0.86–1.17)	.95	0.72 (0.46–1.12)	.15
Low HDL at follow-up	1.01 (0.83–1.23)	.89	1.03 (0.56–1.86)	.94
TG ≥150 mg/dL at follow-up	1.35 (1.11–1.62)	<.001	2.09 (1.29–3.37)	.003
Education ≥16 year	0.95 (0.77–1.17)	.63	0.94 (0.60–1.47)	.77

BP, blood pressure; LDL, low-density lipoprotein; HDL high-density lipoprotein; TG, triglyceride.
[a]*p* values were derived from multivariate logistic regression.

Increasing age and high BMI at follow-up, higher change of BMI, and high baseline LDL level increased the risk of high LDL at follow-up. Also, *H. pylori* eradication decreased the risk of low HDL (adjusted OR, 0.68; 95% CI, 0.49–0.96) at follow-up (Table 4). High BMI at follow-up, female sex, and low baseline HDL increased the risk of low HDL at follow-up. In contrast, high TG was not affected by baseline infection status (Table 2) or *H. pylori* eradication (Table 4). High TG was associated with male sex, current smoker status, increasing BMI at follow-up, higher change of BMI, and high baseline TG (Table 4).

High blood pressure had no association with *H. pylori* eradication, but had a positive association with male sex, increasing age at follow-up, current smoker status, high BMI at follow-up, and high TG at follow-up (Table 5). *Helicobacter pylori* eradication did not decrease the risk of cardiovascular disease at follow-up, but there was a markedly decreased risk of cardiovascular disease in the persistent *H. pylori*-negative group (adjusted OR, 0.57; 95% CI, 0.35–0.94) compared with that in the persistent infected group (Table 5). Increasing age and high TG at follow-up increased the risk of cardiovascular disease at follow-up.

Discussion

Our results showed that current infection with *H. pylori* had a positive association with high LDL, low HDL, and cardiovascular disease. Successful *H. pylori* eradication decreased the risk of high LDL and low HDL, but unfortunately it did not decrease the risk of cardiovascular disease at mean age of 49 years.

Epidemiological studies based on serologic findings have suggested an association between chronic *H. pylori* infection and lipid abnormality [16], yet controversies still exist [17]. Individuals who are serologically positive for *H. pylori* have been reported to have lower HDL cholesterol concentrations and higher TG concentrations [16,18]. In a previous study, current infection of *H. pylori* was shown to correlate with lower HDL values, lower apolipoprotein A1 concentrations, and higher apolipoprotein B concentrations [9]. However, a meta-analysis [19] showed no correlation between *H. pylori* infection and the concentrations of total cholesterol or TGs. A prospective study of 618 Japanese patients with acute myocardial infarction and 967 controls showed no detrimental effect of *H. pylori* infection on total and HDL cholesterol [20]. Smaller studies, including 70–80 persons, suggest that successful eradication of *H. pylori* decreases LDL and total cholesterol and increases HDL [11,12]. A 58-person study showed no significant changes in TG, HDL, LDL, and total cholesterol levels after eradication of *H. pylori* [21]. Our large cohort study confirmed that current infection with *H. pylori* increased the risk of high LDL and low HDL, and eradication of *H. pylori* decreased the risk of high LDL and low HDL at a 2-year follow-up.

Another dispute remains regarding *H. pylori* infection and cardiovascular disease [22]. Several studies

have shown a positive association between *H. pylori* seropositivity and ischemic heart disease or myocardial infarction [23,24]. A higher sero-prevalence of *H. pylori* has also been reported in patients with unstable angina (OR: 3.82, 95% CI: 1.27–12.04) [23]. In a meta-analysis of five prospective studies, *H. pylori* seropositivity did not increase the risk for ischemic heart disease [25]. Smaller studies (<200 cases) did not show any positive correlation between serologically [26] or histologically [10] documented *H. pylori* infection and the risk for ischemic heart disease. A longitudinal observational study suggested that *H. pylori* infection does not increase ischemic heart disease or acute myocardial infarction [27]. *Helicobacter pylori* seropositivity in older persons (mean age 69 years) is not associated with cardiovascular disease in a mean follow-up period of 10 years [28]. The association between CagA-bearing *H. pylori* strains and ischemic heart disease also has been controversial [29,30].

