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## Association between Monocyte Count and Risk of Incident CKD and Progression to ESRD

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### Abstract

**Background and objectives** Experimental evidence suggests a role for monocytes in the biology of kidney disease progression; however, whether monocyte count is associated with risk of incident CKD, CKD progression, and ESRD has not been examined in large epidemiologic studies.

**Design, settings, participants, & measurements** We built a longitudinal observational cohort of 1,594,700 United States veterans with at least one eGFR during fiscal year 2004 (date of last eGFR during this period designated time zero) and no prior history of ESRD, dialysis, or kidney transplant. Cohort participants were followed until September 30, 2013 or death. Monocyte count closest to and before time zero was categorized in quartiles: quartile 1,  $>0.00$  to  $\leq 0.40$  thousand cells per cubic millimeter (k/cmm); quartile 2,  $>0.40$  to  $\leq 0.55$  k/cmm; quartile 3,  $>0.55$  to  $\leq 0.70$  k/cmm; and quartile 4,  $>0.70$  k/cmm. Survival models were built to examine the association between monocyte count and risk of incident eGFR  $<60$  ml/min per 1.73 m<sup>2</sup>, risk of incident CKD, and risk of CKD progression defined as doubling of serum creatinine, eGFR decline  $\geq 30\%$ , or the composite outcome of ESRD, dialysis, or renal transplantation.

**Results** Over a median follow-up of 9.2 years (interquartile range, 8.3–9.4); in adjusted survival models, there was a graded association between monocyte counts and risk of renal outcomes. Compared with quartile 1, quartile 4 was associated with higher risk of incident eGFR  $<60$  ml/min per 1.73 m<sup>2</sup> (hazard ratio, 1.13; 95% confidence interval, 1.12 to 1.14) and risk of incident CKD (hazard ratio, 1.15; 95% confidence interval, 1.13 to 1.16). Quartile 4 was associated with higher risk of doubling of serum creatinine (hazard ratio, 1.22; 95% confidence interval, 1.20 to 1.24),  $\geq 30\%$  eGFR decline (hazard ratio, 1.18; 95% confidence interval, 1.17 to 1.19), and the composite renal end point (hazard ratio, 1.19; 95% confidence interval, 1.16 to 1.22). Cubic spline analyses of the relationship between monocyte count levels and renal outcomes showed a linear relationship, in which risk was higher with higher monocyte count. Results were robust to changes in sensitivity analyses.

**Conclusions** Our results show a significant association between higher monocyte count and risks of incident CKD and CKD progression to ESRD.

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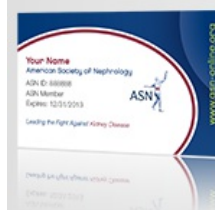
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