PRELIMINARY REPORT

Serum Sialic Acid as an Indicator of Change in Coronary Artery Disease

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We measured serum levels of total sialic acid (TSA) by an enzymatic method in 74 men who completed the St Thomas' Atherosclerosis Regression Study (STARS). Coronary artery disease (CAD) was assessed as the change (Δ) in mean absolute width of coronary segments (MAWS) over 3 years by a computerized technique. ΔTSA was significantly correlated with ΔMAWS ($r = -.50$, $P < .001$) after adjusting for age, blood pressure, smoking status, and plasma low-density lipoprotein (LDL) cholesterol. The relative risk of progression of CAD for a ΔTSA exceeding 10 mg/dL as compared with a ΔTSA not exceeding 10 mg/dL was 4.6 (95% confidence interval, 2.4 to 8.7). We conclude that serial measurement of serum TSA levels may be a useful indicator of the progression of CAD.

SIALIC ACID REFERS TO acetylated derivatives of neuraminic acid that are constituents of acute-phase glycoproteins and are highly concentrated on the surface of vascular endothelia.[1-3] An elevated serum sialic acid concentration occurs in both dyslipidemia[4] and diabetes mellitus[5] and predicts cardiovascular mortality.[6,7] To assess its role as a marker of coronary artery disease (CAD), we examined the correlation between changes in serum total sialic acid (TSA) and changes in coronary luminal dimensions over 3 years in patients in the St Thomas' Atherosclerosis Regression Study (STARS).

SUBJECTS AND METHODS

The design, clinical details, method of quantitative cineangiography, and principal results of the STARS were published elsewhere.[8] Briefly, 74 middle-aged men with CAD and hypercholesterolemia (6.1 to 10.0 mmol/L) were randomly assigned to diet and cholestyramine, diet, and usual care[8]; cholesterol decreased by 25%, 14%, and 0%, respectively. Angiography was repeated after 3 years, with quantitative image analysis of paired coronary segments being performed by edge-detection algorithm.[8] The principal end point was the change (in millimeters) in mean absolute width of coronary segments (ΔMAWS) per patient. The STARS showed improvement in ΔMAWS with diet and cholestyramine and diet treatment. In the present analysis, patients were defined as showing progression of CAD if ΔMAWS was less than −0.14 mm and as showing regression if ΔMAWS was greater than 0.14 mean.[8] The serum TSA concentration was measured at the beginning and end of the study using a commercial method (Boehringer Mannheim, Lewes, Sussex, UK) based on a coupled-enzyme assay system incorporating neuraminidase, aldolase, and pyruvate oxidase linked to a peroxidase dye; the interassay coefficient of variation was 3.8%. Comparisons were made by ANOVA. The correlation between ΔTSA and ΔMAWS was adjusted for age, blood pressure, smoking status, in-trial low-density lipoprotein (LDL) cholesterol, treatment group, and baseline TSA by multiple regression analysis. The relative risk of progression of CAD for ΔTSA greater than 10 mg/dL as compared with ΔTSA not exceeding 10 mg/dL was also calculated.

RESULTS

The mean ± SEM serum TSA concentrations in the diet and cholestyramine, diet, and usual care groups were 66.4 ± 2.8, 66.3 ± 3.0, and 68.2 ± 2.2 mg/dL, respectively ($P = .86$). Figure 1 shows a significant inverse correlation between ΔMAWS (decrease equals progression of CAD) and ΔTSA in data pooled from the three treatment groups; this correlation persisted after adjusting for other variables, including in-trial LDL cholesterol, treatment group, and baseline TSA. ΔTSA was correlated significantly with in-trial LDL cholesterol ($r = .28$, $P = .02$), but not with serum triglyceride. The mean ± SEM ΔTSA for patients showing progression (n = 20), no change (n = 33), and regression (n = 21) of CAD was 5.5 ± 3.3, −1.0 ± 1.3, and −11.8 ± 3.3 mg/dL ($P < .001$). The relative risk of progression of CAD for ΔTSA exceeding 10 mg/dL as compared with that not exceeding 10 mg/dL was 4.6 (95% confidence interval, 2.4 to 8.7).

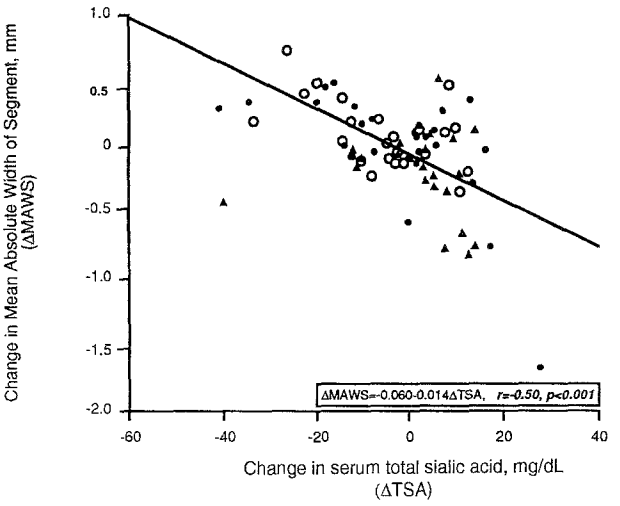

Fig 1. Scattergram and regression line showing association between ΔMAWS and ΔTSA in STARS patients. Treatment group assignment and adjusted linear regression equations are also shown. (○) Diet + cholestyramine; (●) diet; (▲) usual care.

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DISCUSSION

We present novel evidence for a strong and independent correlation between change in serum TSA and change in angiographically defined CAD. An increase in serum TSA greater than 10 mg/dL over 3 years was associated with a fourfold increased risk of CAD progression.

This result is compatible with reports that elevated serum TSA predicts cardiovascular mortality.[6,7] However, we did not find that a single in-trial value of TSA was a better correlate of angiographic progression than ΔTSA. This might have been due to differences both in baseline TSA and in smoking habit among patients,[9] but we adjusted for these variables in regression analysis. We did not confirm the association of serum TSA with triglycerides,[4] probably due to differences in patient characteristics and study design.

Our finding is consistent with the hypothesis that serum TSA reflects changes in atherosclerosis. Acute-phase proteins are highly sialylated and may increase as part of the atherogenic "chronic inflammatory response".[2,10] Serum ΔTSA may also result directly from damage to vascular endothelium, which is rich in sialic acids.[3] We suggest that changes in serum TSA may reflect both atherotic and sclerotic components of atherosclerosis,[11] given the independent correlations of ΔTSA with ΔMAWS and in-trial LDL cholesterol.

In conclusion, serial measurement of TSA levels may be useful to assess the course of CAD and its response to interventions in at-risk patients.

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