学 位 論 文 の 要 旨

氏名　公受　伸之

学 位 論 文 名　HEPATITIS C VIRUS INFECTION AS A RISK FACTOR OF INCREASED AORTIC STIFFNESS AND CARDIOVASCULAR EVENT IN DIALYSIS PATIENTS

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論 文 内 容 の 要 旨

BACKGROUND

Although many epidemiological studies indicate that infectious agents, including cytomegalovirus, *Chlamydia pneumoniae*, helicobacter pylori, herpes simplex virus, and hepatitis A virus, may predispose patients to atherosclerosis and can result in adverse clinical events by causing inflammatory and autoimmune responses, the role of hepatitis C virus (HCV) infection, prevalent in dialysis patients, in the pathogenesis of arteriosclerosis or atherosclerosis and cardiovascular events is unclear. The primary objective of this research was to examine whether HCV infection is associated with increased aortic pulse wave velocity (PWV) - a marker of arterial stiffness - and cardiovascular events in chronic hemodialysis patients.

SUBJECTS AND METHODS

A prospective cohort study was conducted in 94 dialysis outpatients (mean age 64±12 years, mean duration of dialysis 12.0±7.6 years) from October 2002 to October 2004. The cause of renal failure was chronic glomerulonephritis in 47%, diabetic nephropathy in 24%, and hypertensive nephrosclerosis in 8% of the patients. Measurements included carotid-femoral PWV, echocardiographic parameters, serum HCV-RNA (positive in 17 patients), and several biochemical data. Multiple logistic regression and Cox proportional hazard model analysis were used to assess independent determinants of high aortic PWV (≥10.0 m/sec, mean value), after adjusting several risk factors and duration of dialysis. Survival and cardiovascular events, including cerebral and peripheral vascular event, were evaluated after the 2-year follow-up.

RESULTS AND DISCUSSION

In comparison with non-dialysis control subjects, our dialysis patients had significantly higher PWV value (10.0 ± 2.4 vs. 8.3 ± 1.7 m/sec, $p<0.0001$). Duration of dialysis, serum transaminase levels, and PWV were significantly higher in patients with positive serum HCV-RNA. PWV did not correlate with duration of dialysis in both HCV positive and negative group.

Multivariate analysis indicated mean blood pressure, hemoglobin A1c and HCV viremia to be independent determinants of high PWV, after adjusting other risk factors including duration of dialysis.

During the follow-up period, 13 patients suffered from cardiovascular events. Prevalence of the diseases at baseline, pulse pressure, left ventricular mass index, HCV viremia and aortic PWV were associated with cardiovascular events. Kaplan-Meier analysis indicated a significant difference in event free rates between HCV positive and negative patients.

In the general population, the link between HCV and arterial damage remains controversial. In the present study, HCV positive patients were dialyzed significantly longer than HCV negative patients. However, multivariate analysis showed that persistent HCV infection in dialysis patients is closely associated with increased aortic stiffness, left ventricular hypertrophy and

cardiac overload, independently of duration of dialysis. Large cohort studies are needed to pursue the possibility that HCV infection exacerbates arteriosclerosis or atherosclerosis and results in cardiovascular events in dialysis patients.

We would like to propose several possible mechanisms, including HCV-associated immunological vasculitis, oxidative stress, and aggravation of insulin resistance in dialysis patients.

CONCLUSION

HCV infection is likely to be closely associated with increased aortic stiffness and cardiovascular event in dialysis patients.