

学位論文の要旨

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学位論文名 *Helicobacter pylori* Infection Does Not Accelerate the Age-Related Progression of Arteriosclerosis : A 4-Year Follow-Up Study

発表雑誌名 Journal of Gastroenterology and Hepatology
(巻, 初頁~終頁, 年) (23,e373-e378, 2008)

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論文内容の要旨

INTRODUCTION

Infection with *Helicobacter pylori* (*H. pylori*), a pathogen significantly involved in a number of gastroduodenal diseases, has been suggested to be related to lipid metabolism, an important pathogenic factor for cardiovascular diseases. It has been demonstrated that long-term infection with *H. pylori* plays an important role in reducing serum high-density lipoprotein cholesterol (HDL-C) concentrations in Japanese subjects. However, whether *H. pylori* infection accelerates the development of arteriosclerosis has not been fully elucidated. We attempted to clarify the influence of *H. pylori* infection on arteriosclerosis progression.

MATERIALS AND METHODS

This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Shimane Institute of Health Science. The study subjects were chosen from individuals who attended Shimane Institute of Health Science for an annual medical

check-up, of whom 302 were chosen to determine the degree of arteriosclerosis twice at this medical center, once between April 2000 and March 2001 and again between April 2004 and March 2005. Individuals with a history of gastric surgery or eradication therapy for *H. pylori* infection were excluded. Those with cardiovascular diseases or taking medication for hypertension, hyperlipidemia, diabetes mellitus, liver diseases, or upper gastrointestinal diseases were also excluded, in order to eliminate the influence of medication on the parameters of arteriosclerosis and serum level of lipids, which were investigated in this study. Thus, a total of 258 subjects (mean age 49.3 years at enrollment, range 34-70 years, 183 males) were finally enrolled in this study.

After obtaining written informed consent, a precise medical history was taken, a physical examination was carried out, and hematological and biochemical blood tests were performed. In this study, the factors used for assessing cardiovascular risk were gender, age, body mass index (BMI), smoking and drinking (equivalent to over 50 ml of alcohol per day) habits, serum total cholesterol, triglyceride, HDLC and fasting blood glucose levels, and leukocyte count. The severity of arteriosclerosis was determined by use of an automated device that non-invasively determined systolic blood pressure (SBP), heart-carotid pulse wave velocity (HCPWV), bilateral heart-ankle PWVs (HAPWVs), and bilateral ankle brachial indices (ABIs) simultaneously. *H. pylori* infection status was determined using assays for serum anti-*H. pylori* IgG antibodies. Arteriosclerotic parameters at enrollment and after 4 years were compared between the subjects, which were divided into groups based on the presence of *H. pylori* infection. In addition, changes in arteriosclerotic parameters during the 4-year study period were compared between the groups.

A chi-squared test and Mann-Whitney U test were used to compare the values for *H. pylori*-seropositive and seronegative individuals. Analysis of covariance (ANCOVA) was performed to adjust for confounding factors (age, sex, body mass index, and smoking and drinking habits). Differences of $p < 0.05$ were considered to be statistically significant.

RESULTS AND DISCUSSION

The 258 subjects were divided into *H. pylori*-seropositive (n=166, 64.3%) and seronegative (n=92) groups. The HDLC level in *H. pylori*-seropositive subjects was significantly lower than in the *H. pylori*-seronegative group at enrollment, after adjusting for confounding factors. The raw values for HCPWV and HAPWVs in *H. pylori*-seropositive subjects at enrollment tended to be higher. However, a comparison between the groups after adjusting for confounding factors did not reveal significant differences for any of the arteriosclerotic parameters.

All arteriosclerotic parameters except for right ABI (p=0.067) were significantly increased after 4 years in comparison with at enrollment, whereas adjusted values for all arteriosclerotic parameters after 4 years were not significantly different between the groups. There were also no differences between the *H. pylori*-seropositive and seronegative groups for percent changes of SBP, HCPWV, and HAPWVs, which were calculated using the following formula: (value after 4 years - value at enrolment / value at enrolment) x100. In addition, after dividing between male and female subjects, there were no significant differences between the groups.

The results of this study showed that the aging is an important factor for the development of arteriosclerosis, while *H. pylori* infection did not influence the age-related progression of arteriosclerosis. Since this study was not performed in a population-based manner, additional large scale prospective studies, including of subjects undergoing eradication therapy, are recommended to confirm the influence of *H. pylori* infection on the progression of arteriosclerosis and occurrence of cardiovascular diseases.

CONCLUSION

H. pylori infection does not accelerate the age-related progression of arteriosclerosis in healthy Japanese individuals.