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The association of metabolic syndrome and QRS|T angle in US adults (NHANES III)

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Abstract

Background: Spatial QRS|T angle is a predictor of cardiovascular events. Those with metabolic syndrome have an increased risk of cardiovascular morbidity and mortality. This study investigated the association between metabolic syndrome and spatial QRS|T angle.

Methods: We obtained data from the National Health and Nutritional Examination Survey III on 6,249 adults. We calculated spatial QRS|T angle from the standard 12-lead electrocardiogram and classified it as abnormal, borderline, or normal. We identified metabolic syndrome if at least three of the following were present: abdominal obesity, elevated blood pressure, elevated triglycerides, decreased high-density lipoprotein (HDL), and impaired fasting glucose. We used weighted logistic regression to estimate the effect of metabolic syndrome and its components on QRS|T angle while stratifying by gender and adjusting for age, race, smoking status, heart rate, PR, QT, and QRS interval, and QRS amplitude.

Results: Among men and women, metabolic syndrome, the number of components present, elevated blood pressure, and impaired fasting glucose were positively associated with QRS|T angle. Among women, decreased HDL and abdominal obesity were also positively associated with QRS|T angle.

Conclusions: This study suggests that persons with metabolic syndrome may be at increased risk for ventricular arrhythmias. The use of spatial QRS|T angle to assess this cardiovascular risk is warranted.

KEYWORDS

cardiac arrhythmias, cardiovascular disease, electrocardiography, metabolic syndrome, surveys

1 | INTRODUCTION

QRS|T angle is a quantitative characterization of depolarization and repolarization abnormalities of the heart (Narayanan & Chugh, 2016; Oehler, Feldman, Henrikson, & Tereshchenko, 2014; Voulgari, Pagoni, Tesfaye, & Tentolouris, 2013). Spatial QRS|T angle can be derived from the results of an electrocardiogram (ECG) and used to identify those who have high risk of ventricular arrhythmias (Narayanan & Chugh, 2016; Oehler et al., 2014; Voulgari et al., 2013; Zhang et al., 2015). A meta-analysis of 22 studies conducted by Zhang et al. (2015) found that those with wide spatial QRS|T angle were 40% more likely to die of any cause and 71% more likely to die of cardiac causes than those with normal spatial QRS|T angle (RR = 1.40, 95% CI = 1.32–1.48;

RR = 1.71, 95% CI = 1.54–1.90, respectively). Wide spatial QRS|T angle was associated with all-cause and cardiac mortality in the general population and patients who had cardiovascular disease (Zhang et al., 2015); it is an established risk factor of cardiovascular morbidity and mortality (Narayanan & Chugh, 2016; Oehler et al., 2014; Voulgari et al., 2013; Whang et al., 2012; Zhang et al., 2015). Whang et al. (2012) studied the association between wide QRS|T angle and mortality (all-cause and cardiovascular) using national data obtained from the third National Health and Nutrition Examination Survey (NHANES). In this American population of adults 40 years and older, Whang et al. (2012) concluded that an abnormally wide QRS|T angle was associated with an increased hazard ratio of all-cause and cardiovascular mortality in women and men.

Metabolic syndrome (MetS) is a complex disease defined by the presence of at least three of five metabolic abnormalities (hypertension, abdominal obesity, impaired fasting glucose, elevated triglycerides, and decreased high-density lipoproteins) (Heart & Lung, and Blood Institute., 2002). Using data collected with the NHANES in years 2003–2012, Aguilar, Bhuket, Torres, Liu, and Wong (2015) estimated the prevalence of MetS to be around one-third of the US adult population (20 years and older). Among older adults, 60 years and older, the prevalence increases to 50% (Aguilar et al., 2015). Those who met criteria for MetS are at a higher risk of cardiovascular morbidity and mortality (Mccullough, 2011; Mottillo et al., 2010). The presence of MetS has been associated with several ECG markers of cardiovascular disease (e.g., QRS complex duration, QT interval, T-wave axis) in a population-based cohort (Elffers et al., 2017). Using data obtained from NHANES III, Faramawi, Sall, and Kareem (2008) determined the presence of MetS was associated with ECG markers of cardiovascular disease: T-wave axis deviation and QT interval. Spatial QRS|T angle has also been associated with the components of MetS: hypertension, obesity, and type-2 diabetes (Voulgari et al., 2013). The association between MetS and QRS|T angle deviation has never been explored in a population-based (representative) sample. Therefore, we sought to determine if MetS is a risk factor for spatial QRS|T angle in the American adults of the NHANES III.

