Soluble thrombomodulin as a predictor of incident coronary heart disease and symptomless carotid artery atherosclerosis in the Atherosclerosis Risk in Communities (ARIC) Study: a case-cohort study

Veikko Salomaa, Carmen Matei, Nena Aleksic, Leticia Sansores-Garcia, Aaron R Folsom, Harinder Juneja, Lloyd E Chambless, Kenneth K Wu

Department of Epidemiology and Health Promotion, National Public Health Institute, FIN 00300 Helsinki, Finland (V Salomaa MD); Division of Haematology-Oncology, University of Texas Medical School, Houston, TX, USA (C Matei MD, N Aleksic MD, L Sansores-Garcia MD, H Juneja MD, Prof K K Wu MD); Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis, MN (Prof A R Folsom MD); and Collaborative Studies Coordinating Center, University of North Carolina, Chapel Hill, NC (Prof L E Chambless PhD)

Background: Small amounts of soluble thrombomodulin in plasma are thought to reflect endothelial damage. In a case-cohort study, we examined whether soluble thrombomodulin is a predictor of incident coronary heart disease and carotid artery atherosclerosis.

Methods: The study population consisted of 14170 black and white participants from the Atherosclerosis Risk in Communities (ARIC) study, who did not have cardiovascular disease at the start of the study and who we followed up for 6 years. After appropriate exclusions, we analysed 258 cases of incident coronary heart disease and 449 cases of carotid atherosclerosis. A stratified random sample of 753 individuals from the ARIC cohort was used as the comparison group. We used EIA to measure soluble thrombomodulin in plasma samples from both groups. For the analysis, we used quintiles of soluble thrombomodulin concentrations (<24·7, 24·8-30·6, 30·7-40·2, 40·3-55·2, and 55·3 ng/mL).

Findings: Soluble thrombomodulin showed a strong, graded, inverse association with incident coronary heart disease (p=0·005). The adjusted rate ratio of the highest quintile of soluble thrombomodulin compared with the lowest quintile was 0·29 (95% CI 0·15-0·57). The association with carotid atherosclerosis, however, tended to be positive, especially among white participants (odds ratio 2·94 [1·15-7·51] for highest vs lowest quintile). The relation of soluble thrombomodulin to incident coronary heart disease and carotid atherosclerosis was dependent on factor VIII coagulant activity (p=0·06 and 0·003, respectively).

Interpretation: The prospective association of soluble thrombomodulin with incident coronary heart disease differs from its cross-sectional association with carotid atherosclerosis. In healthy people, plasma concentrations of soluble thrombomodulin may reflect endothelial expression of thrombomodulin. Thus, a high concentration of soluble thrombomodulin may be associated with a decreased risk of coronary heart disease.

Abstract Related to MS #543A