Objectives: The goal of the study described here was to determine whether dietary ω-3 polyunsaturated fatty acid (PUFA) intake modulates the association between APOB Ins/Del polymorphism and obesity in type 2 diabetic patients. Methods: In this cross-sectional study, 700 patients with type 2 diabetes were recruited in Tehran. Weight and waist circumference (WC) were measured, and body mass index (BMI) was calculated. Dietary intake was assessed using a validated semi quantitative food frequency questionnaire. APOB genotyping was performed with 8% polyacrylamide gel electrophoresis. Results: We observed a significant interaction between Ins/Del genotype and dietary ω-3 PUFA intake with respect to BMI, WC, and obesity risk in both unadjusted (P = 0.007, P =0.001, and P = 0.021, respectively) and adjusted (P = 0.007, P = 0.04, and P = 0.002, respectively) samples. Thus, the carriers of the Del allele were only associated with lower BMI (P = 0.01) and WC (P = 0.002) among individuals with high ω-3 PUFA intake (≥0.6% of energy), but not in those with low ω-3 PUFA intake (<0.6%). Also, when dietary ω-3 PUFA was <0.6%, general obesity risk in carriers of the Del allele was about 1.6 times higher than that of Ins/Ins homozygotes (odds ratio = 1.59, 95% confidence interval: 1.05–2.52, P = 0.039). But with high ω-3 PUFA intake (≥0.6%), the risk was 0.46 times lower (odds ratio ¼ 0.46, 95% confidence interval: 0.25–0.79, P = 0.003). Moreover, a similar interaction was observed in central obesity only in men after adjustment for confounder variables (P = 0.041). Conclusions: These findings support the hypothesis that a diet high in ω-3 PUFA (≥0.6%) can decrease the obesity risk in carriers of the Del allele of ApoB gene.

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