Histomolecular fibrotic profile and an extent of the atrial and ventricular electroanatomical substrate in patients with atrial fibrillation and heart failure

V. Orshanskaya, V.S. Orshanskaya, A.V. Kamenev, L.B. Mitrofanova, L.A. Belyakova, V.A. Titov, M.A. Naimushin, E.N. Mikhaylov, R.B. Tatarskiy, O.M. Moiseeva, D.S. Lebedev

Almazov Federal Research Heart Centre, Saint Petersburg, Russian Federation
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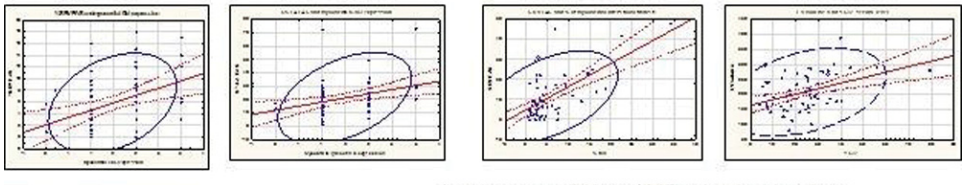
Background and purpose: The aim of this pilot study was to investigate the association between an extent of the atrial and ventricular electroanatomical substrate, serum fibrotic biomarkers and histological and immune-histochemical myocardial characteristics in ipatients with atrial fibrillation and heart failure.

Methods: We prospectively analyzed electroanatomical ultra-high density bipolar maps (HDBM) in 72 patients with AF and CHF, who underwent circular pulmonary veins (PVs) isolation. LA areas outside PVs ostia with bipolar signals ≤0.75mV, associated with local conduction velocity delay were considered as EAS and measured. Relative area of low voltage zones in right (RV) and left ventricles (RV) with bipolar signals in range of 0,5–1,5 mV were also consistently measured. Endomyocardial biopsy samples were taken from low, mediate and high septal areas of RV; histological and immune-histochemical staining was performed and an extent of myocardial interstitial fibrosis (MIF) was calculated. Before the operation we measured plasma MMP2, MMP9, TIMP, MMPs/TIMPs, galectin 3 (Gal3), TGF, soluble ST2 and the cross-linked collagen I/III synthesis and degradation product levels. The patients were divided into groups according to their ejection fraction Simpson (EF) (groups 1: EF≥50%, groups 2: EF 40–49%, and groups 3: EF<40%).

Results: The data of electroanatomical mapping, serum biomarkers and myocardial expression are presented in the table. According to results of correlation analysis, an extent of LA EAS were correlated with Gal3 and PIIICP plasma level and Gal3 myocardial expression and MIF extent (Rs=0,40, 0,45 and 0,42 respectively). The relative extent of LV EAS was correlated with MMP9 serum level (Rs=0,38); LV volume (LVV) was correlated with sST2 serum level and RVV was correlated with CD 133 myocardial expression (Rs=0,42) (picture 1). The patients with lower EF had larger extent of the LA EAS, (group 3: 28±12.4% vs. 1: 17.7±11.6%, p=0.03), an extent of LV EAS and LVV (group 3: 8,4±4,5% vs. 1: 5,1±3,8% p=0.02; group 3 vs group 1 p=0,05 relatively),higher Gal3 plasma level (group 1: 7,1±2 vs. group 2: 8,9±1,5, p=0.05) and higher MIF extent (group 2: 134±56 vs. 3: 151±30 p=0.04) (picture 2).

Conclusion: Our data suggest that relative extent of LA EAS in patients with atrial fibrillation is associated with Gal3 plasma level and Gal3 myocardial expression; severity of myocardial remodeling is connected to CD 3/133 myocardial expression and myocardial interstitial fibrosis extent, especially in patients with HF with restricted LV ejection fraction.

Correlations between the electroanatomical mapping data, serum biomarkers and myocardial expression



Biomarkers, myocardial interstitial fibrosis and EAS in patients with AF and preserved, mid-range and reduced EF