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ABSTRACT

07 – Basic research

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Extensive Association Analysis Between Polymorphisms of PON Gene Cluster, Haplotypes, and Enzyme Activity with Myocardial Infarction in a Tunisian Population

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Background Polymorphisms of paraoxonase gene (PON) cluster have been investigated in numerous studies for their association with myocardial infarction (MI) but the results have been inconsistent. The present study was designed to explore the distribution of PON1, PON2 and PON3 polymorphisms, including genotyping, lipid profile, and PON1 activity, and their association with PON1 activity and MI in a Tunisian population.

Methods We conducted a case-control study, including 380 MI cases and 350 controls. Genotyping for PON1, PON2, and PON3 variants was performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) techniques. The enzymatic activity of PON1 was measured by a kinetic method using paraoxon as a substrate.



Results We reported that of the 12 genotyped variants two were monomorphic (PON1-R160G and PON3-D107D), and ten showed allelic frequency $\geq 5\%$. Statistical analyzes identified a protective variant (PON1-824G/A) and four susceptibility variants for the risk of IDM (PON1: Q192R, -108C/T and 162G/A), PON2-S311C. The study of the lipid profile according to the genotypes revealed that only the S311C variant was associated with apo-B and HDL-c levels. We also reported low activity of PON1 in IDM patients compared to controls. This activity was affected by the Q192R polymorphism, is negatively correlated with age and positively with HDL-c and apo-A1 concentrations. Measurement of the linkage disequilibrium (LD) between pairs of loci revealed that D' varied between (0 and 0.53), whereas the correlation coefficient between alleles r^2 varied from (0 to 0.18), reflects low interaction and high recombination between alleles. Analysis of the haplotypes per gene showed that the QLTAAG and RLTGGA combinations were aggravating the risk of MI, while the QLTGAA combination was protective.

Conclusion Our finding suggested that genetic polymorphisms of PON may play a role in the susceptibility to MI among Tunisian population.

Disclosure of interest The authors declare that they have no competing interest.

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