Association of γ-Glutamyltransferase with Atherosclerosis

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The Japanese government has legally provided a γ-glutamyltransferase (γ-GTP) examination for assessing hepatic function with aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in communities and occupational areas since 1980s. In particular, it is well known that γ-GTP levels increase due to the alcohol-related liver dysfunction; therefore, γ-GTP is very common for Japanese people who regularly drink alcohol.

Besides alcoholic hepatitis, nonalcoholic fatty liver disease (NAFLD) is recently being focused on as a public health issue. NAFLD is defined by the presence of steatohepatitis without the excess alcohol consumption, which is closely associated with insulin resistance and atherosclerosis. NAFLD was greatly associated with cardiovascular disease (CVD) and cancer. Although the mechanism that associates NAFLD with atherosclerosis is yet unclear, insulin resistance derived from the accumulation of triglycerides and free fatty acids in hepatocytes and proinflammatory processes in adipose tissue may contribute to the mechanism of atherosclerosis.

The hepatic function plays a key role in the connection between hepatic parasympathetic function and skeletal muscle insulin resistance as explained by the actions of hepatic insulin sensitizing substance released from the liver. Because of this pathway, the hepatic dysfunction may cause impaired peripheral insulin sensitivity and increase the risk of CVD.

The study by Li Y, et al. in the current issue of Journal of Atherosclerosis and Thrombosis documents that an elevation of γ-GTP levels had a great impact on mortality from CVD in the Evidence for Cardiovascular Prevention from Observational Cohorts in Japan (EPOCH-JAPAN). Subjects were approximately 40,000 healthy men and women with normal AST and ALT levels. Furthermore, the hazard ratios of γ-GTP elevation were significantly increased among alcohol non-drinkers for stroke (in men and women) and coronary heart disease (only in women) mortality. The increase in γ-GTP was no longer caused by the alcohol-related health issue. This prospective study provides evidence that γ-GTP is a risk factor for CVD mortality independent of alcohol drinking habits.

This study excluded individuals with abnormal ranges of AST and ALT from baseline examinations. Thereby, the effect of NAFLD on elevated γ-GTP levels may be less. Further, considering the pathological mechanism for the γ-GTP elevation except for NAFLD, what mechanism associated γ-GTP levels with development of atherosclerosis? As discussed in the article, γ-GTP levels may present conditions of oxidative stress or inflammation as expressed in markers of C-reactive protein, interleukin-6, oxidized low-density lipoproteins, and soluble intercellular adhesion molecule-1, which are associated with vascular injury and atherosclerosis.

With regard to potential explanations, elevated γ-GTP level is already considered to not be a mere marker of alcoholic liver dysfunction. Regardless of alcohol drinking, individuals who have a higher level of γ-GTP should pay attention to an increased risk of CVD mortality. Causes of increased γ-GTP levels and methods to intervene in future investigations require clarification; however, the assessment of hepatic function will be useful for CVD prediction and prevention.

Conflict of Interest

None.

References

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