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SERUM CYSTATIN C LEVELS AND LONG-TERM MORTALITY AMONG SUBJECTS WITH NORMAL CREATININE-BASED ESTIMATED GLOMERULAR FILTRATION RATES

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Objectives: The objective of this study was to evaluate the prognostic value of cystatin C (Cys-C) in the subjects with normal glomerular filtration rates (eGFR).

Methods: We selected the subjects aged ≥ 40 in the Third National Health and Nutrition Examination Survey (NHANES III) who were found to have Modification of Diet in Renal Disease (MDRD) eGFR ≥ 60 ml/min/1.73m2. These subjects were categorized into the high (>90th percentile), medium (10~90th percentile), and low Cys-C levels (<10th percentile). All-cause and cause-specific mortality were obtained from the NHANES III-linked follow-up file through December 31, 2000. Cox regression models, adjusted for age, sex, MDRD eGFR, the presence of microalbuminuria, and the status of diabetes, hypertension, and current smoking, were applied to estimate the hazard ratios (HR) and 95% confidence intervals (95% CI) of various types of mortality among the three Cys-C strata.

Results: There were291, 2470, and 306 subjects with the high, medium, and low Cys-C levels, representing 6.57x106, 52.65x106, and 6.57 x 106 adult US subjects. The serum Cys-C level was 1.29±0.010, 0.89±0.003, and 0.67±0.004 mg/L, respectively. A total of 300 cardiovascular events and 394 non-cardiovascular events developed within the 14-year follow-up. After adjustment for MDRD eGFR and other potential risk factors, the subjects with the high and medium Cys-C levels, as compared to those with the low Cys-C level, were found to have increased risk for all-cause mortality (high vs. low: HR: 3.68, 95% CI: 1.93~7.01, $p < 0.001$; medium vs. low: HR: 1.97, 95% CI: 1.02~3.80, $p = 0.043$), cardiovascular mortality (HR: 8.24, 95% CI: 2.53~26.8, $p < 0.001$; HR: 5.12, 95% CI: 1.52~17.2, $p = 0.009$), and cardiac mortality (HR: 21.7, 95% CI: 6.03~77.9, $p <0.001$; HR: 13.5, 95% CI: 3.45~53.2, $p <0.001$). Non-cardiovascular mortality was statistically higher in the high Cys-C group than in the low-level group (HR: 3.13, 95% CI: 1.37~7.11, $p = 0.008$).

Conclusions: The results of the national cohort have demonstrated that serum Cys-C level is prognostic of long-term mortality in the subjects with relatively normal renal function, independent of conventional risk factors such as MDRD eGFR and microalbuminuria.