# 学 位 論 文 の 要 旨

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| 学 位 論 文 名 | A Study of Arteriosclerosis in Healthy Subjects With HBV and HCV Infection |
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## 論 文 内 容 の 要 旨

### INTRODUCTION

Bacterial and viral infections with pathogens such as *Chlamydia pneumoniae,* Epstein-Barr virus, *Cytomegalovirus*, *Herpes simplex* and *Helicobacter pylori* have been shown to affect the serum fibrinogen and lipid levels, which are well-knqwn risk factors for cardiovascular disease. In patients with liver cirrhosis due to chronic infection with Hepatitis B virus (HBV) and hepatitis C virus (HCV), low levels of serum fibrinogen and lipids may have a favorable effect in the prevention of arteriosclerosis. However, it remains unclear whether HBV or HCV infection can affect the development of arteriosclerosis. In this study, we performed a cross-sectional study to assess the severity of arteriosclerosis in cases with HBV infection and HCV infection by measuring the ankle brachial index (ABI) and pulse wave velocity (PWV).

### MATERIALS AND METHODS

All subjects who visited Shimane Environment and Health Public Corporation for an annual medical check-up between April 2001 and September 2002 were considered for enrolment in this prospective study. Written informed consent was obtained from each subject in accordance with the Helsinki Declaration. Individuals were excluded from the study if there was a history of gastric surgery, cardiovascular disease, or if they were taking medication for hypertension, hyperlipidemia, diabetes mellitus, liver disease or upper gastrointestinal disease. None of the subjects had a history of anti-viral therapy, such as interferon therapy. In total, 1806 study subjects were enrolled.

The factors that were used to assess the degree of cardiovascular risk were the serum

total cholesterol, high-density lipoprotein cholesterol (HDLC), triglyceride and fasting blood glucose levels. The severity of arteriosclerosis was assessed using the systolic blood pressure, bilateral ABIs, heart-carotid PWV (HCPWV) and heart-ankle PWV (HAPWV). An automated PWV/ABI recording device with an applanation tonometry unit (TU-100 23BZ0428; Nippon Colin Company, Komaki, Aichi, Japan) was used to measure the ABI, HCPWV and HAPWV. ABI was demonstrated to reflect the degree of arterial occlusion of the lower extremities, and PWV was shown to be a marker for arterial wall stiffness. In order to minimize psychosomatic effects in the subjects, the measurements of ABI and PWV were performed twice and the second value was used for the analysis.

Statistical analysis was performed using the chi-squared test for comparison between each group and the control group; the Mann-Whitney U test was also applied when a significant difference was observed using the Kruskal-Wallis test. In addition, analysis of covariance (ANCOVA) was done to adjust for confounding factors, to allow comparison between individuals with and without HBV infection and HCV infection. The SPSS (Ver. 12.0 for Windows; SPSS Inc., Chicago, IL, USA) was used to perform the statistical analyses. Differences were considered to be statistically significant where $p<0.05$.

## RESULTS AND DISCUSSION

Of the 1806 subjects who participated in the study, 39 (2.2%) were seropositive for HBs antigen (HBV positive group), and 31 (1.7%) were seropositive for HCV antibody (HCV positive group). None of the study subjects had seropositivity for both HBV and HCV. Therefore, the remaining 1736 subjects were considered to be normal controls (control group). The male/female ratio and the percentage of habitual smokers and drinkers in the HBV positive group were significantly different from those in the control group. The serum total cholesterol level in the HBV and HCV positive groups was significantly lower than that in the control group, and triglyceride in the HCV positive group was significantly lower than that in the control group. Although ALT levels in the majority of subjects with HBV and HCV infection were within the normal range, there were significant differences in ALT levels between the control subjects and the subjects with HBV and HCV infection. The serum albumin level was similar between the groups, and none of the study subjects showed low albuminemia (<3.5 g). There were no significant differences in systolic blood pressure, ABI and PWV between the groups.

Adjusted cardiovascular parameters in the subjects with HBV and HCV infection and the control subjects were calculated by analysis of covariance to adjust for confounding

factors (sex, age, body mass index, and smoking and drinking habits). Adjusted serum levels of total cholesterol and triglyceride in the subjects with HBV and HCV infection were lower than those in the control subjects, and right ABI in the subjects with HBV infection was significantly lower than that in the control subjects. However, the adjusted three parameters of PWV did not differ significantly between the groups. Since total cholesterol and triglyceride levels in the subjects with HBV and HCV infection were lower than those in the control subjects, we performed additional analysis of covariance to adjust for serum lipids and glucose levels. Arteriosclerotic parameters did not differ between the groups, except for right ABI in the subjects with HBV infection. Therefore, the results of this study showed that the presence of HBV or HCV infection was not a significant risk factor for development of arteriosclerosis.

Previously, one study had found that the presence of chronic hepatitis due to HBV or HCV infection was not a risk factor for the development of carotid atherosclerosis by using an ultrasound Doppler method. On the other hand, another study, which was conducted on Japanese subjects who participated in general health screening, demonstrated that the presence of HBV and HCV infection is associated with an increased prevalence of atherosclerotic lesions in the carotid artery. This study was performed by manually measuring atherosclerotic plaques and intima-media thickening using ultrasonography. On the other hand, PWV, by which we assessed the degree of arteriosclerosis in this study, has been established as a simple, reproducible and reliable index for evaluating the elastic properties of the aorta, and there is a direct correlation between PWV and the degree of aortic stiffness. Our study findings showed that the presence of HBV or HCV infection was not a significant risk factor for development of arteriosclerosis. The results of our study need to be confirmed using a larger prospective population-based study by examining the time-course changes in arteriosclerotic parameters in patients with different liver diseases.

## CONCLUSION

The present study has shown that infection with HBV or HCV does not influence the severity of arteriosclerosis, as assessed by ABI and PWV in healthy subjects.