P6191

Proprotein convertase subtilisin/kexin type 9 (PCSK9) plasma levels are associated with the metabolic syndrome in patients with stable coronary artery disease

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On behalf of EVINCI study

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Background: PCSK9 is a key regulator of serum LDL-cholesterol levels. The relation of PCSK9 with other components of cardiovascular and coronary artery disease (CAD) risk is still debated.

Purpose: To evaluate the association of PCSK9 plasma levels with cardiovascular and coronary risk profile, in patients with symptoms of suspected stable CAD enrolled in the EVINCI study.

Methods: PCSK9 was measured in 522 patients (60.4±8.8 years, 318 males) with symptoms of stable CAD Individual risk was characterized by clinical and bio-humoral variables, including lipid/glucose/inflammatory profiles. Obstructive CAD was firstly ruled-in by multimodality non-invasive imaging and, subsequently, assessed by invasive coronary angiography.

Results: Patients were divided into groups according to PCSK9 quartiles: I (<138 ng/mL), II-III (138–264 ng/mL), and IV (>264 ng/mL) (Table). The prevalence of obstructive CAD at invasive angiography and statin treatment did not differ among groups. Compared with patients in quartile IV, patients in quartile I, had a higher prevalence of metabolic syndrome and higher values of body mass index. Among biomarkers, all cholesterol lipoproteins levels progressively increased from quartile I to IV, while insulin and HOMA index values decreased (Table). At multivariable analyses adjusted for medical treatment, the only clinical or bio-humoral variables independently associated with PCSK9 levels were presence of the metabolic syndrome (Coeff. –0.195, SE 0.05, $p<0.0001$) and HDL cholesterol levels (Coeff. 0.444, SE 0.06, $p<0.0001$), respectively.

Conclusion: In patients with stable CAD, low plasma levels of PCSK9 are associated with the prevalence of metabolic syndrome and its individual components, including, in particular, HDL cholesterol.

Table 1

Clinical Variables	Quartile I <138 ng/L (n=130)	Quartile II–III 138–264 ng/L (n=261)	Quartile IV >264 ng/L (n=131)	Biomarkers	Quartile I <138 ng/L (n=130)	Quartile II–III 138–264 ng/L (n=261)	Quartile IV >264 ng/L (n=131)
Age, years	61±9	60±9	61±8	Glucose, mg/dL	110±30	117±41	109±29
Male gender	86 (66)	161 (62)	71 (55)	Insulin, mUI/mL	13.3±12.5*	11.3±10.1	10.3±10.1
Family history	38 (29)#	86 (33)	58 (44)	HOMA index	3.9±4.5*	3.5±4.1	2.9±3.3
Hypertension	78 (60)	164 (63)	88 (67)	Tryglicerides, mg/dL	128±86	128±87	118±68
Hypercholesterolemia	72 (55)	158 (61)	81 (62)	Total cholesterol, mg/dL	171±43*	181±45	203±55
Diabetes mellitus	43 (33)	91 (35)	37 (28)	LDL, mg/dL	99±36*	104±38	119±45
Metabolic Syndrome	45 (35)#	72 (28)	19 (15)	HDL, mg/dL	46±13*	52±15	61±19
BMI, kg/m^2	28.02±4.00*	28.03±4.25	26.95±4.56	Total/HDL cholesterol	3.8±1.2*	3.7±1.2	3.5±1.1
Significant CAD at ICA	18 (14)	46 (18)	24 (18)	hs-CRP, mg/dL	0.41±0.61	0.39±1.38	0.41±0.83
Statins treatment	68 (52)	143 (55)	58 (44)	Interleukin 6, ng/L	1.60±2.75	1.30±2.49	1.30±1.68

Chi square test: #$p<0.05$. ANOVA: I vs. IV Quartile: *$p<0.05$.