Paraoxonase polymorphism Met-Leu 54 is associated with fatal myocardial infarction in type 2 diabetic patients

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Coronary heart disease (CHD) is the dominant cause of early mortality in Type 2 diabetes mellitus. Oxidation of low-density lipoproteins (LDL) contributes to the development of cardiovascular disease. Paraoxonase, an HDL-associated enzyme, provides protection against the oxidation of LDL and several studies have implicated polymorphisms as risk factors for heart disease. Two polymorphisms of paraoxonase Gln-Arg 191 and Met-Leu 54 were evaluated by PCR-RFLP in 169 Type 2 diabetic patients with cardiovascular disease (angina n=56, non-fatal myocardial infarction (MI) n=95 and fatal MI n=18) and 169 control diabetic subjects without evidence of heart disease. Cases and controls were matched for gender, duration of diabetes, age at diagnosis and for fasting plasma glucose, blood pressure, LDL, and HDL after 3 months diet therapy. The proportion of patients with LL in control, angina, nonfatal MI and fatal MI was 41%, 39%, 45%, and 78%, χ^2 for trend, $p< 0.04$. For fatal MI, the association of LL compared with controls was $p< 0.006$. The addition of data from the 191 poymorphism only slightly increases the association. In conclusion, there was a trend for association of the paraoxonase 54 polymorphism with MI, with the major effect being for fatal MI. This would be in keeping with decreased activity of paraoxonase, increasing the liquidity and decreasing the stability of atheromatous plaques.