ORIGINAL ARTICLE

Sleep-disordered breathing and electrocardiographic QRS-T angle: The MESA study

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Abstract

Introduction: Sleep-disordered breathing (SDB) has been linked to sudden cardiac death (SCD) but the mechanism is unclear. Abnormal QRS-T angle, a novel electrocardiographic (ECG) marker of ventricular repolarization, has been linked to adverse cardiovascular outcomes including SCD. We hypothesized that individuals with SDB have more pronounced abnormality in QRS-T angle.

Methods: We performed a cross-sectional analysis from the Multi-Ethnic Study of Atherosclerosis (MESA) Exam Sleep ancillary study. We calculated the odds ratio (OR) of abnormal frontal and spatial QRS-T angle (defined as >sex-specific 95th percentile thresholds) related to the apnea-hypopnea index (AHI) using logistic regression, adjusting for demographics, body habitus, cardiovascular risks, and prevalent cardiovascular disease. Linear associations between AHI and frontal and spatial QRS-T angle, separately, were also examined using multiple regression models.

Results: A total of 1,804 participants (mean age 67.9 ($\pm$ 9.0) years, 55.3% women and 64.1% non-whites) were included in the study. Sleep-disordered breathing was common among participants (median AHI 8.6 events/hr IQR [3.2–19.5/hr]). Higher AHI was associated with the odds of abnormal frontal ($\geq 81^\circ$ in men and $\geq 79^\circ$ in women) and spatial QRS-T angle ($\geq 129.7^\circ$ in men and $\geq 115.9^\circ$ in women; OR [95%CI]: 1.25 [1.02–1.51], $p = 0.03$; 1.23 [1.01–1.50], $p = 0.04$ respectively per 1 SD [16.8 events/hr] increase in AHI). Similarly, linear associations were observed (frontal QRS-T angle: beta coefficient: 2.30° [0.92, 3.66], $p = 0.001$; spatial QRS-T angle: beta coefficient: 2.16° [0.67, 3.64], $p = 0.005$).

Conclusion: In a racially/ethnically diverse community cohort, severity of SDB is associated with abnormal ventricular repolarization as measured by QRS-T angle.

KEYWORDS

arrhythmia, electrocardiography, sleep apnea, sleep-disordered breathing

1 | INTRODUCTION

Sleep-disordered breathing (SDB) is a common condition affecting at least 10%–20% of the general US population. It is increasingly

recognized as a risk factor for cardiovascular (CV) morbidity such as hypertension, stroke, and heart failure (HF) as well as overall mortality (Gottlieb et al., 2010; Peppard, Young, Palta, & Skatrud, 2000; Redline et al., 2010; Young et al., 2008). Sleep-disordered

breathing has also been linked to an increased risk of sudden cardiac death (SCD) (Gami et al., 2013). In addition, in patients with HF, SDB has been shown to increase the risk of potentially malignant arrhythmias based on a higher risk of appropriate therapy by implantable cardioverter defibrillator (Kwon et al., 2017). Electrocardiographic (ECG) markers of either depolarization or repolarization have been implicated as predictors of SCD. Among them, QRS-T angle is a less studied but a promising vectorcardiographic ECG parameter that takes into account both ventricular depolarization and repolarization. Thus, QRS-T angle is an integrated marker for heterogeneity of action potential morphology related to ventricular structural abnormality (depolarization) or pathophysiological changes in ionic channels (repolarization). Both frontal and spatial QRS-T angles have been shown to predict CV mortality as well as SCD in general populations (Aro et al., 2012; Kardys et al., 2003). However, QRS-T angle has not been studied in relation to SDB in a community-based population. In this study, we tested the hypothesis that QRS-T angles are more abnormal in association with increasing severity of SDB.

