Association between atherosclerosis and gastric biomarkers concerning *Helicobacter pylori* infection in a Chinese healthy population

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ABSTRACT

Background: Studies have suggested that *Helicobacter pylori* (Hp) infection is associated with atherosclerotic process, while the relationship between pepsinogens, gastrin and atherosclerosis is unknown.
Aim: The aim of the study was to observe association of Hp infection on atherosclerotic parameters and blood pressure, and explore the relationship between atherosclerotic parameters, blood pressure and gastric biomarkers in a healthy population.
Methods: 395 subjects were chosen and received physical examinations, carotid artery ultrasound, peripheral atherosclerosis measurement, and testing of serum pepsinogen (PG) I and II, Hp antibody, and gastrin-17 (G-17) levels. Analyses were conducted by Student's *t*-test, ANOVA, Pearson correlation, multiple linear regression and binary logistic regression.
Results: In Hp-infected subjects, right carotid intima media thickness (R-CIMT) were higher (P = 0.027) and left ankle brachial index were higher in 45–64 years compared to 35–44 years group (P = 0.039, P = 0.016). Hp-IgG, PGI and G-17 respectively positively correlated with CIMT, pulse wave velocity and systolic blood pressure (P = 0.044, P = 0.013, P = 0.021). The unadjusted OR in subjects with elevated CIMT for quartile IV of PGI was 3.542 (95% CI, 1.491–8.411), the adjusted OR was 2.916 (95% CI, 1.035–8.216). The unadjusted OR in subjects with elevated CIMT for quartile III of G-17 was 4.351 (95% CI, 1.670–11.336) and for quartile IV was 3.108 (95% CI, 1.149–8.406), the adjusted OR for quartile III was 4.962 (95% CI, 1.515–16.258).
Conclusions: Hp infection, higher levels of PGI and G-17 may contribute to atherosclerotic process by influencing atherosclerotic parameters and blood pressure in a healthy population, the influence on CIMT was most significant.

1. Introduction

As the prevalence and mortality of cardiovascular diseases increase especially in elderly population, atherosclerosis and its related diseases have become the hotspots of researches. Since Patel et al. (Patel et al., 1995) founded that *Helicobacter pylori* (Hp) infection is independently associated with coronary heart disease as well as cardiovascular risk factors including fibrinogen concentration and total leucocyte count in the '90 for the first time, more and more attention has been paid to the influence of Hp infection on the development of arteriosclerosis. Studies have suggested that Hp infection is significantly related to the most important risk factors for cardiovascular diseases such as hypertension, diabetes mellitus as well as elevated low density lipoprotein cholesterol

(LDL-C) levels and decreased high density lipoprotein cholesterol (HDL-C) levels (Longo-Mbenza et al., 2012; Kim et al., 2011; Albaker, 2011). Hp is even regarded as a risk factor which plays an important role in the formation of atherosclerotic plaque (Izadi et al., 2012).

In clinic, the parameters of atherosclerosis include carotid intima media thickness (CIMT), pulse wave velocity (PWV) and ankle brachial index (ABI). CIMT reflects the early structural changes relevant to ageing in the arterial wall (Han et al., 2013). PWV refers to the conduction velocity of pulse wave in the artery, which is used to reflect the degree of stiffness of the arterial wall. ABI is the ratio of the systolic blood pressures between ankle artery and brachial artery, which represents the degree of stenosis and obstruction of lower extremity artery. (Honda et al., 2008; Adachi et al., 2003).

It has been shown that Hp infection is related to greater intima media thickness in patients with atherosclerotic stroke (Diomedi et al., 2004). Another study has suggested that Hp positivity is independently associated with increased PWV levels in younger individuals (Yoshikawa et al., 2007). It has also been found that the mean systolic blood pressure is higher in Hp-infected subjects compared to those non-infected (Kopacova et al., 2014).

The gastric biomarkers include pepsinogen (PG) and gastrin-17 (G-17). Serum levels of pepsinogens represent the number of cells and glands in gastric corpus mucosa and serum G-17 level reflects the function and structure of gastric antral mucosa. Combined test of pepsinogen, G-17 and Hp-IgG levels is significant in clinic for general evaluation of gastric mucosal secretion (Iijima et al., 2009; Kikuchi et al., 2011). However, to date, very few studies have observed the relationship between pepsinogen, G-17 and atherosclerosis, whether pepsinogen and G-17 are also associated with atherosclerotic process, is still unknown. The aim of the current study was to observe coexistence of Hp infection on atherosclerotic parameters and blood pressure, and explore the relationship between atherosclerotic parameters, blood pressure and serum gastric biomarkers in a healthy Chinese population.

