Residual Associations of Inflammatory Markers with eGFR after Accounting for Measured GFR in a Community-Based Cohort without CKD.

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Abstract: eGFR on the basis of creatinine (eGFRcre) associates differently with cardiovascular disease and mortality than eGFR on the basis of cystatin C (eGFRcys). This may be related to risk factors affecting the level of creatinine and cystatin C along non-GFR pathways, which may confound the association between eGFR and outcome. Nontraditional risk factors are usually not measured in epidemiologic studies of eGFR and cannot be adjusted for to reduce confounding. We examined whether the inflammatory markers soluble TNF receptor type 2 (sTNFR2), C-reactive protein (CRP), and fibrinogen associated differently with eGFR than with measured GFR (mGFR).

GFR was measured by iohexol clearance in 1627 middle-aged participants without kidney disease, diabetes, or cardiovascular disease enrolled in the Renal Iohexol Clearance Survey Study from the Sixth Tromsø Study between 2007 and 2009. Generalized estimating equations were used to assess the residual associations between eGFR (eGFRcre, eGFRcys, and eGFR on the basis of creatinine and cystatin C) and the inflammatory markers relative to mGFR.

sTNFR2, CRP, and fibrinogen were associated with a higher eGFRcre after accounting for mGFR in multivariable-adjusted models (2.63 ml/min per 1.73 m(2); 95% confidence interval [95% CI], 2.1 to 3.2 per SD increase in sTNFR2, 0.93 ml/min per 1.73 m(2); 95% CI, 0.3 to 1.5 per SD increase in log CRP, and 1.19 ml/min per 1.73 m(2); 95% CI, 0.6 to 1.8 per SD increase in fibrinogen). sTNFR2 and CRP were inversely associated with eGFRcys (-1.4 ml/min per 1.73 m(2); 95% CI, -2.1 to -0.6 per SD increase in sTNFR2, and -0.76 ml/min per 1.73 m(2); 95% CI, -1.4 to -0.1 per SD increase in log CRP).

eGFRcre and eGFRcys are associated with inflammatory factors after accounting for mGFR but in opposite directions. These non-GFR-related associations may bias risk estimates by eGFR and, in part, explain the different risks predicted by eGFRcre and eGFRcys in longitudinal studies.

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