Role of Genetic Polymorphisms of ion channels in the pathophysiology of coronary microvascular dysfunction and ischemic heart disease: an update

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Background: Ischemic heart disease (IHD) is classically associated with coronary artery disease (CAD) and conventional cardiovascular risk factors. However, IHD may exhibit in the absence of CAD, because of different pathophysiological mechanisms, such as the presence of specific genetic variants of ion channels, which act mainly in the microcirculation. Recently, we reported the correlation between some single nucleotide polymorphisms (SNPs) of ion channels genes and the presence of IHD, independently from the presence of conventional cardiovascular risk factors. The goal of this study is to confirm the results of the previous study on a bigger population and discover new SNPs of ion channels genes which may be associated with IHD.

Methods: A prospective, observational, single-center study was conducted on patients candidates for coronary angiography. Patients were divided in three groups: G1, coronary artery disease; G2, microvascular disfunction; G3, normal. Genetic polymorphisms relative to KCNJ11 encoding for the Kir6.1 and Kir6.2 subunits of K-ATP channels and KCNE1 encoding for the MinK subunit of IKs channels were analyzed.

Results: 603 consecutive patients (G1: 409; G2:76; G3:118) were enrolled. Genetic analysis for the three groups showed a statistically significant difference for the SNP S38G of KCNE1 (p=0.001) and for the variants rs5215, rs5218, rs5219 of KCNJ11 (p<0.0001), as well as comparing G1-G3 (S38G p=0.006; rs5215, rs5218 and rs5219 p<0.0001). Regarding G1-G2 we confirmed differences only for the variants rs5215 (p<0.0001), rs5218 (p=0.005) and rs5219 (p=0.024), while regarding G2-G3 we found differences for the variants S38G, rs5215 e rs5219 (p<0.0001). A multivariate analysis was performed and highlighted that the SNP rs5215_GG of KCNJ11 may represent an IHD independent protective factor (p<0.0001; OR: 0.036; 95.0% CI: 0.018-0.069).

Conclusion: These results confirm the importance of genetic susceptibility and the role of SNPs of ion channels genes in the determinism of IHD, independently from the conventional cardiovascular risk factors. Moreover, these results may represent a future perspective for a genic therapy for IHD.