Supplementary Online Content

Chalazan B, Mol D, Darbar FA, et al. Association of rare genetic variants and early-onset atrial fibrillation in ethnic minority individuals. *JAMA Cardiol*. Published online May 5, 2021. doi:10.1001/jamacardio.2021.0994

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Baseline clinical characteristics of African American, European American and Hispanic/Latinx probands with early-onset atrial fibrillation (EOAF).

Category	European American (n=132)	African American (n=147)	Hispanic/Latinx (n=77)	*P*-value
Gender (male)	100 (75.8%)	82 (55.8%)	48 (62.3%)	.002
Age of onset	58.0 (52.0-62.0)	55.0 (46.0-59.0)	51.5 (44.0-59.0)	<.0001
Paroxysmal AF	105 (79.6%)	118 (80.3%)	54 (70.1%)	.18
Persistent AF	19 (14.4%)	21 (14.3%)	15 (19.5%)	.54
Permanent AF	8 (6.1%)	8 (5.4%)	8 (10.4%)	.35
Family history	43 (32.6%)	13 (8.8%)	11 (14.3%)	<.0001
Body mass index (kg/m^2)	31.5 (27.8-37.8)	33.3 (28.4-41.0)	30.1 (26.4-36.0)	.01
Obstructive sleep apnea	9 (6.8%)	14 (9.5%)	7 (9.1%)	.70
Hyperthyroidism	1 (0.8%)	1 (0.7%)	1 (1.3%)	.64
Coronary artery disease	16 (12.1%)	16 (10.9%)	12 (15.6%)	.59
Valve heart disease	2 (1.5%)	7 (4.8%)	12 (15.6%)	<.0001
Congestive heart failure	22 (16.7%)	45 (30.6%)	13 (16.9%)	.009
Hypertension	76 (57.6%)	87 (59.2%)	23 (29.9%)	<.0001
Type II diabetes	24 (18.2%)	42 (28.6%)	12 (15.6%)	.04
Stroke	7 (5.3%)	9 (6.1%)	6 (7.8%)	.77
Vascular disease	3 (2.3%)	5 (3.4%)	3 (3.9%)	.79

AA, African American; H/L, Hispanic/Latinx; $CHADS_2$-VASC, Congestive Heart Failure, Hypertension, Age, Diabetes, Stroke, Vascular Disease and Sex.

eTable 2. In-silico scores for pathogenic or likely pathogenic variants in African American and Hispanic/Latinx probands with EOAF.

STUDY ID	Ethnicity	Gene	GERP++ RS Score	SIFT Score	Polyphen2 HDIV Score	Polyphen2 HVAR Score	PROVEAN Score	MutationTasterScore	CADD Score
UIC-	H/L	*TTN*	5.81	-	-	-	-	1.00	69.00
UIC-	AA	*PITX2*	5.37	0.00	0.99	0.98	-6.59	1.00	34.00
UIC-	H/L	*TTN*	4.54	-	-	-	-	1.00	36.00
UIC-	H/L	*CACNA1C*	-	-	-	-	-	-	23.90
UIC-	AA	*TTN*	6.07	-	-	-	-	1.00	63.00
UIC-	AA	*SCN5A*	3.29	-	-	-	-	1.00	37.00
UIC-	H/L	*TTN*	-	-	-	-	-	1.00	23.60
UIC-	AA	*TTN*	4.54	-	-	-	-	1.00	36.00
UIC-	AA	*TTN*	5.56	-	-	-	-	1.00	71.00
UIC-	AA	*PITX2*	5.37	0.00	1.00	0.98	-2.83	1.00	33.00
UIC-	AA	*KCNQ1*	6.10	0.00	1.00	1.00	-5.87	1.00	23.30
UIC-	AA	*PITX2*	4.63	0.00	1.00	0.98	-4.22	1.00	27.20
VA-	AA	*TTN*	5.55	-	-	-	-	1.00	73.00
VA-	AA	*SCN5A*	4.30	0.00	1.00	0.99	-5.85	1.00	31.00
VA-	AA	*TTN*	-	-	-	-	-	1.00	23.60

AA, African American; H/L, Hispanic/Latinx; GERP, Genomic Evolutionary Rate Profiling (Rejected Substitution); SIFT, Sorting Intolerant From Tolerant; PolyPhen2, Polymorphism Phenotyping (Version 2); PROVEAN, Protein Variation Effect Analyzer; CADD, Combined Annotation Dependent Depletion.

eTable 3. In-Silico scores for co-segregating variants of unknown significance in African American and Hispanic/Latinx probands with EOAF.

Ethnicity	Gene	GERP++ RS Score	SIFT Score	Polyphen2 HDIV Score	Polyphen2 HVAR Score	PROVEAN Score	MutationTaster Score	CADD Score
AA	*KCNE5*	4.80	0.00	1.00	1.00	-4.58	0.99	29.10
AA	*SCN10*	3.30	0.00	1.00	1.00	-7.75	1.00	29.10
H/L	*TTN*	5.93	0.00	1.00	1.00	-6.88	1.00	24.10
H/L	*NPPA*	5.84	0.00	1.00	0.97	-6.40	0.99	26.20
AA	*MYH6*	4.63	0.00	1.00	1.00	-4.96	1.00	32.00
H/L	*MYH6*	4.63	0.00	1.00	1.00	-4.32	1.00	28.40

AA, African American; H/L, Hispanic/Latinx; GERP, Genomic Evolutionary Rate Profiling (Rejected Substitution); SIFT, Sorting Intolerant From Tolerant; PolyPhen2, Polymorphism Phenotyping (Version 2); PROVEAN, Protein Variation Effect Analyzer; CADD, Combined Annotation Dependent Depletion.

