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Circulating Levels of Endostatin Are Increased in Young Nondiabetic First-Degree Relatives of Patients With Type 1 Diabetes

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Introduction: Previous study at our institution demonstrated dyslipidemic changes in healthy normoglycemic first-degree relatives (FDR) of patients with type 1 diabetes (T1D). In the present study of the same cohort, we aimed to assess circulating levels of novel biomarkers for atherosclerosis and their relationship to the lipid profile and the diabetes-risk HLA DQ2/8 genotype.

Methods: Plasma endostatin, cathepsin S, MMP-9, ICAM-1, VCAM-1 and VEGFr1 were assessed in 70 healthy FDR of patients with T1D (age 12.7±0.6 , female: 32) and in 23 age-matched control individuals (age: 11.7±1.0 years; female: 11). Human leukocyte antigen (HLA) genotype 2/8 was assessed in dried blood spots by the DELFIA method. Data are expressed as mean and standard error of the mean.

Results: There was no difference in age, body mass index, arterial blood pressure and C-peptide levels between the FDR and control groups ($p>0.2$). In the FDR group, plasma endostatin was significantly higher than in controls ($p=0.008$), whereas cathepsin S, MMP-9 and CAMs-1 plasma levels did not differ between the groups ($p>0.3$). Endostatin correlated with both total cholesterol and LDL cholesterol ($p=0.04$, $r=0.2$ for both) but showed no association with HLA-DQ 2/8 in the FDR group.

Conclusion: To our knowledge, this is the first study indicating elevated levels of endostatin in young normoglycemic individuals at risk for T1D, supporting the hypothesis that early vascular disease may develop before the onset of T1D via mechanisms unrelated to the glycemic levels.