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Overweight is Not a Diabetes Risk Factor for Insulin-sensitive Individuals: CARDIA 30-year Follow Up

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Abstract

Introduction: Overweight and obese are widely reported risk factors for type 2 diabetes. However, the true risk may be obscured by effect modification. Hypothesis: The extent to which overweight or obese increases diabetes risk is modified by insulin resistance status. Specific Aim: Estimate the association of overweight and obese with incident type 2 diabetes, accounting for interacting variables. Methods: We conducted a retrospective cohort study of CARDIA: Coronary Artery Risk Development in Young Adults. Participants ages 18-30 at baseline were followed for 30 years. In this study (n=4,855), the primary outcome was time to incident diabetes. Cox proportional hazards regression models were summarized with hazard ratios (HR) and 95% confidence intervals (CI). Results: In a risk-factor-adjusted model without interacting variables, participants overweight at baseline had twice the risk of future diabetes compared to normal weight participants (HR 2.03, 95% CI: 1.65, 2.49; $p<0.0001$). However, after exploring interacting variables, overweight was not a risk factor among insulin-sensitive participants below the bottom tertile of HOMA2-IR, homeostatic model assessment of insulin resistance: HR 1.37, 95% CI: 0.83, 2.25, $p=0.2165$. By contrast, overweight was a significant risk factor for those above the top two tertiles of HOMA2-IR: HR 2.21; 95% CI: 1.75, 2.79, $p<0.0001$. The effect modification for overweight participants was confirmed using Cox models stratified by HOMA2-IR categories. Obese at baseline was a diabetes risk factor regardless of insulin resistance status. Conclusion: Overweight at baseline was not a diabetes risk factor for insulin-sensitive CARDIA participants. If confirmed, these findings could impact weight-loss recommendations.

Keywords: insulin resistance, hyperinsulinemia, overweight, obese, effect modification

Abbreviations: CARDIA, Coronary Artery Risk Development in Young Adults Study; HR, hazard ratio; CI, confidence interval; HOMA2-IR, homeostatic model assessment of insulin resistance version 2

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