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Longitudinal associations of plasma fatty acid composition with type 2 diabetes incidence and indices of insulin secretion and insulin sensitivity in the Finnish Diabetes Prevention Study

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Background: There is evidence that desaturase enzymes and proportion of certain fatty acids (FA) in plasma are associated with type 2 diabetes risk (T2D). Less is known of plasma FAs in relation to insulin sensitivity and secretion.

Methods: Originally, 522 middle-aged, overweight people with impaired glucose tolerance were randomized into a control or lifestyle intervention group in the Finnish Diabetes Prevention Study. Lifestyle intervention reduced the incidence of T2D by 58%. Total plasma FA composition was measured using gas chromatography among 409 people at baseline and selected annual visits during the intervention period lasting for one to six years. T2D incidence during an extended 14-year follow-up was analysed with Cox regression. Mixed models were used to examine longitudinal associations (>1000 observations) of FAs with subsequent year's indices of Matsuda insulin sensitivity (ISI), acute-phase insulin secretion (InsAUC30/GlucAUC30) and disposition (DI30=ISI*InsAUC30/GlucAUC30), and yearly changes of ISI (Δ ISI) and homeostatic model assessment β -cell function (Δ HOMA- β). Adjustments were made for intervention, sex, smoking, age, BMI, alcohol consumption, serum triglyceride concentration and level of physical activity.

Results: Proportions of 20:5n-3, 22:5n-3, 22:6n-3 and Δ 5 desaturase activity (20:4n-6/20:3n-6, Δ 5D) were related to decreased incidence of T2D (HR per 1SD: 0.78, 0.77, 0.79 and 0.80, $P < 0.05$). Δ 5D was associated with low InsAUC30/GlucAUC30 ($\beta = -0.07$, $P = 0.01$), whereas pentadecanoic acid (15:0) associated with high InsAUC30/GlucAUC30 ($\beta = 0.04$, $P = 0.05$). Both 22:5n-3 and 22:6n-3 associated with improved Δ HOMA- β (both $\beta = 0.06$, $P < 0.05$), whereas 20:3n-6 was associated with low ISI ($\beta = -0.07$, $P = 0.03$) and 14:0 with improved Δ ISI ($\beta = 0.07$, $P = 0.03$). DI30 was not associated with FAs.

Conclusions: Marine PUFAs and Δ 5D activity predicted decreased incidence of T2D. However, these associations were only partly explained by the underlying pathogenic mechanisms of T2D, i.e. insulin secretion and sensitivity.

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