2 | METHODS

2.1 | Participants

The Multi-Ethnic Study of Atherosclerosis (MESA) is an ethnically diverse community cohort of men and women aged 45–84 years without known cardiovascular disease (CVD; history of coronary heart disease, HF, or stroke) at enrollment in 2000–2002. Participants were recruited from six U.S. communities (Forsyth County, NC; Northern Manhattan and the Bronx, NY; Baltimore County, MD; St. Paul, MN; Chicago, IL; and Los Angeles County, CA) and self-identified as White, Chinese, African American or Hispanic. Participants underwent up to five follow-up exams, with sleep data collected in conjunction with Exam 5 (2010–2012). All participants with available polysomnography (PSG) and 12-lead surface ECG administered at MESA Exam 5 were included. Participants with any of the following were excluded from this analysis: those with pacemaker, complete heart block or any intraventricular conduction delay (QRS > 120 ms) noted on 12-lead ECG at visit 5, and those on class I or III antiarrhythmic agents. Those using continuous positive airway pressure, oral appliances, or oxygen therapy were not eligible for the MESA Sleep study ($n = 113$). The research protocols were approved by the Institutional Review Boards at each participating institution, and all participants gave written informed consent.

2.2 | Sleep study data

An overnight in-home PSG was performed as part of the MESA Sleep Study (2010–2013), employing standard channels recommended by American Academy of Sleep Medicine (AASM). The

sleep records were electronically transmitted to a centralized reading center (Brigham and Women's Hospital, Harvard Medical School, Boston, MA) for manual scoring by trained technicians, blinded to all clinical data. Apnea was scored in the presence of more than 90% of airflow reduction by a thermocouple signal in reference to the pre-event baseline for longer than 10 s and was further specified as obstructive or central on the basis of the presence of respiratory effort recorded using inductance plethysmography. Hypopneas were scored in the presence of more than 30% of airflow amplitude reduction by nasal pressure flow signal in reference to the pre-event baseline for longer than 10 s; only hypopneas with >4% desaturation were included in the AHI for this study. The apnea-hypopnea index (AHI) was defined as the number of total apneas plus hypopneas per hour (hr) of sleep. Inter- and intrascorer intraclass correlation coefficients for the AHI ranged from 0.95 to 0.99. Nocturnal hypoxemia was evaluated as time spent with oxygen saturation (SpO_2) less than 90% ($\%\text{SpO}_2 < 90$).

2.3 | Electrocardiography

Standard 12-lead ECGs (GE MAC 1200 model; GE, Milwaukee, WI) were digitally recorded at a 10 mm/mV calibration and speed of 25 mm/s in all participants using standardized procedures on visit 5. ECG reading was performed centrally at the Epidemiological Cardiology Research Center (EPICARE), Wake Forest School of Medicine, Winston-Salem, NC. All ECGs were inspected visually for inadequate quality. ECG measurements, QRS and T axis were automatically obtained by software (GE Marquette 12-SL program 2001 version [GE Marquette, Milwaukee, WI]). Frontal QRS-T angle was defined by the absolute value of the difference between the frontal plane QRS axis and T axis. If a difference is greater than 180° , then the value was subtracted from 360° . The spatial QRS/T angle ($\text{QRS}/\text{T}_{\text{spatial}}$) is the angle between the mean QRS vector and T vector from three-dimensional plane. The mean spatial QRS and T vectors were calculated from quasi-orthogonal X, Y, and Z leads reconstructed from the standard ECG leads by a matrix transformation method (Edenbrandt & Pahlm, 1988; Zhang, Prineas, Case, Soliman, & Rautaharju, 2007). Abnormal QRS-T angle was defined by $\geq$ sex-specific 95th percentile, similar to previous studies (Walsh et al., 2013; Zhang et al., 2007).

2.4 | Covariates

Demographic characteristics (age, sex, race/ethnicity), smoking status, medication use, body habitus (body mass index; BMI), and blood pressure were based on information from the exam 5 visit. Blood samples were collected and assayed for fasting glucose level, low density lipoprotein (LDL), and high density lipoprotein (HDL) cholesterol. Diabetes (American Diabetes Association Fasting Criteria 2003) and hypertension (Joint National Committee VI 1997), as well as prevalent coronary heart disease and HF based on surveillance were also included as covariates.

