

Insulin Resistance Mediates the Link Between Dietary Inflammatory Index and Advanced Cardiovascular–Kidney–Metabolic Syndrome Stages: NHANES 2007–2018

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Background

Cardiovascular–Kidney–Metabolic (CKM) syndrome represents a continuum of progressive dysfunction involving metabolic, renal, and cardiovascular systems, and is classified into five distinct stages. Individuals in advanced stages face substantially elevated risks of all-cause and cardiovascular-related mortality. Emerging evidence highlights chronic low-grade inflammation and insulin resistance (IR) as pivotal drivers of CKM progression. The Dietary Inflammatory Index (DII), a validated tool to quantify the inflammatory potential of diet, may play a role in CKM progression; however, its association with CKM staging remain unexplored.

Purpose

The purpose of this study was to investigate whether dietary inflammatory potential, as assessed by the DII, is associated with progression to advanced stages of CKM syndrome in U.S. adults, and to explore whether IR mediates this relationship.

Methods

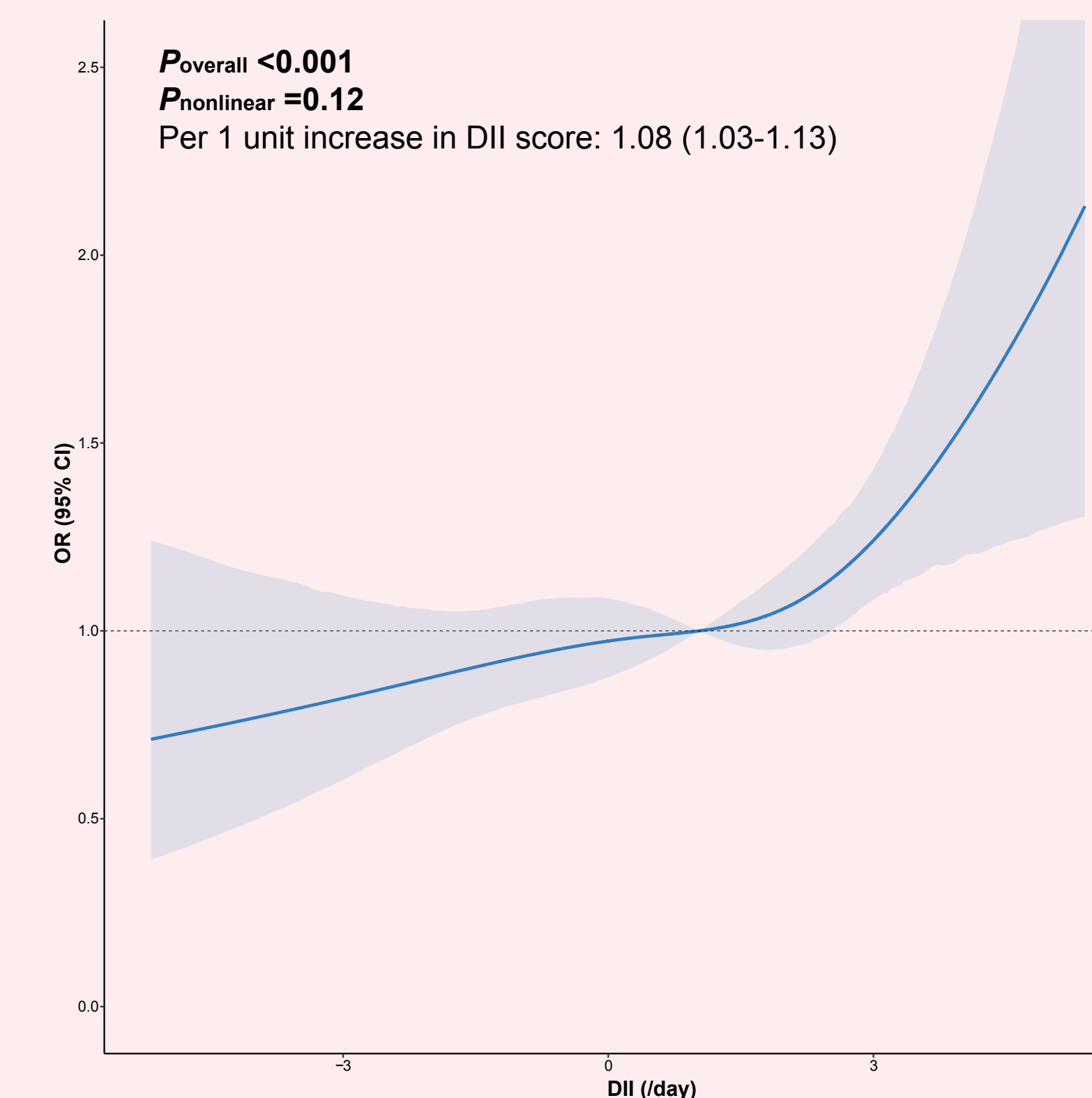
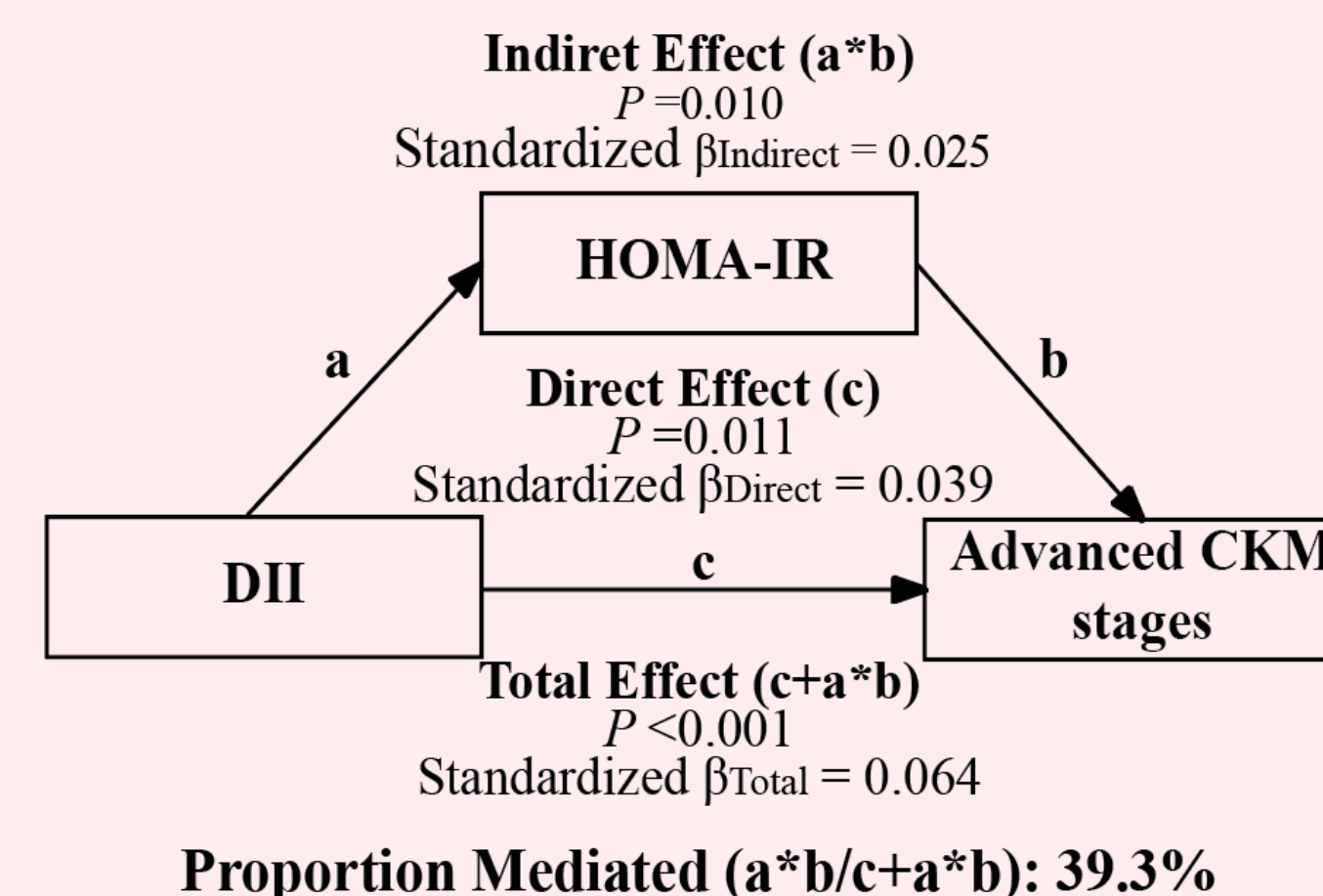
We conducted a cross-sectional analysis using data from the U.S. National Health and Nutrition Examination Survey (NHANES) spanning 2007–2018. DII scores were calculated from 24-hour dietary recall data. Advanced CKM was defined as stage 3 or 4 according to American Heart Association guidelines, representing individuals with established or high-risk cardiovascular disease. IR was estimated using the HOMA-IR index, calculated by fasting plasma glucose (mmol/L) \times fasting insulin (mIU/L) / 22.5.

