Impact of Insulin-resistance, Body Mass Index and Dietary Fat Intakes on Apolipoprotein B-48 Kinetic

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Substantial evidence exists indicating that elevated plasma levels of apolipoprotein (apo) B-48-containing lipoproteins are associated with increased cardiovascular disease risk. Overaccumulation of apoB-48-containing lipoproteins of intestinal origin observed in patients with insulin-resistance (IR) is thought to be attributable to both elevated intestinal production and reduced clearance of these lipoproteins. The objective of this study was to assess the relative contribution of IR, anthropometry, and dietary fat content on triglyceride (TG)-rich lipoprotein (TRL) apoB-48 kinetic. The in vivo kinetic of TRL apoB-48 was measured in 131 men with primed-constant infusion of L-[5,5,5-D3]leucine. TRL apoB-48 production rate (PR) and fractional catabolism rate (FCR) were determined by multi-compartmental modeling, while TRL apoB-48 pool size (PS) was measured by ELISA. IR was defined by TG levels > 1.5 mmol/L and Homeostasis Model Assessment of IR (HOMA-IR) > 2.5. Age was inversely associated with TRL apoB-48 FCR (ρ=-0.21; P=0.02), while BMI was positively correlated with TRL apoB-48 PR (ρ=0.33; P=0.0001) and PS (ρ=0.44; P<0.0001). Fat intake was associated with TRL apoB-48 PR (ρ=0.34; P<0.0001) and PS (ρ=0.35; P=0.0001). HOMA-IR was positively associated with TRL apoB-48 PR (ρ=0.26; P=0.005) and PS (ρ=0.35; P=0.0001). Furthermore, when adjusted for fat intake, TRL apoB-48 PR was significantly higher in IR subjects (n=73) than in insulin-sensitive subjects (Δ=+64%; P<0.0001), and TRL apoB-48 FCR was lower (Δ=-13%; P=0.005). Multiple linear regression analysis showed that IR was the most significant constitutive predictor of TRL apo B-48 PR variance (6.6%; P=0.01), while age and BMI were not significantly associated with PR. In conclusion, these results suggest that IR is a major factor contributing to TRL apoB-48 overaccumulation, possibly through increased production and decreased clearance, independent of age, BMI and fat intake.