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Serum Apolipoprotein M Levels are Correlated with Biomarkers of Coagulation

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Background and Objective

Low-density lipoprotein cholesterol (LDL-C) is called "bad cholesterol", because it causes arteriosclerosis. Increased serum LDL-C level was associated with not only arteriosclerosis, but also activation of coagulation cascade leading to thromboembolism.[1,2] On the other hand, high-density lipoprotein cholesterol (HDL-C), called "good cholesterol" by extracting cholesterol from peripheral tissues, regulates activation of platelets, coagulation factors and vascular endothelial function to suppress excessive activation of coagulation cascade.[3,4] We reported that HDL-C modulates vascular endothelial function via sphingosine 1-phosphate (S1P)/S1P specific receptors and via apolipoprotein A (ApoA)/scavenger receptor class B type I (SR-BI), which are accumulated at high concentrations in HDL-C.[5] The major carrier of plasma SIP has been thought to be ApoA, but Apolipoprotein M (ApoM), which is highly associated with HDL, was recently reported to be a major carrier of S1P.[6] Inhibition of arteriosclerosis by regulating vascular endothelial function by S1P in HDL-C bound to ApoM has been reported[7]. Furthermore, association between HDL-C/ApoM and venous thromboembolism (VTE) has also been reported. Lower plasma levels of HDL-C and ApoM are associated with higher risk of recurrent VTE,[8,9] suggesting that ApoM has not only anti-arteriosclerotic effect but also anti-thrombotic effect. The role of ApoM in coagulation remains unclear.

Materials and methods

Serum samples from 233 Japanese participants including with impaired glucose tolerance (n＝7), diabetes mellitus (n＝12), hypertension (n＝34), dyslipidemia (n＝66), and healthy controls (n=115) were analyzed and the association between ApoM and coagulation markers was analyzed.

Results

In all subjects (223 patients), serum ApoM levels were positively correlated with age (r＝0.284, p＜0.001), total cholesterol (TC; r＝0.477, p＜0.001), HDL-C (r＝0.234, p＜0.001), and LDL-C (r＝0.331, p＜0.001). Furthermore, serum ApoM levels were correlated with activated partial thromboplastin time (APTT; r＝− 0.226, p＝0.001) and prothrombin time (PT, %; r＝0.326, p＜0.001). These results indicated that higher serum ApoM levels were correlated with shorter coagulation time.

Separate analysis of the 115 healthy controls showed that ApoM levels were positively correlated with age, TC, HDL-C and LDL-C. Higher serum ApoM levels were correlated with shorter PT (%). These results indicated that the coagulation time becomes shorter as the serum ApoM levels are higher.

Conclusions

This study demonstrated that the coagulation time is shorter as the serum ApoM levels are higher in Japanese subjects including patients with diabetes mellitus, hypertension, or dyslipidemia, and healthy controls. This was an unexpected result. In this study we confirmed that serum ApoM levels were positively correlated with HDL-C, TC and LDL-C in line with previous reports.[10,11] We also found negative correlations between HDL-C levels and biomarkers of coagulation[6,10,11] (the higher the HDL-C levels, the longer the coagulation time). These results suggest that HDL-C suppress excessive activation of coagulation cascade. On the other hand, increase in serum ApoM levels were correlated with shortening of the coagulation time. As shown in previous reports,[1,2] increase in serum LDL-C levels were correlated with shorter coagulation time. Previous study showed that statin treatment significantly decreased plasma LDL-C level, ApoM and hypercoagulability.[14] These facts suggest that the association between higher serum ApoM levels and shorter coagulation time linked with slow turnover of plasma LDL levels.

In conclusion, serum ApoM levels were correlated with biomarkers of coagulation. Further study is needed to clarify the physiological role of ApoM in coagulation.

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