Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies.

Abstract

AIMS:
Little is known about the long-term association between low-carbohydrate diets (LCDs) and mortality. We evaluated the link between LCD and overall or cause-specific mortality using both individual data and pooled prospective studies.

METHODS AND RESULTS:
Data on diets from the National Health and Nutrition Examination Survey (NHANES; 1999-2010) were analysed. Multivariable Cox proportional hazards were applied to determine the hazard ratios and 95% confidence intervals (CIs) for mortality for each quartile of the LCD score, with the lowest quartile (Q1-with the highest carbohydrates intake) used as reference. We used adjusted Cox regression to determine the risk ratio (RR) and 95% CI, as well as random effects models and generic inverse variance methods to synthesize quantitative and pooled data, followed by a leave-one-out method for sensitivity analysis. Overall, 24 825 participants from NHANES study were included (mean follow-up 6.4 years). After adjustment, participants with the lowest carbohydrates intake (quartile 4 of LCD) had the highest risk of overall (32%), cardiovascular disease (CVD) (50%), cerebrovascular (51%), and cancer (36%) mortality. In the same model, the association between LCD and overall mortality was stronger in the non-obese (48%) than in the obese (19%) participants. Findings on pooled data of nine prospective cohort studies with 462 934 participants (mean follow-up 16.1 years) indicated a positive association between LCD and overall (RR 1.22, 95% CI 1.06-1.39, $P < 0.001$, $I2 = 8.6$), CVD (RR 1.13, 95% CI 1.02-1.24, $P < 0.001$, $I2 = 11.2$), and cancer mortality (RR 1.08, 95% CI 1.01-1.14, $P = 0.02$, $I2 = 10.3$). These findings were robust in sensitivity analyses.

CONCLUSION:
Our study suggests a potentially unfavourable association of LCD with overall and cause-specific mortality, based on both new analyses of an established cohort and by pooling previous cohort studies. Given the nature of the study, causality cannot be proven; we cannot rule out residual bias. Nevertheless, further studies are needed to extend these important findings, which if confirmed, may suggest a need to rethink recommendations for LCD in clinical practice.

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