Statistical analyses were performed after adjusting for covariates, including age, sex, race, education level, smoking status, physical activity, and total energy intake.

Results

Among 12,993 eligible participants, 2,167 (16.68%) were classified as having advanced CKM stages. The weighted mean DII was 0.87 ± 2.04 , and the median HOMA-IR was 2.51 (1.51–4.32). Participants in advanced CKM stages exhibited significantly higher DII scores (1.20 ± 2.03 vs. 0.82 ± 2.03 , $P < 0.001$) and HOMA-IR levels ($3.18 [1.77–5.70]$ vs. $2.43 [1.48–4.15]$, $P < 0.001$) compared to those in earlier stages (0–2). Weighted logistic analysis showed that individuals in the highest DII quartile (≥ 2.42) had a significantly increased risk of advanced CKM (adjusted odds ratio: 1.39; 95% confidence interval: 1.08–1.78; $P = 0.010$) compared to those in the lowest quartile (< 0.69). Weighted Restricted cubic spline models demonstrated a linear positive association between DII and advanced CKM stages ($P_{\text{overall}} < 0.001$; $P_{\text{nonlinear}} = 0.12$).

Mediation analysis indicated that HOMA-IR accounted for 39.3% of the positive association between DII and advanced CKM stages.



Conclusions

A diet with higher inflammatory potential, reflected by elevated DII scores, is significantly associated with progression to advanced CKM stages. This relationship is partially mediated by insulin resistance. These findings underscore the potential of DII as a modifiable risk factor for CKM prevention and highlight the importance of anti-inflammatory dietary strategies in managing cardiometabolic health.

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