Combined effect of smoking and the -148C>T fibrinogen polymorphism and the risk of Myocardial Infarction in the Maltese population

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Fibrinogen is a soluble glycoprotein that acts as a clotting factor and acute phase reactant. Plasma fibrinogen levels are affected by environmental and demographic factors including gender, advancing age and seasonality. Polymorphisms within the three fibrinogen genes, *FGA*, *FGB*, and *FGG*, encoding the Aα, Bβ and γ chains respectively, also influence plasma fibrinogen levels. The fibrinogen genes have been extensively studied. However, there are conflicting results on whether individual single nucleotide polymorphisms (SNPs) within these genes confer an increased risk of Myocardial Infarction (MI). The -148C>T SNP (rs1800787) is a promoter SNP in *FGB*, the rate-limiting gene in fibrinogen synthesis. In this study, 1062 samples from the Maltese Acute Myocardial Infarction (MAMI) Study were tested for the -148C>T SNP using PCR-RFLP (polymerase chain reaction and restriction fragment length polymorphism) with *Hind III*. The allele frequencies for the wildtype -148*C and the mutant -148*T were 78% and 22% respectively. In the MAMI collection, this SNP alone did not have an effect on fibrinogen levels or risk of MI [C/T: Odds Ratio (OR) 1.11 (95% Confidence Interval (CI) 0.82–1.51); T/T: OR 1.59 (95% CI 0.86–2.94)]. However, amongst those who never smoked, the risk of MI increased with increasing number of the T allele [C/T: OR 1.91 (95% CI 1.10–3.33); T/T: OR 3.40 (95% CI 1.05–11.00)]. In smokers, the -148CC and CT genotypes were associated with a three-fold increased risk of MI [C/C: OR 3.54 (95% CI 2.12–5.93); C/T: OR 3.09 (95% CI 1.78–5.38)] and this risk doubled in those with the -148TT genotype [OR 5.90 (95% CI 1.73–20.10)]. These observations suggest that smoking status modifies the risk of MI associated with the -148C>T genotype and may, in part, account for the conflicting data reported in other studies.