Electrophysiology

PREVALENCE OF DISEASE-ASSOCIATED CARDIOMYOPATHY GENE VARIANTS IN ETHNIC MINORITIES WITH ATRIAL FIBRILLATION

Moderated Poster Contributions
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Background: African-American (AA) and Hispanic-LatinX (HL) individuals with atrial fibrillation (AF) experience lower prevalence yet poorer clinical outcomes compared to Caucasians. While pathogenic/likely pathogenic (P/LP) arrhythmia and cardiomyopathy (CM) gene variants have been identified in 10% of Caucasians with early-onset AF and are associated with increased mortality, the prevalence of P/LP CM gene variants in ethnic minorities with AF remains unknown.

Methods: We performed whole exome sequencing in 305 predominantly AA/HL individuals with AF at University of Illinois Health and Jesse Brown VA Medical Center. We examined 22 candidate genes strongly associated with CM and selected variants with appropriate read depths (≥ x20) with exclusion of multiallelic calls and genotype quality scores ≥20. Pathogenicity was determined by applying guideline-based criteria from the American College of Medical Genetics.

Results: Among 305 patients (mean age 60 ± 14 years, 50% male, 65% AA, 34% HL), 12/305 (3.9%) carried P/LP variants in CM genes (Figure 1). Compared to patients without P/LP variants, those with P/LP variants had lower rates of hypertension (58% vs 85%, p=0.012) and higher rates of congestive heart failure (75% vs 37%, p=0.008).

Conclusion: Disease-associated CM gene variants were found in 3.9% of AA/HL individuals with AF. These findings may provide valuable insight into the role of genetics in explaining differential AF prevalence and outcomes across race-ethnicity.

a)

Gene	Race/ Ethnicity	Chr:Pos	Ref/Alt	Variant (DNA)	Variant (Protein)	Mutation Type	Inheritance	ACMG Classification
ACTC1	Hispanic	15:34793398	C/T	c.301G>A	p.Glu101Lys	Missense	Dominant	P
CSRP3	Black	11:19186265	C/T	c.365G>A	p.Arg122Gln	Missense	Dominant	LP
CSRP3	Black	11:19186265	C/T	c.365G>A	p.Arg122Gln	Missense	Dominant	LP
DES	Black	2:219420943	T/C	c.1013T>C	p.Leu338Pro	Missense	Dominant	LP
LMNA	Black	1:156136231	G/-	c.1175delG	p.Ser392Thrfs*88	Frameshift	Dominant	LP
MYBPC3	Hispanic	11:47339785	G/A	c.1933C>T	p.Pro645Ser	Missense	Dominant	LP
MYBPC3	Black	11:47332932	G/T	c.3372C>A	p.Cys1124Ter	Stop Gain	Dominant	P
TTN	Black	2:178565416	G/A	c.80716C>T	p.Arg26906Ter	Stop Gain	Dominant	P
TTN	Black	2:178605696	C/A	c.53599G>T	p.Glu17867Ter	Stop Gain	Dominant	P
TTN	Hispanic	2:178672653	C/A	c.34837G>T	p.Glu11613Ter	Stop Gain	Dominant	LP
TTN	Hispanic	2:178776533	G/T	c.5331C>A	p.Cys1777Ter	Stop Gain	Dominant	LP
TTN	Black	2:178769894	G/A	c.8687C>T	p.Thr2896Ile	Missense	Dominant	LP

b)

	P/LP Variant Present n = 12		P/LP Variant Absent n=293		P value
Age (years; mean, SD)	54.8	13.3	60.4	13.9	0.188
BMI (kg/m^2; mean, SD)	33.2	11.6	33.4	9.4	0.927
Male sex	50.0%	6	50.2%	147	0.991
Ethnicity					0.999
White	0.0%	0	0.3%	1	
Black	66.7%	8	65.2%	191	
Hispanic	33.3%	4	34.1%	100	
Other	0.0%	0	0.3%	1	
Diabetes	25.0%	3	39.0%	114	0.327
Hypertension	58.3%	7	85.3%	249	0.012
Sleep apnea	8.3%	1	17.6%	51	0.403
Coronary artery disease	8.3%	1	23.6%	69	0.217
COPD/Asthma	25.0%	3	19.3%	56	0.626
Family history of AF	16.7%	2	11.0%	31	0.542
Tobacco use	25.0%	3	29.4%	85	0.742
Alcohol use	25.0%	3	10.7%	31	0.126
Congestive heart failure	75.0%	9	36.9%	107	0.008
Prior stroke/TIA	41.7%	5	20.3%	59	0.077
Prior myocardial infarction	8.3%	1	11.4%	33	0.744

Figure 1. a) P/LP variants in CM genes; **b)** baseline characteristics of ethnic minority cohort. All demographics are reported as percentage, number of subjects unless otherwise specified. (SD = standard deviation, BMI = body mass index, COPD = chronic obstructive pulmonary disease, TIA = transient ischemic attack)