2.5 | Statistical analysis

Main exposure SDB variables were continuously measured AHI and %SpO₂90. Baseline characteristics of participants were summarized by severity of SDB based on AHI quartiles. We calculated the odds ratio (OR) of dependent variables, abnormal frontal and spatial QRS-T angle, in association with exposure to SDB variables of interest using logistic regression models: (a) Model 1 adjusted for age, race, sex, and field center; (b) Model 2 additionally adjusted for body mass index, smoking status, systolic blood pressure, antihypertensive medications, diabetes, HDL cholesterol, LDL cholesterol, lipid-lowering medications; and (c) Model 3 additionally adjusted for prevalent coronary heart disease and prevalent HF. Linear associations between continuous frontal and spatial QRS-T angle, separately, with continuously measured AHI values were also examined. For linear regression, we calculated regression coefficient (β) per 1 SD of predictor variable of interest. Linearity assumptions were checked in all sleep exposures with the frontal and spatial QRS-T angles and were found to mostly satisfy them in most instances. Effect modification by age, sex, and race/ethnicity was tested by including each cross product term in the model. In case of significant interaction ($p < 0.1$), we performed stratified analyses as appropriate using the same statistical models. All conclusions were based on model 3 unless specified otherwise. Finally, a final sensitivity analysis was performed after excluding central apneas from the derived AHI. All analyses were performed using SAS version 9.3 (SAS institute, Cary, NC). A p value < 0.05 was considered statistically significant.

3 | RESULTS

A total of 1,804 participants were included in our study. Mean age (SD) of the cohort was 67.9 (9.0) years, 55.3% were women, and 64.1% of the cohort were non-whites. SDB was common among participants (median AHI: 8.6 events/hr IQR [3.2–19.5/hr]). Baseline characteristics of the study participants overall and by AHI quartiles are shown in Table 1. Participants with higher AHI tended to be men, more obese, and had a higher prevalence of CVD risk factors including hypertension, diabetes, and lower HDL-C.

Mean (SD) QRS-T angles were 28.3° (27.5) and 65.2° (30.3) for frontal and spatial indices, respectively (Table 2). Based on the sex-specific 95th percentile cut off, abnormal frontal QRS-T angle was defined by $\geq 81^\circ$ in men and $\geq 79^\circ$ in women and spatial QRS-T angle was defined by $\geq 129.7^\circ$ in men and $\geq 115.9^\circ$ in women.

In both unadjusted and adjusted models, higher AHI was associated with higher odds of both abnormal frontal and spatial QRS-T angle (OR [95%CI]: 1.25 [1.02–1.51], $p = 0.03$; 1.23 [1.01–1.50], $p = 0.04$ respectively, per 1 SD higher AHI [16.8 events/hr]; Table 3). Similarly, linear associations were observed (frontal QRS-T angle: beta coefficient [degrees per 1 SD events/hr]: 2.30° [0.92, 3.66], $p = 0.001$; spatial QRS-T angle: beta coefficient: 2.16° [0.67, 3.64], $p = 0.005$; Table 4, Figure 1). An interaction between AHI and sex was found in analysis in which continuous spatial QRS-T angle was

designated as outcome. Stratified results showed that the association was present in men but not in women for continuous spatial QRS-T angle (Table 5). Similar results were found between %SpO₂90 and QRS-T angle. With each SD higher %SpO₂90, there was higher odds of abnormal frontal and spatial QRS-T angle (OR [95%CI]: 1.16 [1.01–1.34], $p = 0.04$; 1.22 [1.04–1.41], $p = 0.01$ respectively; Supporting Information Table S1). Linear associations were observed (frontal QRS-T angle: beta coefficient: 3.05° [1.76, 4.34], $p < 0.001$; spatial QRS-T angle: beta coefficient: 2.29° [0.89, 3.70], $p = 0.001$; Supporting Information Table S2). Similar to AHI, an interaction was present between %SpO₂90 and sex when considering spatial QRS-T angle as an outcome (Supporting Information Table S3). Significant association was found only in men but not in women. No interactions were found with age or race/ethnicity. Sensitivity analyses limiting respiratory events to obstructive AHI yielded similar results for the linear model but attenuated results for the logistic model (Supporting Information Tables S4–S6).

