PCSK9 IN DIABETIC KIDNEY DISEASE

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OBJECTIVES

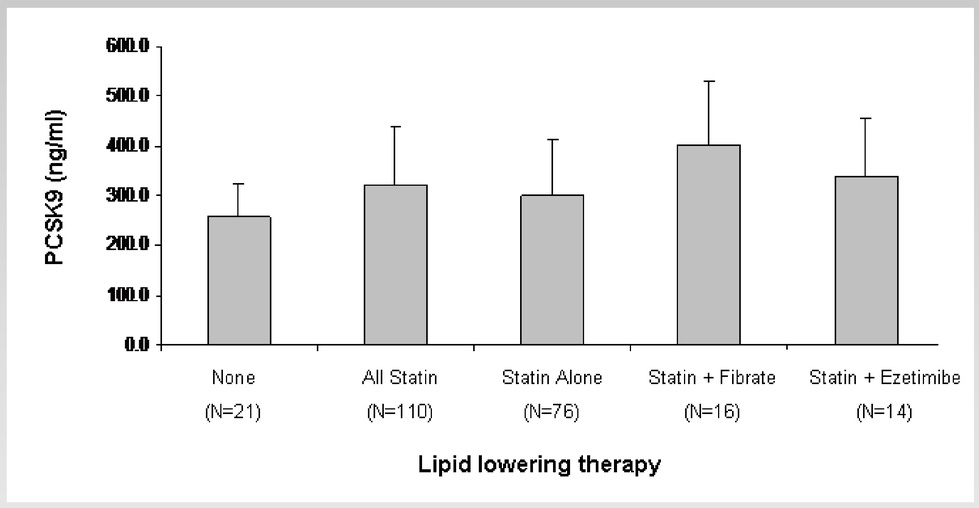
Chronic Kidney Disease (CKD) and, specifically, diabetic kidney disease, is among the fastest increasing causes of death worldwide. A better understanding of the factors contributing to the high mortality may help design novel monitoring and therapeutic approaches.

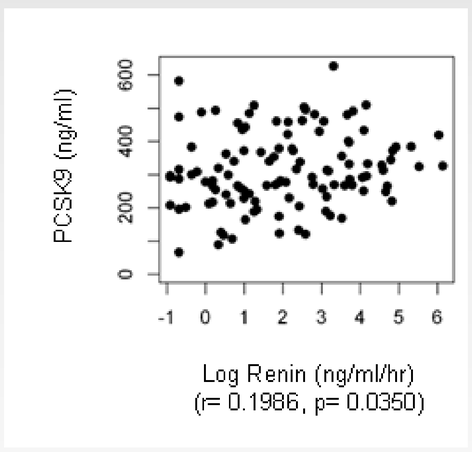
Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) downregulates hepatic LDL receptor (LDLR) expression, thus increasing LDL levels. Adding anti-PCSK9 agents to standard lipid lowering therapy further reduces the incidence of cardiovascular events. Whether this applies to CKD patients and what the selection criteria might be to intensify therapy remains unknown.

To identify factors influencing plasma PCSK9 in diabetic kidney disease patients.

METHODS

This is a cross-sectional analysis of baseline data from patients with one-hundred thirty four diabetic CKD not on dialysis on regular follow-up visits in the diabetic nephropathy clinic. Mean age was 67.9 13.9 years and a majority was male (92/134, 69%). This population was borderline obese with mean BMI 29.7 4.2 kg/m2. 40 laboratory parameters potentially related to cardiovascular risk and echocardiogram were prospectively assessed. CKD stage distribution among those patients was 16 (11.9%) stage 1, 36 (26.9%) stage 2, 29 (21.6%) stage 3A, 33 (24.6%) stage 3B and 20 (14.9%) stage 4. Albuminuria 30-300 mg/g Cr was present in 56 patients (41.8%), 300-1000 in 26 (19.4%) and >1000 in 17 patients (12.7%).





RESULTS

Plasma PCSK9 levels were 309.8±113.9 ng/ml. Plasma PCSK9 was not influenced by eGFR or albuminuria, but was higher in patients on lipid lowering therapy.

In univariate analysis, plasma PCSK9 had a significant positive correlation with serum total iron binding capacity (r=0.2087, p=0.0155), vitamin E (r=0.2132, p=0.029), phosphaturia (r=0.2565, p=0.003) and plasma renin (r=0.1986, p=0.035), and there was a trend towards a positive correlation with total serum cholesterol (r=0.1566, p=0.078).

In multivariate models, only therapy with fibrate and statin (p=0.0005), and Log renin (p=0.0126) remained independently correlated with plasma PCSK9. However, multivariate models explained very little of the PCSK9 variability, the best obtained r^2 was 0.12.

CONCLUSIONS

In diabetic kidney disease, therapy with lipid lowering drugs and specially the fibrate/statin combination were independent predictors of higher PCSK9 levels. The increased PCSK9 may limit the therapeutic benefit of these drugs. The biomarker potential of PCSK9 levels to identify diabetic kidney disease patients that may benefit from anti-PCSK9 strategies should be studied.

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