P1079

Non-valvular atrial fibrillation recurrence after sinus rhythm restoring at 1-year follow-up: predictors and risk stratification considering rs10465885 polymorphism in connexin-40 gene

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Purpose: to establish the predictors of non-valvular atrial fibrillation (AF) recurrence after sinus rhythm restoring (SRR) in patients (pts) with AF at 1-year follow-up (AFr1y), and provide AFr1y risk stratification, considering single nucleotide polymorphism rs10465885 in connexin-40 gene (SNP-Cx40).

Methods. We enrolled 186 pts before the age of 65 years (mean age (55 ± 10) years; males 123 [66,1%]) with AF (paroxysmal – 86, persistent – 72, stable – 28 pts; first onset (FO) AF – 48 pts). Clinical, laboratory and echocardiographic data were analyzed. SNP-Cx40 was genotyped by real time polymerase chain reaction (T – reference, C – minor allele) in 112 pts. Genotype distribution of SNP-Cx40 was as follows: TT – 25,9% (n = 29); CT – 49,1% (n = 55); CC – 25,0% (n = 28). SRR was performed in 112 cases (102 pts) with non-permanent AF: 30 – pharmacological cardioversion (PCV), 62 – direct-current cardioversion (DCV), 20 cases – radiofrequency ablation (RFA). AFr1y occurred in 74 (66,1%) of 112 cases. We performed Artificial Neural networks (ANNs) analysis to select the AFr1y predictors. While AFr1y risk stratification, we considered the activation function value (Y) of the certain ANN model and its relation to Y cut-off value (Ycrit). In case of Y > Ycrit, the AFr1y risk was considered as «high».

Results. Genetic algorithm Input Selection revealed the set of parameters, associated with AFr1y, included SRR type, SNP-Cx40, and baseline clinical (body mass index, global cardiovascular risk, heart failure (HF) stage, CHA2DS2-VASc score, AF anamnesis duration, average AF event duration, FO AF), laboratory (fasting glucose level, estimated glomerular filtration rate, red cell distribution width, total serum cholesterol level) and echocardiographic (left atrial dimension (LAD), left ventricular (LV) mid-wall fractional shortening degree, LV hypertrophy degree) characteristics.

In order to obtain the maximal reduction of predictors, we built non-linear multilayer perceptron model (MLP5) on the basis of set of 5 the most sensitive parameters, included SRR type, SNP-Cx40, HF stage, LAD and FO AF. The area under curve for MLP5 (0,808 [CI 0,723-0,876]) was higher than 0,5 ($p < 0,001$), with Ycrit = 0,503.

The rs10465885 CC genotype was associated with AFr1y high risk in pts without HF and mildly increased LAD – both after PCV (FO AF with known precise event duration (PED); Y = 0,906) or DCV (FO AF with unknown PED; Y = 0,911). Additionally, rs10465885 CC genotype was associated with AFr1y high risk after RFA in pts without HF and normal or mildly increased LAD (Y = 0,912), and in pts with HF B or C1 stage (according to modified AHA/ACC classification) with moderately increased LAD (Y = 0,912).

Conclusions. AFr1y was non-linearly associated with SRR type, SNP-Cx40 and certain phenotypic parameters, including HF stage, FO AF and LAD. These parameters could be used for AFr1y risk stratification, with the selection of phenotype-genotype high risk groups, considering SNP-Cx40.