4 | DISCUSSION

In this study we found that severity of SDB as determined by either AHI or degree of nocturnal hypoxemia (%SpO₂90) was associated with higher daytime frontal and spatial QRS-T angle.

Sleep-disordered breathing, of which obstructive sleep apnea is the most common type in the community, is a highly prevalent chronic disorder associated with a wide range of health impairments. In particular, SDB has been linked to CVD risks and outcomes including hypertension, stroke, atrial fibrillation, and mortality (Gottlieb et al., 2010; Kwon et al., 2015; Marin, Carrizo, Vicente, & Agusti, 2005; Marshall, Wong, Cullen, Knuiman, & Grunstein, 2014; Peppard et al., 2000; Redline et al., 2004). Sleep-disordered breathing has also been suggested as an independent risk factor for SCD in the general population (Gami, Howard, Olson, & Somers, 2005; Gami et al., 2013). Furthermore, high risk patients such as those with HF, are at increased risk of appropriate implantable cardioverter-defibrillator (ICD) therapy, a surrogate marker for malignant ventricular arrhythmia (Kwon et al., 2017). Consequently, there has been increasing interest in searching for electrocardiographic (ECG) markers that identify people at risk for future development of sustained ventricular arrhythmia or SCD in the context of SDB.

QRS-T angle is a unique ECG-based measure of ventricular repolarization that takes into account ventricular depolarization. Spatial QRS-T angle is the angle between QRS and T-wave vectors in three-dimensional space, whereas frontal QRS-T angle is the projection of spatial QRS-T angle onto the frontal plane. A number of observational studies have demonstrated that both frontal and spatial QRS-T angle are predictive of incident CVD and mortality (Aro et al., 2012; Borleffs et al., 2009; Pavri et al., 2008; Walsh et al., 2013; Whang et al., 2012; Zhang et al., 2007). One of the earliest investigations from a large population-based cohort in Rotterdam showed that abnormal spatial QRS-T angle ($>130^\circ$) was predictive of future fatal cardiac events including CV and sudden death, and total mortality.

TABLE 1 Baseline characteristics of the full cohort and by apnea–hypopnea index (AHI) quartile, Multi-Ethnic Study of Atherosclerosis Sleep Study, 2010–2013

	Full cohort (n = 1,804)	AHI quartile (events/hr)				p-value*
		0–3.19 (n = 451)	3.20–8.63 (n = 451)	8.64–19.46 (n = 451)	19.47–102.91 (n = 451)	
Age, years	67.9 ± 9.0	66.3 ± 8.8	68.2 ± 9.0	68.6 ± 9.0	68.5 ± 8.8	0.0002
Sex						
Female	997 (55.3)	307 (68.1)	284 (63.0)	236 (52.3)	170 (37.7)	<0.0001
Male	807 (44.7)	144 (31.9)	167 (37.0)	215 (47.7)	281 (62.3)	
Race						
White	648 (35.9)	184 (40.8)	172 (38.1)	156 (34.6)	136 (30.2)	0.004
Chinese	226 (12.5)	50 (11.1)	58 (12.9)	47 (10.4)	71 (15.7)	
African American	489 (27.1)	126 (27.9)	124 (27.5)	122 (27.1)	117 (25.9)	
Hispanic	441 (24.5)	91 (20.2)	97 (21.5)	126 (27.9)	127 (28.2)	
Body mass index, kg/m ²	28.6 ± 5.6	26.3 ± 4.9	28.1 ± 5.1	29.4 ± 5.2	30.8 ± 6.1	<0.0001
Diabetes	341 (18.9)	57 (12.6)	71 (15.7)	98 (21.7)	115 (25.5)	<0.0001
HDL cholesterol, mg/dl	55.8 ± 16.3	61.1 ± 18.5	56.6 ± 15.0	54.2 ± 16.1	51.3 ± 13.6	<0.0001
LDL cholesterol, mg/dl	107.2 ± 32.0	109.3 ± 32.3	107.8 ± 30.7	107.7 ± 32.2	103.9 ± 32.7	0.07
Lipid-lowering medications	667 (37)	144 (31.9)	165 (36.6)	172 (38.1)	186 (41.2)	0.03
Smoking status						
Never	860 (47.7)	236 (52.3)	220 (48.8)	208 (46.1)	196 (43.4)	0.05
Former	819 (45.4)	186 (41.3)	192 (42.6)	212 (47.0)	229 (50.8)	
Current	125 (6.9)	29 (6.4)	39 (8.6)	31 (6.9)	26 (5.8)	
Antihypertensive medications	933 (51.7)	198 (43.9)	235 (52.1)	240 (53.2)	260 (57.7)	0.001
Systolic blood pressure, mmHg	122.5 ± 20.4	120.4 ± 21.9	121.4 ± 20.1	124.2 ± 19.9	124.1 ± 19.3	0.01
Prevalent coronary heart disease	32 (1.8)	7 (1.6)	7 (1.6)	11 (2.4)	7 (1.6)	0.68
Prevalent heart failure	19 (1.1)	3 (0.7)	4 (0.9)	3 (0.7)	9 (2.0)	0.23

