Non-valvular atrial fibrillation recurrence after sinus rhythm restoring at different follow-up periods: phenotype-genotype high-risk groups, considering rs10465885 polymorphism in connexin-40 gene

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Purpose: to provide risk stratification of non-valvular atrial fibrillation (AF) recurrence after sinus rhythm restoring (SRR) in patients (pts) with AF at different follow-up periods (3 months (AFr3m), 12 months (AFr12m) and 18 months [AFr18m]), based on phenotype-genotype high-risk groups, considering rs10465885 polymorphism in connexin-40 gene (SNP-Cx40).

Methods. We enrolled 186 pts (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 PCR (T – reference, C – minor allele) in 112 pts. The genotypes were distributed 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). AFr3m occurred in 53 (43,4%) of 122 available cases; AFr12m – 65,5% (76/116); AFr18m – 75,2% (79/105). The Artificial Neural networks (ANNs) analysis was performed to select the AF recurrence predictors. We considered the ANN activation function value (Y) and its relation to Y cut-off value (Ycrit). In case of Y > Ycrit, the AF recurrence risk was considered as «high».

Results. We built three nonlinear ANN models (multilayer perceptrons) for AFr3m (Ycrit = 0,496), AFr12m (Ycrit = 0,503) and AFr18m (Ycrit = 0,720) risk prediction.

In case of SNP-Cx40 CC genotype carriage, we determined the additional increase of AFr3m risk after PCV in pts with CHA2DS2-VASc score «0» and normal (Y = 0,629) or mildly decreased (Y = 0,616) left ventricular mid-wall fractional shortening, and in the case of its moderate decrease – both after PCV (Y = 0,585) and DCV (Y = 0,627).

The CC genotype was associated with AFr12m high risk in pts without heart failure (HF) and mildly increased left atrial dimension (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, CC genotype was associated with AFr12m 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).

The high-risk groups of AFr18m in pts with CC genotype were as follows (Y = 0,913): after RFA in pts with recurrent AF and presence of episodes lasting ≥7 days; after PCA in case of FO AF with unknown PED and index episode lasting ≥1 month; after DCV in case of FO AF with unknown PED and index episode lasting ≥12 months.

Conclusion. AFr3m, AFr12m and AFr18m, besides SNP-Cx40, were non-linearly associated with SRR type, and certain clinical and echocardiographic phenotypic parameters, which could be used for AF recurrence risk stratification, with the selection of phenotype-genotype high-risk groups, considering SNP-Cx40.