Although there are many serologic studies for the association between *H. pylori* and ischemic heart disease, reports on the association between current infection of *H. pylori* and ischemic heart disease are rare [10,31]. Two studies using histology showed no association between *H. pylori* and ischemic heart disease, but the number of subjects included in each group (<150) was small [10,31]. A previous study revealed a higher rate of *H. pylori* stool antigen positivity in 28 patients with acute coronary heart disease compared to 40 controls [32]. Furthermore, the effect of *H. pylori* eradication on development of cardiovascular disease is not known even if *H. pylori* eradication decreased the adverse events or cardiac death in acute coronary syndrome [33,34]. In our large cohort study, current infection of *H. pylori* increased the risk of cardiovascular disease up to 3.3-fold at baseline, but *H. pylori* eradication failed to decrease the risk of cardiovascular disease at a mean follow-up period of 2 years. The plausible mechanisms for *H. pylori*-induced cardiovascular disease include *H. pylori*-induced atherogenic-modified lipid profile, systemic increase of inflammatory cytokines, *H. pylori*-induced platelet aggregation, and hypercoagulation [35]. One plausible explanation why *H. pylori* eradication failed to reduce cardiovascular disease at follow-up could be that 2 years is too short to evaluate the effect of *H. pylori* eradication on cardiovascular diseases, which are results of chronic exposures to risk factors. A second explanation could be that although the effect of *H. pylori* on lipids is reversible, *H. pylori*-induced atherosclerosis may be irreversible. Actually, mean age of eradication was 48.8 years, which is the beginning age of increased cardiovascular diseases. Earlier eradications, before development of atherosclerosis, may reduce the development of cardiovascular disease. In the future, the long-term effect of *H. pylori* eradication on cardiovascular disease in a younger age group should be studied. However, one interesting thing is that persistent negative group continued to be low prevalence of cardiovascular disease compared to persistent *H. pylori* positive group (1.5% vs 2.3%). Furthermore, persistent *H. pylori*-negative group reduced the risk of cardiovascular disease to 57% comparing to persistent positive group at follow-up in adjusted analysis. This longitudinal study suggests at least the causal relationship of *H. pylori* with cardiovascular disease.

Our study results that high LDL had a positive association with male sex, increasing age, increasing body mass index, and current smoker status are in agreement with previous epidemiologic studies. Increasing BMI and current smoker status had a positive association with high TG and low HDL. However, high TG was related with male sex but low HDL was related with female sex. The reason that the risk of low HDL was higher in females than males may be due to a higher cutoff value of HDL in females. When cardiovascular disease at follow-up was simultaneously adjusted for many confounding factors and three lipid profiles (LDL, HDL, TG), it had a strong positive association with TG rather than LDL or HDL.

Strengths of this study were that it evaluated the effect of both current infection with *H. pylori* and its eradication on lipids and cardiovascular disease using a cross-sectional design and a large prospective cohort. Our study overcame many limitations of previous studies of the association between *H. pylori* and lipids or cardiovascular disease, such as small sample size, serologic detection of *H. pylori*, and absence of treatment effect. Nonetheless, this study had limitations. For example, the mean follow-up duration of 2 years appears to be too short to evaluate the effect of *H. pylori* eradication on cardiovascular disease. In the future, longer term follow-up studies are needed. Second, even if the rapid urease test with a sensitivity of 98% and specificity of 100% [15], it has a chance of giving a false-negative result. Therefore, we excluded the spontaneous positive conversion of *H. pylori.* Third, we did not consider diet and physical activity. However, even if physical activity and diet factors independently affect cardiovascular disease, the effect would be primarily via increase of body fat mass and induction of lipid abnormalities. In essence, therefore, we adjusted for lipid profile and BMI, which are markers of body fat mass, instead of physical activity and diet factors.

In conclusion, current infection of *H. pylori* had a positive association with high LDL, low HDL, and cardiovascular disease. Successful *H. pylori* eradication

decreased the risk of high LDL and low HDL, but did not decrease the risk of cardiovascular disease at a 2-year follow-up. However, persistent *H. pylori*-negative group continued to reduce the risk of cardiovascular disease comparing to persistent positive group at a 2-year follow-up. In the future, we need to evaluate the effect of *H. pylori* eradication on development of cardiovascular disease with a longer term follow-up study in a younger age group.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1 Change of lipid profile and blood pressure by *Helicobacter pylori* eradication.

Table S2 Cardiovascular disease at baseline and follow-up by *Helicobacter pylori* status.

