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Association of endothelial NO-synthase gene polymorphism with the left ventricle diastolic dysfunction and pulmonary hypertension in patients with heart failure and preserved ejection fraction

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Topic(s): Heart Failure with Preserved Ejection Fraction

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Introduction. Pulmonary hypertension (PH) develops in 50-80% of patients with left-sided heart failure (HF), regardless to the left ventricle (LV) ejection fraction (EF). Endothelial NO-synthase (eNOS) activity plays important role in the development of PH in patients (pts) with heart failure with preserved ejection fraction (HFpEF). Genetic polymorphisms of eNOS may affect the severity of the left ventricle (LV) diastolic dysfunction (DD) and the elastic properties of systemic arteries in pts with HFpEF.

Purpose. To determine the polymorphism of the eNOS gene 786T>C rs 2070744 and the association of the corresponding genotypes with the severity of LV DD, PH and elastic properties of the arteries in patients with arterial hypertension (AH) and HFpEF.

Methods. We included 69 hemodynamically stable pts with AH and HFpEF (58.1% men, 67.4 ± 10.2 years; NYHA II-III). All patients underwent NT – proBNP evaluation; echocardiography; applanation tonometry; 6-minute walk test (6MWT); endothelium-dependent, flow-mediated vasodilation (FMD); LV myocardium mass index (LVMI), arterial elastance (Ea), ventricular elastance (Ees), their ratio (Ea/Ees) and systemic arterial complaence (SAC) were also calculated. Genotyping for eNOS 3 was performed by polymerase chain reaction in the real-time. Genomic DNA samples were isolated from stabilized blood. Patients were divided into 3 groups, according to genotype.

Results. "Wild" homozygous TT genotype was found in 34 (49.3%) pts (TT group), heterozygous TC genotype – in 21 (30.4%) pts (TC group), "mutant" homozygous CC genotype – in 14 (20.3%) pts (CC group). Pts did not differ in gender (19 (55.9%), 12 (60%), 11 (61.1%) men, respectively), age (67.1 ± 8.9, 65.4 ± 10.6, 64.9 ± 10.3 years, respectively), and the prevalence of comorbidities (all p> 0.05). In pts of CC group, compared with TT and TC, there was the worst result of 6MWT (314.3 ± 69.1, 371.8 ± 77.7, 385.7 ± 85.4 m, respectively); higher NT-proBNP level (806.9 ± 369.7, 668.1 ± 317.8, 636.9 ± 433.2 pg/ml, respectively); greater LVMI (187.4 ± 37.1, 182.2 ± 25.7, 195.2 ± 28.5 g/m2 respectively); more pronounced LV DD, according to average e' (4.7 ± 0.6, 5 ± 1.7, 5.3 ± 0.8 sm/sec, respectively) and E/e' ratio (15.9 ± 2.1, 14.5 ± 1.3, 15.1 ± 1.5, respectively); the highest systolic pulmonary artery pressure (50 ± 19.9; 39.6 ± 10.3; 40 ± 19.2 mmHg, respectively); worse elastic properties of arteries according to augmentation index (33.8±4.9, 26.5±4.6, 27.3±5.6, respectively), pulse wave velocity (13,1±0.7, 12.2±0.8, 12.4±1.1 sm/sec, respectively), SAC (1,1±0.2, 1,6±0.2, 1,55±0.3 ml/mmHg, respectively), Ea (2,3±0.2, 1,9±0.3, 2,1±0.3, respectively) and worse results of the FMD (8,1±2.5,10,1±4,5, 9,8±2,2, respectively, (all p <0.05).

Conclusions. Compared to other polymorphisms, the CC genotype of the NOS3 rs 2070744 gene is associated with more impaired LV diastolic function and systemic arteries elasticity, and greater PH in patients with AH and HFpEF.
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