Notes. Results are shown as n (%) for categorical variables and mean ± standard deviation for continuous variables.

HDL: high-density lipoprotein; LDL: low-density lipoprotein.

*p-value for difference between the AHI quartiles.

Intriguingly, spatial QRS-T angle was found to be by far the strongest marker when compared to other classical CV risk factors and traditional ECG risk indicators such as left ventricular hypertrophy, left bundle branch block, T-wave inversion and QTc interval (Kardys et al., 2003). In National Health and Nutrition Examination Survey III participants without clinically evident CVD at the start of the study, abnormal spatial QRS-T angle (136° for men 121° for women) was associated with a doubling of the risk for CV death including suspected SCD (Whang et al., 2012). Frontal QRS-T angle was also shown to be predictive of CV outcomes. In a large study involving the Finnish general population, high frontal QRS-T angle (>100°) conferred a threefold increased risk of SCD over a 30-year follow up period (Aro et al., 2012). Notably, in a previous analysis in the MESA cohort, adults free of CVD at baseline but with extreme frontal QRS-T angle (95th percentile) at baseline (MESA visit 1) had a higher incidence of composite outcomes of CVD (Walsh et al., 2013). In addition to general population studies, there have been numerous studies linking

QRS-T angle to adverse CVD outcomes in patients with known CVD. In patients with either ischemic or nonischemic cardiomyopathy with ICD, baseline high QRS-T angle was shown to be a strong predictor of appropriate ICD therapy, a surrogate for potentially malignant ventricular arrhythmias (Borleffs et al., 2009; Pavri et al., 2008).

The aim of the present analysis was to examine QRS-T angle in relation to SDB. Severity of SDB as measured by either AHI or %SpO₂90 was associated with higher odds of having abnormally high QRS-T angle after accounting for multiple factors that may have an influence on the relationship. The consistent results across predictors (AHI and %SpO₂90) as well as across outcomes (frontal and spatial QRS-T angle) lend credence to our findings. One SD increased in either the AHI or %SpO₂90 was each associated with an approximately 20% increased odds of an abnormal QRS-T angle, measured by either the frontal or spatial QRS-T angle. Similar strength of associations between frontal and spatial QRS-T angles may imply that frontal QRS-T angle, which is more readily available

TABLE 2 Frontal and spatial QRS-T angle distribution overall, by race, and by sex, Multi-Ethnic Study of Atherosclerosis Sleep Study, 2010–2013

	Frontal QRS-T Angle (°)			Spatial QRS-T Angle (°)		
	Mean	SD	Median	Mean	SD	Median
Overall	28.3	27.5	20	65.2	30.3	60.5
Race						
White	27.7	25.9	21	64.7	27.9	60.1
Chinese	22.1	23.8	13	60.0	29.4	57.7
Black	31.8	32.2	22	69.4	33.2	64.1
Hispanic	28.5	25.5	21	63.9	30.4	59.8
Sex						
Female	28.3	26.9	21	60.1	28.9	55.9
Male	28.3	28.4	20	71.5	30.9	67.7

compared to spatial QRS-T angle, could be conveniently referenced in terms of possible risk estimation for patients with SDB. The abnormal cutoff value (95th percentile of the QRS-T angle) used in our study was patterned after comparable large-scale studies. It is important to note that different cutoff values were used for each sex given the reported gender difference in the distribution of QRS-T angle (Schreurs et al., 2010). Modeling QRS-T angle as a continuous variable yielded similar results although interaction with sex was observed for spatial QRS-T angle. The