2. Methods

2.1. Study subjects

This was a cross-sectional study of a healthy population defined as having no cardiovascular, respiratory, digestive, endocrine, urinary and neurological system diseases, and absence of chronic infectious and neoplastic diseases as well as no history of psychiatric disorders. We screened 505 healthy people out of 1500 volunteers from all walks of life in 15 communities in Shenyang, China between September 2007 and June 2008. The screening included investigations on symptoms, family history, medical history, diets, smoking and alcohol intake which were acquired by a questionnaire completed by each participant. Physical examinations (such as measurement of blood pressure, chest radiograph, electrocardiogram *etc.*) were performed along with biochemical tests including liver function, renal function, uric acid, blood lipids and fasting blood glucose (FBG) levels. A total of 395 subjects (168 males and 227 females) from the 505 people with a mean age of 59.4 years old (37–87 years old) were recruited from November 2010 to May 2011 by the same screening process. Patients with respiratory, circulatory, digestive, endocrine, urinary, neurological diseases and neoplastic diseases, chronic infections, or abnormal test results and physical examinations, as well as those with psychiatric disorders and unable to complete instructions and self-evaluations were ruled out. Blood sample was obtained and sera were stored at −75 °C until used for testing of gastric biomarker levels. Informed consent was completed by each participant. This study was approved by the Medical Ethics Committees of General Hospital of Chinese People's Liberation Army and China Medical University.

2.2. Carotid artery ultrasound and peripheral atherosclerotic parameters examination

Left and right CIMTs were measured by carotid artery ultrasound (Liang et al., 2014) (Philips iE33 Ultrasound System, Holland), left and right PWVs and ABIs were measured by peripheral atherosclerotic parameters examination (Liang et al., 2014) (form PWV/ABI, Colin Co), all procedures were carried out by professional technicians.

2.3. Serological assay

Serum levels of PG I and II, G-17 as well as Hp antibody were measured with ELISA (González et al., 2012) (Biohit Oyj, Laippatie 1, FIN-00880 Helsinki, Finland). All procedures were conducted according to the instructions of manufacturer.

2.4. Study groups

1. Participants were divided into five age groups (35–44, 45–54, 55–64, 65–74 and ≥ 75 years old).
2. Hp-IgG positive or negative groups (Hp-IgG positive was defined as serum Hp-IgG ≥ 35 EIU) (He et al., 2011).

2.5. Statistical analysis

Levels of atherosclerotic parameters and blood pressure by Hp infection status were compared with Student's *t*-test. Levels of atherosclerotic parameters and blood pressure among age groups by Hp infection status were compared by ANOVA, multiple comparisons were done by Bonferroni method (homogeneity of variance) or Tamhane method (heterogeneity of variance). CIMT, PWV and ABI represented the means of left and right CIMTs, PWVs and ABIs values for each subject respectively and were used for correlation and regression analyses. Relationships among atherosclerotic parameters, blood pressure and serum gastric biomarkers were analyzed by Pearson correlation coefficient matrix. Atherosclerotic parameters and blood pressure as dependent variables respectively and other related factors including gastric biomarkers, FBG, LDL-C and age as independent variables were analyzed by multiple linear regression with stepwise method and multiple-colinearity. Abnormal levels of atherosclerotic parameters and blood pressure as dependent variables respectively and quartiles of gastric biomarkers as independent variables were analyzed by binary logistic regression with quartile I represented the lowest value. We used SPSS V.17.0 for statistical analysis, and a two-sided P value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of atherosclerotic parameters and blood pressure by Hp infection status

Compared to non-infected subjects, levels of right CIMT (R-CIMT) were significantly higher in Hp-infected subjects (P = 0.027), while no significant difference was seen in the levels of other atherosclerotic parameters and blood pressure between the two groups. (Table 1).

3.2. Comparison of atherosclerotic parameters and blood pressure in various age groups by Hp infection status

In Hp-infected subjects, levels of left ABI (L-ABI) were significantly higher in subjects between 45 and 64 years old compared to 35–44 years old group (P = 0.039, P = 0.016), while no significant difference was seen in levels of L-ABI between each age group in non-

Table 1

Comparison of atherosclerotic parameters and blood pressure by Hp infection status (mean ± SD).

	Hp-IgG(+) n = 186	Hp-IgG(−) n = 209	P
L-CIMT(mm)	0.65 ± 0.01	0.63 ± 0.01	0.317
R-CIMT(mm)	0.65 ± 0.01	0.61 ± 0.01	0.027
L-ABI	1.13 ± 0.01	1.13 ± 0.01	0.547
R-ABI	1.15 ± 0.01	1.15 ± 0.01	0.688
L-PWV(m/s)	1679.84 ± 33.95	1668.74 ± 27.86	0.814
R-PWV(m/s)	1659.77 ± 33.38	1635.88 ± 27.86	0.580
SBP(mmHg)	132.78 ± 1.53	130.43 ± 1.28	0.236
DBP(mmHg)	78.48 ± 0.83	77.70 ± 0.67	0.458

Hp-IgG: *Helicobacter pylori*-IgG, L-CIMT: left carotid intima media thickness, R-CIMT: right carotid intima media thickness, L-ABI: left ankle brachial index, R-ABI: right ankle brachial index, L-PWV: left pulse wave velocity, R-PWV: right pulse wave velocity, SBP: systolic blood pressure, DBP: diastolic blood pressure. Hp-IgG (+) is defined as Hp-IgG ≥ 35EIU.