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Association of Insulin-like Growth Factor-1 with Cardiovascular Outcomes in Individuals with or without Chronic Kidney Disease: the UK Biobank Study

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Objectives : Insulin-like growth factor-1 (IGF-1) has been implicated in chronic noncommunicable diseases. We aimed to explore the relationship between IGF-1 and adverse outcomes among individuals with or without CKD.
Methods : We included 359,739 participants without CKD (cohort 1) and 19,249 participants with CKD (cohort 2) from the UK Biobank cohort study. CKD was defined as an estimated glomerular filtration rate<60 ml/min/1.73m^2 or random urine-albumin-to-creatinine-ratio>30mg/g. The main predictor was IGF-1 levels, and the primary outcome was all-cause mortality. The secondary outcome included the major-cardiovascular-event (MACE), defined as a composite of non-fatal ischemic heart disease, non-fatal ischemic stroke, or cardiovascular death.
Results : There were 23,100 (6.4%) deaths (the corresponding incidence rate, 4.74) over a median follow-up of 13.6 years. In cohort 1 without CKD, the adjusted hazard ratios (aHRs) (95% CIs) for all-cause mortality were 1.24 (1.19-1.30), 1.00 (0.96-1.05), 0.98 (0.93-1.02), 1.03, (0.98-1.08), and 1.09 (1.08-1.19), for 1st, 2nd, 3rd, 5th, and 6th sextile groups, respectively, compared with 4th sextile as the reference group. The U-shaped association was similar in both cohorts. In cohort 2, the corresponding HRs (95% CIs) were 1.46 (1.29-1.66), 1.17 (1.02-1.34), 1.20 (1.04-1.37), 1.13 (0.98-1.30), and 1.17 (1.02-1.35), respectively. Notably, we observed a consistent U-shaped association with MACE, only in individuals with CKD. When effect modification was examined, no significant interaction between CKD and IGF-1 levels for the risk of all-cause mortality was observed, while a significant interaction was exhibited for the risk of MACE only in individuals with IGF-1 levels above the median.
Conclusions : This study revealed a U-shaped association between IGF-1 levels with all-cause mortality and cardiovascular outcomes in CKD patients. In individuals with IGF-1 levels above the median, this association was more pronounced in individuals with CKD, suggesting that IGF-1 may serve a more potent prognostic marker in this patient population.