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Low PCSK9 plasma level is an independent predictor of coronary atherosclerotic burden in patients with stable coronary artery disease

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On behalf of EVINCI study

Funding Acknowledgement: AMGEN grant, EU FP7-CP-FP506 2007 project (grant agreement no. 222915)

Background: Circulating proprotein convertase subtilisin/kexin type 9 (PCSK9) is a key regulator of LDL cholesterol levels and has emerged as a new therapeutic target in coronary artery disease (CAD). Plasma PCSK9 levels have also been related to other components of the lipid profile associated with atherosclerotic risk.

Purpose: Aim of the present study was to evaluate the relationship of plasma PCSK9 levels with lipid profile and measures of coronary atherosclerotic burden and risk in patients with stable CAD enrolled in the European EValuation of INtegrated Cardiac Imaging (EVINCI) study.

Methods: PCSK9 was measured in 412 patients (60.3±8.6 years, 256 males) with symptoms of stable CAD fully characterized by clinical risk factors, bio-humoral profiles, and treatment. All patients underwent coronary computed tomography (CT) angiography to assess the presence and characteristics of coronary atherosclerosis. We calculated an individual CT risk score, expressing the coronary atherosclerotic burden, combining extent, severity, composition, and location of plaques.

Results: Patients were divided in groups according to PCSK9 quartiles: I (<136 ng/mL), II-III (136–266 ng/mL), and IV quartile (>266 ng/mL). LDL and HDL-cholesterol levels were significantly lower while total/HDL-cholesterol ratio was significantly higher in patients in the quartile I than in those in quartile IV (Figure A). CT angiography documented normal vessels in 30 and obstructive CAD in 35% of cases. Compared with patients with the highest levels (quartile IV), patients with the lowest PCSK9 levels (quartile I) had a higher CT risk score, a higher number of mixed plaque and higher hs-cTnI plasma levels (Figure B). PCSK9 itself was not associated with obstructive CAD. At multivariable analysis including clinical variables, medications and lipid variables PCSK9 was an independent predictor of the CT risk score (Coefficient - 0.129 (SE 0.03), p<0.0001), together with age, male gender and statin treatment.

Conclusion: PCSK9 levels are independently and inversely associated with the coronary atherosclerotic burden in patients with stable CAD.

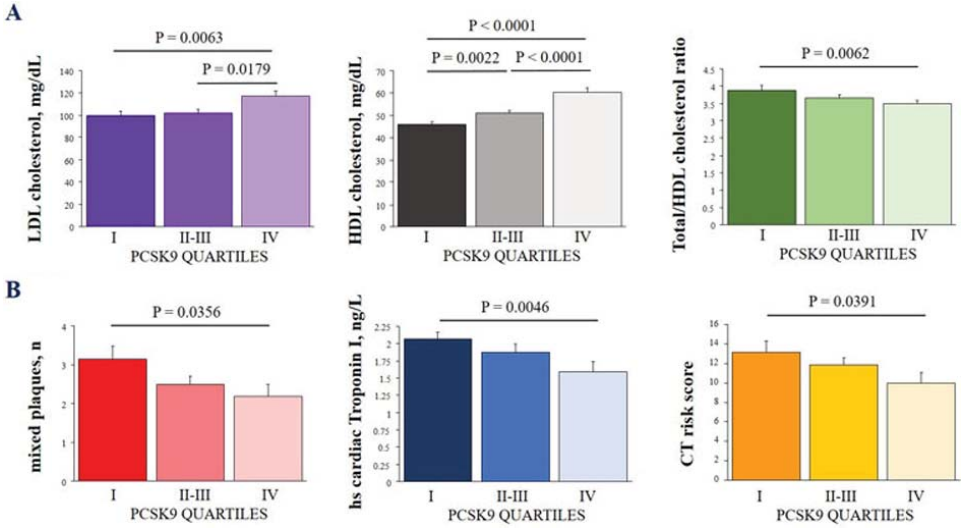

Figure 1