ASSESSING THE COMBINED EFFECTS TWO SINGLE NUCLEOTIDE GENETIC POLYMORPHISMS OF FIBRINOGEN GENES ON THE COAGULATION CASCADE IN PATIENTS WITH STABLE ANGINA

ACC Moderated Poster Contributions
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Background: Studies have shown that genetic polymorphisms such as the G58A and the G455A polymorphisms on alpha and beta chain genes of fibrinogen respectively are associated with fibrinogen plasma levels in healthy individuals, but their effects on thrombotic process in patients with coronary artery disease (CAD) are unclear. In the present study we examined the combined effect of these polymorphisms on prothrombotic profile of patients with CAD.

Methods: The study population consisted of 439 patients with CAD and 283 healthy individuals (controls), evaluated by coronary angiography or exercise test. The G455A (beta chain) and the G58A (alpha chain) polymorphisms were estimated by polymerase chain reaction (PCR) and appropriate restriction enzymes. Fibrinogen levels were measured by immunonephelometry, while plasma levels of factors (f) V, X, plasminogen were measured by standard coagulometry techniques.

Results: The genotype distribution was GG: 39.6%, AG: 40.2%, AA: 20.2% and GG: 37.3%, AG: 49.0%, AA: 13.7% for CAD patients and healthy individuals (G58A) and GG: 48.2%, AG: 40.3%, AA: 11.5% and GG: 50.0%, AG: 34.6%, AA: 15.3% for CAD patients and healthy subjects respectively (G455A). We have shown that both the two polymorphisms had no significant effect on fV and fX levels in the two study groups (p=NS for all). In addition, the G58A polymorphism had no significant effect on fibrinogen and plasminogen both in controls and in CAD (G allele carriers vs AA homozygotes, p=NS for all). Controversially, 455AA homozygotes had significantly higher levels of fibrinogen (426.2±110.9 vs 368.8±92.9, p<0.05), but not plasminogen (p=NS) compared to the carriers of the G allele in controls. Interestingly, 455AA homozygotes had also higher levels of fibrinogen (539.9±132.7 vs 428.3±126.5, p<0.001) and plasminogen (118.7±15.8 vs 110.6±16.2, p<0.05) compared to the carriers of the 455G allele in CAD patients.

Conclusions: We have shown that the G58A polymorphism does not affect the coagulation process. However, the G455A polymorphism modifies significantly this process by increasing fibrinogen levels both in patients with CAD and healthy individuals and this may have important clinical implications.