Plasma PCSK9 levels and atherosclerosis burden in the coronary arteries of patients undergoing coronary angiography

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Background: Plasma PCSK9 levels, a novel and effective therapeutic target for CVD prevention, have been associated with CVD events irrespective of traditional risk factors. Whether PCSK9 levels predict coronary artery disease (CAD) burden and severity is a matter of dispute.

Purpose: To investigate the association between plasma PCSK9 levels and CAD characteristics, including number of major diseased vessels, severity of coronary stenosis, and the burden of coronary calcifications.

Methods: One hundred and one patients undergoing coronary angiography were recruited for this cross-sectional study. The number of major coronary diseased vessels was defined as the presence of ≥1 stenoses ≥50% in diameter of at least one major coronary artery. CAD severity was defined as either the absence of coronary stenosis (no-CAD), CAD<50% or CAD≥50% in one or more coronary arteries. The burden of coronary calcifications was estimated by angiography visual inspection and classified as absent, mild, moderate or severe.

Results: Coronary angiography showed single, double and triple vessel disease in 26 (25.7%), 23 (22.8%) and 21 (20.8%) patients, respectively; 20 (19.8%) and 11 (10.9%) pts had either minimal CAD (<50%) or normal angiographic findings. Also, calcifications were absent in 65 patients (64.4%), and mild, moderate and severe in 23 (22.8%), 11 (10.9%) and 2 (2%) patients, respectively. Plasma PCSK9 levels were significantly associated with age (ρ=0.22, p=0.025) and SBP (ρ=0.21, p=0.034), and were almost doubled in patients with chronic kidney disease (CKD) as compared to those without CKD [164.6 ng/mL (104.6–187.0) vs 94.8 ng/mL (86.8–114.9), p=0.006]. Among patients without CKD, those with CAD≥50% had higher plasma PCSK9 levels than those without [97.1 ng/mL (87.8–143.0) vs 83.2 ng/mL (73.4–102.6), p=0.04]. In the overall population, higher plasma PCSK9 levels were found in pts with triple vessel disease [165.7 ng/mL (121.3–180.5)] than in those with double/single vessel involvement [97.9 ng/mL (87.6–99.8) and 88.4 ng/mL (87.3–97.4), p<0.001 for both comparisons] or without CAD [87.5 ng/mL (74.3–114.9), p=0.001]. Also, a trend toward an increase of plasma PCSK9 levels was found with higher CAD severity [no-CAD: 87.5 ng/mL (74.3–114.9), CAD<50%: 89.1 ng/mL (78.9–105.3), CAD≥50%: 97.6 ng/mL (87.9–155.3), p=0.051], which turned significant after exclusion of CKD patients (p=0.042). Adjustment for age, sex, plasma LDL-cholesterol levels, statin use and CKD abolished the association between PCSK9 and CAD severity but not with the number of significantly diseased vessels and the burden of coronary calcifications.

Conclusions: Circulating PCSK9, whose plasma levels are significantly influenced by the presence of CKD, discriminates patients with significant coronary artery stenosis from those without CAD. In addition, both the number of diseased coronary vessels and total coronary calcifications are independently predicted by an elevated plasma PCSK9 level.