

Complement factor D (adipsin) is positively associated with cfPWV in individuals with T2D: The Maastricht study

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Background: Factor D (FD, also known as adipsin) is the rate-limiting protease of the alternative pathway of complement activation. FD was reported to be associated with a higher risk of stroke, while its relation with coronary heart disease is less clear. Carotid-femoral pulse wave velocity (cfPWV), an indicator for aortic stiffness, is independently associated with coronary heart disease and cerebrovascular disease. We herein investigated the association between FD and cfPWV.

Methods: FD plasma concentrations and cfPWV were measured in 2270 participants (51% men, 60 ± 8.0 years, 26% type 2 diabetes [T2D]; oversampled) of The Maastricht study, a large population-based observational cohort. We conducted multiple linear regression analyses to investigate the association between FD (main independent variable) and cfPWV (outcome) with adjustments for confounders.

Results: Per SD higher FD, cfPWV was 0.415 m/s greater (95% confidence interval (CI) [0.329; 0.501], $P < 0.001$). After adjustment for age, sex, mean arterial pressure and heart rate, this was attenuated (0.089 m/s, 95%CI, [0.014; 0.164], $P = 0.021$), and after additional adjustment for prediabetes and T2D no longer significant (0.065 m/s, 95%CI [-0.010; 0.139], $P = 0.088$). This remained so in the fully adjusted model. Since we observed interaction with T2D ($P_{\text{interaction FD} \times \text{prediabetes}} = 0.107$, $\text{FD} \times \text{T2D} = 0.002$), we stratified on glucose metabolism status. In those with normal glucose metabolism, FD was positively associated with cfPWV, but only in the crude model (0.296 m/s, 95%CI, [0.186; 0.406], $P < 0.001$). In prediabetes, the association of FD with cfPWV was not significant in any model. In T2D patients, the crude association of FD with cfPWV was 0.404 m/s (95% CI [0.244; 0.563], $P < 0.001$). When adjusted for all confounders, this association was attenuated but remained significant (0.177 m/s, 95%CI [0.023; 0.331], $P = 0.025$).

Conclusion: The independent positive association between FD concentrations and aortic stiffening was statistically significant only in individuals with T2D.