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SNP RS3825214 IN THE TBX5 GENE IS ASSOCIATED WITH LONE ATRIAL FIBRILLATION IN CHINESE HAN POPULATION

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Objectives The prolongation of the PR interval has been considered as an increased risk of atrial fibrillation (AF), pacemaker implantation and mortality. Several recent genome-wide association studies (GWAS) have yielded associations between common variants and echocardiogram (ECG) parameters. SNP rs3825214 in TBX5 gene was shown correlating with PR interval, QRS duration, QT interval and verified significant in diseases such as atrial fibrillation, advanced AV block. The aim of this study is to further assess association between SNP rs3825214 and ECG parameters, AF, ventricular tachycardia, as well as some other arrhythmias associating with sudden cardiac death in mainland Chinese Han population.

Methods 692 patients as AF group, 235 patients as VT group, and 856 controls in GeneID population were enrolled for case-control association study. Genotyping was performed using a Rotor-Gene TM 6000 High Resolution Melt system. The associations of both allele and genotype were analysed by rigorous statistical analysis adjusting for potential confounding factors.

Results In contrast to previous GWAS results, we did not found PR interval, QRS duration, QT interval significantly associated with SNP rs3825214, but the PR interval shows a tendency of association ($p=0.057$). QT_c was associated with SNP rs3825214 ($p=0.047$, $\beta=-19.76$). A significant association between G allele of SNP rs3825214 and lone atrial fibrillation (LAF) was arresting ($p=0.002$; $P_{adj}=0.001$, $OR=0.652$). In both AF and LAF group, the distributions were significantly different compared to the control group with p value equals to 0.029 and 0.003 respectively. Assuming a dominant genetic model, the GG shows strong significant association with AF, and especially LAF. The GG genotype could be a profound protective factor under dominant genetic model as the OR was 0.73 after adjusting for sex, age, T2DM, hypertension, stroke, and CAD.

Conclusions The study detected the association of allele G of SNP rs3825214 in TBX5 with QT_c and lone AF for the first time. The findings expand the GWAS results to other ethnic population and provide new insight into the molecular aetiology involved in the pathogenesis of lone AF.