Haplotype analysis of phagocytic NADPH oxidase polymorphisms in Korean atrial fibrillation patients: effect on the systemic oxidative stress burden

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Introduction: Cardiac myocyte nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) activity within the atrial tissue is an important source of oxidative stress during AF. The aim of this study was to determine the role of the polymorphisms of phagocytic NOX on the systemic oxidative stress burden in Korean AF patients.

Methods: A total of 220 consecutive patients, including 103 non-AF and 117 with AF (52 non-paroxysmal AF), were enrolled. We analyzed 25 single nucleotide polymorphisms (SNPs) of 6 subunits of the phagocytic NOX (gp91phox, p22phox, p47phox, p67phox, p40phox, and Rac2). To evaluate the in vivo oxidative stress burden, the plasma level of 8-iso-prostaglandin F2α (8-iso-PGF2α) was measured.

Result: A difference in the distribution of the haplotypes of p22phox was found in the likelihood ratio tests (P=0.0380). The distribution of the C-C-G-G-T and C-T-A-G-T haplotypes differed between the two groups. The oxidative stress burden (8-iso-PGF2α) was higher in the AF group (72.62 ± 46.29 vs. 47.55 ± 38.38 pg/mL, P=0.00004). Among the variables, the presence of AF (β=22.6, P=0.001) and the C-C-G-G-T haplotype (β=17.1, P=0.049) were significant determinants of 8-iso-PGF2α. In the AF patients carrying a haplotype C-C-G-G-T, the 8-iso-PGF2α level was more elevated than in AF patients who did not (91.04 ± 57.64 vs. 68.79 ± 42.93 pg/mL, P=0.05).

Conclusion: The polymorphism in the gene coding phagocytic NOX subunit p22phox significantly differed between the AF and non-AF control groups, and the specific haplotype C-C-G-G-T was associated with AF and an elevated oxidative stress burden in the Korean population.