TABLE 3 Odds ratios (OR) and 95% confidence interval (CI) of abnormal frontal and spatial QRS-T angles estimated per 1-standard deviation (SD)^a difference in apnea-hypopnea index (AHI), Multi-Ethnic Study of Atherosclerosis Sleep Study, 2010–2013

	Frontal QRS-T Angle	Spatial QRS-T Angle
<i>n</i>	1,804	1,804
Abnormal QRS-T angle, <i>n</i>	93	91
Model 1 OR (95% CI)	1.32 (1.09–1.57)	1.29 (1.07–1.54)
<i>p</i> -Value	0.003	0.01
Model 2 OR (95% CI)	1.24 (1.02–1.50)	1.23 (1.01–1.50)
<i>p</i> -Value	0.03	0.04
Model 3 OR (95% CI)	1.25 (1.02–1.51)	1.23 (1.01–1.50)
<i>p</i> -Value	0.03	0.04

Notes. Model 1: Logistic regression adjusted for age, race/ethnicity, and center.

Model 2: Additional adjustment for body mass index, diabetes, smoking status, antihypertensive medications, systolic blood pressure, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and lipid-lower medications.

Model 3: Additional adjustment for prevalent coronary heart disease and prevalent heart failure.

Abnormal frontal QRST angle is defined as a sex-specific cutpoint at the 95th percentile, which was $\geq 81^\circ$ in males and $\geq 79^\circ$ in females for this sample.

Abnormal spatial QRST angle is defined as a sex-specific cutpoint at the 95th percentile, which was $\geq 129.7^\circ$ in males and $\geq 115.9^\circ$ in females for this sample.

^aAHI 1-SD = 16.8 events/hr.

linear association between measures of SDB and spatial QRS-T angle was observed in men but not in women. Given the significant association found between measures of SDB and abnormal spatial QRS-T angle (defined by 95th percentile) in women, this finding suggests that the association is confined to that of severity of SDB with extreme spatial QRS-T angle. The validity and biological underpinning of this finding is uncertain. Gender-specific difference of the prognostic implication of each QRS-T angle in CV outcomes is largely understudied area. In addition, sex-related differences in CV outcomes in SDB remains controversial mainly due to lack of studies carrying adequate power for meaningful sex-based analysis (Shah, Yaggi, & Redline, 2013). SDB has been reported to associate more strongly with incident coronary heart disease and all cause and CVD-related mortality in men compared to women (Gottlieb et al., 2010; Punjabi et al., 2009). On the other hand,

TABLE 4 Linear regression of frontal and spatial QRS-T angles estimated per 1-standard deviation (SD)^a difference in apnea-hypopnea index (AHI), Multi-Ethnic Study of Atherosclerosis Sleep Study, 2010–2013

	Frontal QRS-T Angle	Spatial QRS-T Angle
Model 1 β (95% CI)	2.78° (1.50, 4.06)	2.38° (0.98, 3.77)
<i>p</i> -Value	<0.0001	0.001
Model 2 β (95% CI)	2.26° (0.89, 3.64)	2.18° (0.69, 3.67)
<i>p</i> -Value	0.001	0.004
Model 3 β (95% CI)	2.30° (0.93, 3.66)	2.16° (0.67, 3.64)
<i>p</i> -Value	0.001	0.005

Notes. Model 1: Linear regression adjusted for age, race/ethnicity, and center.

Model 2: Additional adjustment for body mass index, diabetes, smoking status, antihypertensive medications, systolic blood pressure, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and lipid-lower medications.

Model 3: Additional adjustment for prevalent coronary heart disease and prevalent heart failure.

β : absolute difference.

^aAHI 1-SD = 16.8 events/hr.