2 | METHODS

2.1 | Study population

We used the NHANES III datasets to conduct our analyses. The NHANES III, a cross-sectional survey, was conducted from 1988 to 1994 by the National Center for Health Statistics (National Center for Health Statistics, 1994). The survey used a complex multistage probability sampling design to capture a representative sample of noninstitutionalized American citizens (NCHS, 1994). The National Center for Health Statistics institutional review board approved the protocol for NHANES III. The NHANES III researchers obtained written informed consent, interviewed, and examined the participants to collect information on their demographics, health, and behavior (NCHS, 1994). To account for the complex sampling design, a sampling weight was assigned to each participant (NCHS, 1994). The weights assigned for those who completed the examination were used in this analysis.

A total of 9,737 adults, 40 years and older, participated in both the interview and medical examination of NHANES III. We excluded those with a suspected history of myocardial infarction based on self-report or ECG results (n = 758), and those who self-reported congestive heart failure (n = 267). Of the remaining 8,712 adults, 7,542 (86.6%) had sufficient data to determine MetS status. Those who did not complete a 12-lead ECG (n = 839), who had a QRS interval ≥ 120 msec (n = 423), or did not have sufficient data to determine spatial QRS|T angle (n = 31) were excluded. The final sample included 6,249 participants.

2.2 | Measures

2.2.1 | Spatial QRS|T angle

We used standard 12-lead ECGs, conducted during the medical examination, to calculate spatial QRS|T angle. The ECGs were obtained for adults who were 40 years or older using the Marquette MAC 12 Medical Systems, Inc. (Milwaukee, Wisconsin) (NCHS, 1994, 1998). The 12-lead ECG recorded eight independent components simultaneously, sampling data at 250 samples/second/channel (NCHS, 1998). ECG data were analyzed using Minnesota and Novacode computer algorithms to detect ECG abnormalities and obtain durations and amplitudes of the ECG components (Blackburn, Keys, Simonson, Rautaharju, & Punsar, 1960; NCHS, 1998; Rautaharju et al., 1990).

We calculated spatial QRS|T angle from the QRS and T amplitudes of leads V2, V5, V6, and AVF using the formula provided by Rautaharju and colleagues (Rautaharju, Prineas, & Zhang, 2007; Schreurs et al., 2010). We converted the obtained spatial QRS|T angle to degrees and classified spatial QRS|T angle as abnormal, borderline, or normal based on the prior NHANES III study conducted by Whang et al. (2012). They used the sex-specific 75th and 95th percentiles of spatial QRST|T angle to classify spatial QRS|T angle (Whang et al., 2012). Among females, abnormal spatial QRS|T angle was defined as an angle > 120°, borderline as 90–120°, and normal as an angle < 90° (Whang et al., 2012). Among males, abnormal spatial QRS|T angle was defined as an angle > 135°, borderline as 107–135°, and normal as an angle <107° (Whang et al., 2012).

2.2.2 | Metabolic syndrome

We used the guidelines of the Adult Treatment Panel III to define MetS (NHLBI, 2002). MetS has five metabolic components: abdominal obesity, elevated blood pressure, elevated triglycerides, decreased high-density lipoprotein (HDL), and impaired fasting glucose (NHLBI, 2002). We considered the participants who had at least three of five of these components as individuals with MetS (NHLBI, 2002).

TABLE 1 Bivariate analysis of spatial QRS|T angle as classified by Whang et al. stratified by sex

