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GENETIC VARIANTS IN SOX5 AND CAV1 ARE ASSOCIATED WITH ABNORMAL ATRIAL ACTIVATION IN PATIENTS WITH LONE ATRIAL FIBRILLATION

Poster Contributions
Hall C
Monday, March 31, 2014, 9:45 a.m.-10:30 a.m.

Session Title: Arrhythmias and Clinical EP: New Observations on Pathophysiology of Atrial Fibrillation
Abstract Category: 4. Arrhythmias and Clinical EP: AF/SVT
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Background: Abnormal P-wave morphology (PWM) has been associated with history of atrial fibrillation (AF) in earlier studies. Though lone AF is believed to have substantial genetic basis, studies on associations between single nucleotide polymorphisms (SNP) linked to AF and PWM have not been reported. We aimed to assess whether SNPs previously associated with AF (rs2200733, rs2106261 and rs13376333) and SNPs linked to PR interval prolongation and AF (rs11708996, rs6800541, rs3807989, rs251253 and rs11047543) are also linked to P-wave abnormalities.

Methods: Eight SNPs were studied in 249 non-related patients with lone AF (median age 37 [IQR27-44] years, 121 men). Orthogonal PWM was classified as Type 1 - positive in leads X and Y and negative in lead Z (most common in healthy), Type 2 - positive in leads X and Y and biphasic (-/+) in lead Z, and Atypical - all other morphologies.

Results: Presence of risk allele (both in homo- and heterozygous state) of rs11047543 near the gene SOX5 and rs3807989 near the gene CAV1 did not affect either PR or P-wave duration but was linked to a lower prevalence of Type 1 P waves (SOX5: OR 5.7 95%CI 1.3-24.9, p=0.021; CAV1: OR 4.5 95%CI 2.2-9.3, p<0.001, Table). No association was observed in regard to other 6 SNPs.

Conclusion: In patients with lone AF, carrying risk alleles of rs11047543 or rs3807989 is associated with abnormal atrial activation. The association between the SNPs and PWM is a novel finding and supports the causative effect of genetic variation on atrial electrophysiology.

		rs1147543 (SOX5)			rs3807989 (CAV1)		
Alleles		AA/AG	Non-risk allele	P	AA/AG	Non-risk allele	P-value
P-wave morphology	Type 1, n (%)	2 (8%)	54 (32%)	0.010 [Type 1 vs others]	11 (13%)	48 (41%)	<0.001 [Type 1 vs others]
	Type 2, n (%)	13 (50%)	73 (44%)		44 (53%)	44(37%)	
	Atypical, n (%)	11 (42%)	41(24%)		28 (34%)	26 (22%)	
PQ-time (ms)		157±30	163±26	ns	155±27	168±25	ns
P-wave duration (ms)		128±21	125±15	ns	122±17	128±14	ns