ROLE OF GENETIC POLYMORPHISMS IN PREVENTING COMPLICATIONS DEVELOPMENT IN HEART FAILURE PATIENTS

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Background: Implantation of the left ventricular assist device (LVAD) improves heart failure (HF) patient's quality of life before heart transplantation. However, it causes thrombosis and bleeding complications after implantation, which happen due to the anticoagulant/antiplatelet treatment and platelet receptors' dysfunction due to the non-physiological shear-stress (NPSS) of the device. The aim of our study was to identify influence of genetic polymorphisms on complications development in HF patients after device implantation.

Materials and methods We recruited venous blood samples from n = 98 HF patients with implanted LVAD such as HMII, HM3 and HW. Patients were prescribed with warfarin and aspirin treatment according to the clinical protocol. Twenty-four patients had complications after LVAD implantation. DNA samples were genotyped for 21 SNPs encoding blood coagulation system, metabolism of the anticoagulant/antiplatelet drugs. And also, n = 95 healthy control individuals were included for genetic analysis.

Results The distributions of allelic and genotype frequencies of polymorphisms rs8050894 in *VKORC1* and rs5918 in *ITGB3* genes were significantly different between HF patients and healthy control groups ($p < 0.05$). Furthermore, according to the logistic regression analysis four polymorphisms of rs9934438; rs9923231 in *VKORC1*, rs5918 in *ITGB3* and rs2070959 in *UGT1A6* genes were significantly associated with HF patients' complications ($p < 0.05$). Genetic variants of *VKORC1* influence to warfarin's metabolism and on dose effects. We identified that genotypic polymorphisms of *VKORC1* gene could help to prevent over/under-coagulation of warfarin treatment. Gene polymorphism of rs5918 in *ITGB3* encodes platelet receptor GPIIIa. Apart from the impact of NPSS on platelet dysfunction, genotype variants of rs5918 also carries genetically inherited platelet dysfunction. *UGT1A6* gene encodes enzyme which is involved in aspirin metabolism. Genetic polymorphism in *UGT1A6* gene can influence to the expression of different metabolic activities of the enzyme which excretes (faster/slower) aspirin metabolites.

Conclusion Our research identifies that genotyping analysis before LVAD implantation could prevent thrombosis and bleeding complications and help to prescribe correct individual anticoagulant/antithrombotic treatments