

## PLASMA OSTEOPROTEGERIN AND PROGRESSION OF CORONARY ARTERY CALCIFICATION IN TYPE 2 DIABETES

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**Background:** Type 2 diabetes is associated with accelerated atherosclerosis and considered a coronary heart disease (CHD) equivalent. Coronary artery calcification (CAC) measured by cardiac CT has evolved as a quantitative tool for risk prediction in patients with and without diabetes. Initial studies suggest that progression of CAC is associated with an unfavourable prognosis especially in patients with diabetes. We prospectively evaluated the relationship between selected biomarkers and progression of CAC in type 2 diabetic subjects without previous CHD.

**Methods:** 398 asymptomatic type 2 diabetic subjects (mean age = 52±8 years, 61% male, mean HbA<sub>1c</sub> = 8±1.5) were evaluated serially by coronary calcium imaging (mean follow-up = 2.5 ± 0.4 years) using an electron beam CT scanner. Progression/regression of CAC score was defined as a change in square root transformed volumetric CAC score ≥ 2.5 mm<sup>3</sup>, based on previously published data. Demographic data, cardiovascular risk factors, glycemic control, medication use, biomarkers of inflammation (hs-CRP and IL-6) and vascular calcification (osteoprotegerin) were measured at baseline and during follow-up.<sup>1,2</sup>

**Results:** At baseline CAC was present in 211 patients (53%). Progression of CAC was found in 119 patients (29.9%). The likelihood and magnitude of progression increased with increasing baseline CAC severity. Regression of CAC was seen in 3 patients (0.8%). Hs-CRP and IL-6 levels did not correlate with the extent of baseline CAC (r = 0.02 and 0.09 respectively). Plasma OPG levels were positively correlated with age, duration of diabetes and the severity of CAC at baseline (0.42, p<0.0001). Age, male gender, presence of hypertension, baseline HbA<sub>1c</sub>, CAC score, serum IL-6 and plasma OPG were univariate predictors of CAC progression. In a multivariate logistic regression model adjusted for baseline CAC (p<0.0001), serum HbA<sub>1c</sub> (Odds ratio [OR] = 10.5 [95% CI: 2.04, 53.9], p = 0.02), plasma OPG (OR = 2.50 [1.19, 5.22], p = 0.02) and IL-6 (OR = 2.06 [1.13, 3.75], p = 0.05) were independent predictors of CAC progression. Patients in the highest tertile of plasma OPG (>9 pmol/l) had a 2.5 fold increased risk of CAC progression in comparison to those in the lowest tertile of OPG (0 – 5.2 pmol/l).

**Conclusion:** Progression of CAC was frequent in those subjects with pre-existing CAC and unlikely in patients without significant baseline CAC at an average follow-up of 2.5 years. Suboptimal glycemic control was a strong risk factor for progression of CAC in asymptomatic type 2 diabetic subjects. Of the biomarkers studied, only plasma OPG levels predicted the extent of coronary atherosclerotic plaque burden and its progression.

**References:** 1. Anand V et al. Journal of American College of Cardiology 2006; 47:9,1850-57.  
2. Anand V, et al. European Heart Journal 2006; 27:713-721

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