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Association of ketone bodies with adverse cardiorenal outcomes and death : a UK Biobank cohort study

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Objectives: Although recent findings in cellular and animal models have suggested a protective effect of ketone bodies, clinical data are still lacking to support these findings. This study assessed whether ketone body levels were associated with adverse cardiorenal outcomes and death.

Methods: This was a prospective cohort study of 83,027 UK Biobank participants without baseline chronic kidney disease (CKD) and cardiovascular disease who had serum β-hydroxybutyrate and acetoacetate levels measured at the time of study enrolment. The main predictor was β-hydroxybutyrate levels. The primary outcome was the composite of incident CKD, atherosclerotic cardiovascular disease (ASCVD; the composite of fatal and non-fatal cardiovascular events), and all-cause mortality. Secondary outcomes included the individual components of the primary composite outcome.

Results: During a median follow-up of 11.9 years, a total of 8,914 primary outcome events occurred (incidence rate 9.4/1,000 person-years). In the multivariable Cox model, a 1-standard deviation log increase in serum β-hydroxybutyrate level was associated with a 1.06 [95% confidence interval (CI) 1.04-1.09] higher risk of the primary outcome. When stratified into quartiles, compared to Q1, the hazard ratio (95% CI) of Q4 was 1.15 (1.08-1.23) for the primary outcome. This association was consistent for incident CKD, and all-cause mortality. In the multivariable Cox model of acetoacetate levels, the hazard ratio (95% CI) of a 1-standard deviation log increase in serum acetoacetate level was 1.04 (1.01-1.06), 1.05 (1.02-1.09), 1.01 (0.98-1.05), and 1.06 (1.02-1.09) for the primary composite outcome, incident CKD, ASCVD, and all-cause mortality, respectively.

Conclusions: Higher ketone body levels were independently associated with higher risk of adverse cardiorenal outcomes and death.