
# Study of the interaction between modulators of iron homeostasis and the ACE gene in heart failure

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**Introduction**: Heart failure (HF) refers to a clinical syndrome composed of a set of symptoms and/or signs that originate from a structural and/or functional cardiac anomaly and that give rise to the inability to pump blood in sufficient quantity, to meet the body's metabolic needs. In the present work, we intend to understand how the interaction between the I/D variation in the *ACE* gene and possible modulators of iron (Fe) homeostasis influence HF. The modulators under study were: the methemoglobin reductase activity, the *Hfe* gene and heparanase genes (*HPSE*)
**Methodology**: A case-control study was carried out with 252 Portuguese people, 143 with HF and 109 healthy controls. To analyze the polymorphism in the *HPSE* gene (rs4693608) endpoint genotyping (LightCycler480) was performed. To analyze both polymorphisms in the *Hfe* gene (H63D and C282Y), ARMS Multiplex technique was used. For the analysis of the polymorphism in the *ECA* gene (rs4646994 - I/D) a regular PCR was performed. Methaemoglobin reductase activity was obtained using spectrophotometric assay. All necessary statistical tests were performed using the IBM® SPSS® Statistics 26.0 software, with values considered significant for $p < 0.05$.
**Results:** There was an association between HF and: 1) the presence of the D allele of the *HFe* gene (HH vs HD; p=0.049); 2) the presence of the A allele of the *HPSE* gene (AA + GA vs GG; p=0.045; 3) lower levels of methemoglobin reductase activity (p=0.019). It was also found that epistasis between the presence of the H or C allele of the *Hfe* gene and the D allele of the *ACE* gene are protective in HF (p=0.041 for both).
**Conclusion:** Results of this study highlight the role of iron homeostasis and its interaction with *ACE* in HF. Iron is an essential component for the proper functioning of mitochondria, which play an important role in providing energy to the heart muscle. Knowledge of the genotype profile of patients, in modulating genes of iron homeostasis in interaction with the *ACE* gene could be an advantage in the application of a more personalized medicine, allowing preventive counseling and more targeted therapy.