FIGURE 1 Association between apnea-hypopnea index (AHI) and QRS-T angle. (a) Frontal QRS-T angle. (b) Spatial QRS-T angle

prior analyses in MESA have not shown any differences in the associations between left ventricular hypertrophy and SDB in men and women or in glucose impairment (Bakker et al., 2015; Javaheri et al., 2016). Additional well-powered studies, including men and women across the age range, are needed to better understand the sex-related differences in susceptibility to electrophysiological disturbances occurring with SDB. We did not find evidence of effect modification by age or race/ethnicity. However, the power for these analyses was limited. We speculate that attenuation of the results for AHI when central sleep apnea events were excluded is likely related to statistical power as the results remained significant when the QRS-T angle was modeled continuously. In addition, meaningful projection on the role of central sleep apnea in this study is challenged by rarity of the events and our inability to differentiate hypopneas into obstructive versus central. The results of this study are consistent with two recently conducted small-sized sleep clinic-based studies. Gungor et al. (2016) showed higher frontal QRS-T angle in patients with SDB compared to controls. Kicinski et al. (2017) showed a similar finding with spatial QRS-T angle. Likewise, linear associations between AHI and QRS-T angle were shown in both studies. However, these studies were clinic based and are inherently subject to referral bias.

TABLE 5 Linear regression of spatial QRS-T angles estimated per 1-standard deviation (SD)^a difference in apnea-hypopnea index (AHI), by sex, Multi-Ethnic Study of Atherosclerosis Sleep Study, 2010–2013

	Females	Males
N	997	807
Model 1 β (95% CI)	0.40° (−1.77, 2.57)	3.68° (1.82, 5.53)
p-Value	0.72	0.0001
Model 2 β (95% CI)	0.58° (−1.78, 2.94)	2.88° (0.90, 4.86)
p-Value	0.63	0.005
Model 3 β (95% CI)	0.54° (−1.81, 2.90)	2.87° (0.88, 4.85)
p-Value	0.65	0.005

Notes. Model 1: Linear regression adjusted for age, race/ethnicity, and center.

Model 2: Additional adjustment for body mass index, diabetes, smoking status, antihypertensive medications, systolic blood pressure, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and lipid-lower medications.

Model 3: Additional adjustment for prevalent coronary heart disease and prevalent heart failure.

β : absolute difference.

The interaction term between AHI and sex was significant (p -value = 0.02).

^aAHI 1-SD = 16.8 events/hr.

Obstructive respiratory events lead to intermittent hypoxemia, increase in ventricular afterload and disruption of sympatho-vagal balance (Dempsey, Veasey, Morgan, & O'Donnell, 2010). These episodes can increase nocturnal ventricular arrhythmogenicity possibly through ion channel dysfunction (Jiang et al., 2016; Verrier & Josephson, 2009). Such immediate effect of SDB is illustrated by dynamic change in ECG markers of ventricular repolarization in sleep in patients with SDB and its attenuation with continuous positive airway pressure (Kilicaslan et al., 2012; Roche et al., 2003, 2005). Sustained long-term exposure to these events, particularly in the setting of cardiac structural remodeling, may contribute to more permanent instability in myocardial action potential increasing the risk of SCD. Based on our findings, we reason that daytime QRS-T angle may represent a novel signature of such vulnerability in patients with SDB. Future investigations should address whether measurement of abnormal QRS-T angle enhances risk prediction of CV outcomes including SCD in patients with SDB and whether treatment of SDB and the attenuation of the CV risk can be reflected via this ECG marker.

Strengths of this study include objective measurements of SDB and comprehensive examination of resting 12-lead daytime ECGs involving a large, ethnically diverse, community-based cohort. However, the cross-sectional nature of the study prevents us from inferring a temporal association. Moreover, the possibility of residual confounding exists, despite adjusting for several potential confounders.

In conclusion, in a racially/ethnically diverse community cohort, severity of SDB, as measured by AHI or %SpO₂90, is associated with

abnormal ventricular repolarization as measured by either frontal or spatial QRS-T angle. Further research is needed to understand whether measuring QRS-T angle may be of benefit in identifying patients with SDB at risk for SCD.

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CONFLICT OF INTEREST

None declared.

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SUPPORTING INFORMATION

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