CLINICAL NEPHROLOGY - EPIDEMIOLOGY - CLINICAL TRIALS

Association between serum homocysteine and markers of impaired kidney function in adults in the United States

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Background. Circulating homocysteine, a risk factor for cardiovascular disease (CVD), is often elevated in chronic kidney disease and end-stage renal disease (ESRD) patients. Little is known about the risk of elevated homocysteine associated with less advanced renal insufficiency in the community.

Methods. Serum homocysteine concentration measures (umol/L) from the National Health and Nutrition Examination Survey (NHANES) 1991-1994 participants who were aged ≥40 years and fasted ≥6 hours (1558 men and 1829 women) were categorized as <9, 9 to 11.9, 12 to 14.9, and ≥15. Renal function levels were determined by Modified Diet in Renal Disease (MDRD) estimated glomerular filtration rate (GFRest) (mL/min/1.73 m^2) and the urinary albumin-to-creatinine ratio (ACR) (mg/g). Cumulative odds ratios (OR) of exceeding any given homocysteine cut point were computed by gender, using ordinal logistic regression. Each model included GFRest (<60, 60 to 90, ≥90), ACR (<15, 15 to <30, ≥30), age, race/ethnicity, red blood cell folate, serum vitamin B_{12}, and dietary vitamin B_6 intake as independent variables.

Results. The adjusted ORs for elevated homocysteine risk were 9 to 11 times greater in adults with the lowest GFRest levels (<60 mL/min/1.73 m^2) compared to those with normal GFRest levels. Association measures for marginal GFRest levels (60 to 90 mL/min/1.73 m^2) were weaker but significant. Albuminuria (ACR ≥30 mg/g) was a significant, independent renal risk factor for elevated homocysteine in men and women (adjusted OR = 1.78, 95% CI 1.08-2.93, and adjusted OR = 1.83, 95% CI 1.21-2.76, respectively) relative to those with low normal albumin excretion, but high normal albuminuria (ACR = 15-30 mg/g) was not.

Conclusion. In the general population, renal insufficiency is strongly associated with an increased risk of elevated circulating homocysteine, independent of B vitamin status. These results raise the possibility that elevated homocysteine may be an important risk factor to explain the heavy burden of CVD associated with kidney disease.