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PLASMA CYSTATIN C LEVELS AND ITS ASSOCIATION WITH ANGIOGRAPHICALLY DOCUMENTED CORONARY ARTERY IN PATIENTS WITH NORMAL OR MILDLY IMPAIRED RENAL RUNCTION

Objectives Concomitant chronic renal impairment (RI) is frequent in patients with cardiovascular disease and substantially increases morbidity and mortality. Even mild RI is associated with an increased cardiovascular risk, and due to the non-linear relationship between Creatinine (Cr) levels and Glomerular filtration rate (GFR), Cr is unreliable for detecting small reductions in GFR and mild RI. Cystatin C, a cysteine protease inhibitor, is novel marker for renal function that is very sensitive and specific for GFR estimation. Plasma Cysyatin C (PCyC) levels are less influenced by age, gender, race, drugs and muscle mass as compared to Cr and estimation of PCyC levels is known to be a better indicator of mild RI which may not be detectable by Cr measurement. The clinical utility of cystatin C in patients with manifest CAD, with normal or only mild RI merits further investigation, especially in the developing world, where CAD is rising exponentially.

Methods In a prospective study of 150 patients (mean age 57.89 ±9.43 years, 86% males) undergoing coronary angiography, PCyC levels were measured using particle-enhanced nephelometric immunoassay (PENIA) method (N Latex Cys-C, Dade Behring, Deerfield, Illinois) while estimated GFR (eGFR) was calculated from MDRD (Modification of Diet in Renal Disease) study equation. Patients with significant valvular or other structural heart disease, severe symptomatic heart failure, life-threatening arrhythmias, acute and chronic liver disease, infectious, auto-immune and chronic inflammatory disease, cancers and on any form of renal replacement therapy, were excluded.

The mean serum Cr of the cohort was 1.14±0.56 (range 0.64–5.59 mg/dl) while mean e-GFR was 70.97±18.86 ml/min/1.73 m^2 (range (11.25–114.38). Forty of 150 (26%) patients had renal impairment (RI, e-GFR <60 ml/min/1.73 m^2); of these 37 had eGFR 30–60 ml/min/1.73 m^2 while 3 had eGFR <30 ml/min/1.73 m^2. The mean PCyC levels were 1.8+0.72 mg/l (0.51–6.87 mg/l); expectedly patients with RI had significantly higher mean PCyC levels (2.11±1.11 mg/l) as compared to those with normal eGFR (1.36±0.35 mg/dl, p<0.001).

Categorising the patients into two groups according to the median PCyC levels ≥/<1.45 mg/l revealed that those with higher PCyC levels were older, had higher mean number of diseased coronary vessels, more frequently had triple vessel disease (TVD, 46% vs 32%) and diffuse CAD (69% vs 54%, p=0.04) on angiography. The prevalence of hypertension, diabetes, smoking and clinical pattern of presentation of CAD were similar amongst the two groups. Patients with PCyC ≥1.45 mg/dl had a 1.7 times higher Relative risk of having TVD (95% CI 0.89 to 3.36, p=0.04) and a 1.9 times higher RR of having diffuse CAD on coronary angiography (95% CI 0.96 to 3.65, p=0.04)

This association of higher PCyC levels with CAD remained robust even in patients with normal eGFR (n=110). Amongst these patients the median PCyC levels were 1.36 mg/l; patients with PCyC levels≥1.36 mg/l had higher incidence of TVD (46% vs 30%) and diffuse angiographic CAD (71% vs 51%, p <0.03) and higher mean number of diseased coronary vessels. The prevalence of hypertension, diabetes, smoking and clinical pattern of presentation of CAD were similar amongst the two groups.

The Relative risk (RR) of having Triple vessel disease or diffuse CAD on coronary angiography in the 1.91 and 2.3 respectively in

those with PCyC levels>than the median levels.

Results In this study of Indian patients with angiographically documented CAD, higher PCyC levels were associated with more severe CAD. The association of PCyC with severe CAD remains robust even in patients with normal or mildly impaired renal function. Higher levels of Cystatin C in patients with more severe CAD suggest its clinical usefulness as a potential biomarker for identification of high risk CAD patients.