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Relationship between plasma homocysteine concentration and urinary markers of tubulointerstitial injury

To the Editor: Francis et al [1] recently reported that serum homocysteine concentrations are significantly elevated in patients with albuminuria and low glomerular filtration rate (GFR). We previously reported that weanling rats with experimental hyperhomocysteinemia developed significant tubulointerstitial injury [2], but showed little glomerular changes, and no significant increases in proteinuria compared with normal control rats. We concluded that plasma homocysteine correlated with tubulointerstitial injury, rather than with urinary albumin. Here, we report preliminary data on the relationship between plasma homocysteine and urinary markers in healthy subjects. We measured morning urinary albumin, α1-microglobulin, and creatinine concentrations, and plasma homocysteine and creatinine in samples obtained during annual health checkups from 273 healthy consented subjects (males 174, females 99, mean age 45.7 ± 12.0 years, ±SD). Plasma homocysteine correlated significantly with plasma creatinine ($r = 0.347$, $P < 0.0001$) and urinary α1-microglobulin/creatinine ratio (Fig. 1B), but not with urinary albumin/creatinine ratio (Fig. 1A). Our experimental and clinical data suggest that elevation of plasma homocysteine might cause subclinical tubulointerstitial damage that is not associated with albuminuria. In contrast, several studies, including the study by Francis et al, have shown that renal dysfunction would induce hyperhomocysteinemia [1, 3, 4]. Unfortunately, markers of tubulointerstitial injury were not measured in these studies. We propose that hyperhomocysteinemia per se could cause subclinical renal interstitial injury, and that reduced renal function promotes further rise in plasma homocysteine. Thus, both hyperhomocysteinemia and renal injury are associated with each other as pathogenic processes, creating a vicious cycle that results in further deterioration of renal function.

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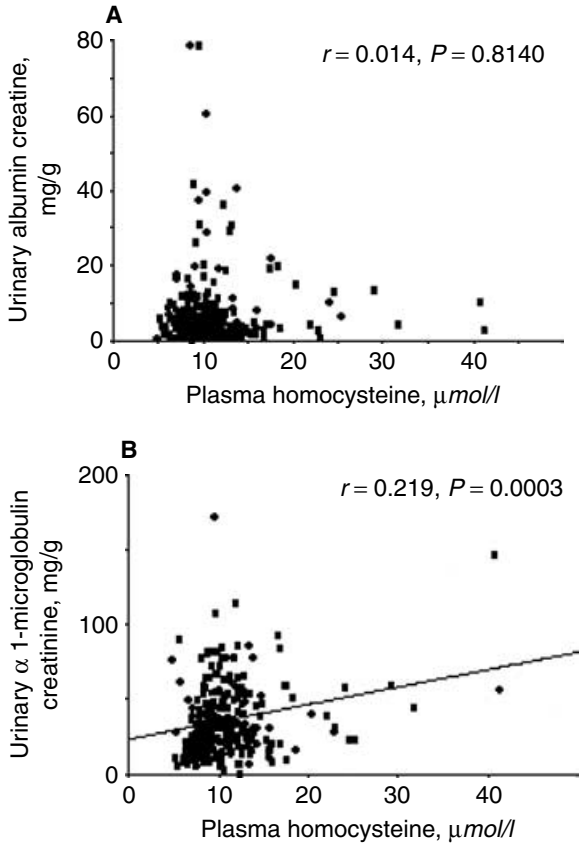

Fig. 1. Correlation between plasma homocysteine concentration and urinary albumin/creatinine (*A*) and urinary α-1 microglobulin/creatinine ratios (*B*). Plasma homocysteine correlated significantly with urinary α-1 microglobulin/creatinine ratio ($r = 0.219$, $P = 0.0003$), but not with urinary albumin/creatinine ratio ($r = 0.014$, $P = 0.8140$).

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REFERENCES

1. FRANCIS ME, EGGERS PW, HOSTETTER TH, BRIGGS JP: Association between serum homocysteine and markers of impaired kidney function in adults in the United States. *Kidney Int* 66:303–312, 2004
2. KUMAGAI H, KATOH S, HIROSAWA K, *et al*: Renal tubulointerstitial injury in weanling rats with hyperhomocysteinemia. *Kidney Int* 62:1219–1228, 2002
3. WILCKEN DEL, GUPTA VJ: Sulphur-containing amino acids in chronic renal failure with particular reference to homocysteine and cysteine-homocysteine mixed disulphide. *Eur J Clin Invest* 9:301–307, 1979
4. GUTTORMSEN AB, UELAND PM, SVARSTAD E, REFSUM H: Kinetic basis of hyperhomocysteinemia in patients with chronic renal failure. *Kidney Int* 52:495–502, 1997