	Men (*N* = 2,904)				Women (*n* = 3,345)			
	Spatial QRS|T				Spatial QRS|T			
	Abnormal (*N* = 186)	Borderline (*N* = 639)	Normal (*N* = 2,079)	*p*-Value	Abnormal (*N* = 186)	Borderline (*N* = 639)	Normal (*N* = 2,079)	*p*-Value
Race[a]								
White	124 (85.8)	442 (86.3)	1,533 (87.8)		163 (86.5)	513 (88.1)	1,770 (87.2)	
Black	59 (13.7)	176 (10.8)	475 (8.2)		71 (13.0)	163 (8.9)	568 (8.9)	
Other	3 (0.5)	21 (2.9)	71 (4.0)	.0004	1 (0.5)	14 (3.0)	82 (3.9)	.0014
Smoking [a]								
Current smoker	53 (33.7)	198 (30.4)	582 (24.5)		55 (28.0)	131 (20.2)	418 (18.7)	
Former smoker	80 (42.7)	269 (43.8)	889 (45.3)		40 (23.1)	143 (25.9)	546 (25.8)	
Nonsmoker	53 (23.6)	172 (25.8)	608 (30.1)	.1728	140 (48.93)	416 (53.8)	1,456 (55.5)	.3049
Metabolic syndrome[a]								
Yes	92 (56.6)	266 (36.8)	719 (34.5)		151 (59.5)	343 (44.5)	987 (32.9)	
No	94 (43.4)	373 (63.2)	1,360 (65.5)	.0200	84 (40.5)	347 (55.5)	1,433 (67.2)	<.0001
Number metabolic syndrome components present[a]								
0	12 (7.7)	73 (16.9)	327 (16.9)		17 (9.1)	79 (15.9)	349 (21.3)	
1	52 (19.5)	170 (26.5)	590 (27.6)		40 (19.7)	141 (22.5)	587 (26.6)	
2	30 (16.2)	130 (19.8)	443 (21.1)		27 (11.8)	127 (17.1)	497 (19.3)	
3	50 (28.3)	151 (20.1)	435 (19.9)		79 (32.0)	181 (23.4)	581 (19.7)	
4	27 (18.6)	90 (12.5)	220 (10.4)		49 (18.8)	115 (15.8)	293 (9.5)	
5	15 (9.7)	25 (4.2)	64 (4.2)	.0042[b]	23 (8.7)	47 (5.4)	113 (3.7)	<.0001[b]
Elevated blood pressure[a,c]								
Yes	155 (76.2)	448 (61.1)	1,211 (54.0)		188 (74.0)	463 (59.3)	1,398 (49.7)	
No	31 (23.8)	191 (38.9)	868 (46.0)	.0002	47 (26.0)	227 (40.7)	1,022 (50.3)	<.0001
Impaired fasting blood glucose[a,d,f]								
Yes	81 (51.9)	247 (34.2)	700 (29.6)		95 (33.7)	229 (28.6)	676 (21.0)	
No	105 (48.1)	392 (65.8)	1,379 (70.4)	.0038	140 (66.3)	461 (71.4)	1,743 (79.0)	.0078
Decreased High-density lipoprotein cholesterol[a,e,f]								
Yes	68 (44.4)	220 (38.5)	708 (37.1)		107 (51.0)	287 (41.2)	908 (34.9)	
No	113 (55.6)	409 (61.5)	1,330 (62.9)	.5334	120 (49.0)	387 (58.8)	1,476 (65.1)	.0008
Elevated triglycerides[a,f,g]								
Yes	56 (43.5)	205 (38.1)	647 (42.7)		84 (38.4)	204 (39.4)	604 (29.0)	

(Continues)

TABLE 1 (Continued)

	Men (*N* = 2,904)				Women (*n* = 3,345)			
	Spatial QRS|T				Spatial QRS|T			
	Abnormal (*N* = 186)	Borderline (*N* = 639)	Normal (*N* = 2,079)	*p*-Value	Abnormal (*N* = 186)	Borderline (*N* = 639)	Normal (*N* = 2,079)	*p*-Value
No	93 (56.5)	291 (61.9)	999 (57.3)	.3926	103 (61.6)	338 (60.6)	1,312 (71.0)	.0061
Abdominal obesity[a,f,h]								
Yes	85 (52.5)	248 (33.8)	715 (37.1)		168 (70.1)	450 (57.8)	1,475 (52.6)	
No	98 (47.5)	382 (66.2)	1,334 (62.9)	.022	61 (29.9)	231 (42.2)	898 (47.4)	.0006
Age[i]	59.61 (1.56)	55.48 (0.81)	54.42 (0.39)	.0053	61.03 (1.02)	57.15 (1.01)	55.74 (0.41)	<.0001
Heart rate[i]	69.93 (1.29)	67.04 (0.57)	66.25 (0.41)	.0335	70.71 (1.7)	70.86 (0.6)	68.62 (0.3)	.0037
PR Interval, msec[i]	175.76 (2.52)	165.21 (2.34)	164.15 (1.08)	.0003	159.95 (2.55)	159.82 (1.25)	159.06 (0.86)	.8910
QRS Interval, msec[i]	100.94 (0.94)	99.47 (0.53)	99.45 (0.53)	.2971	95.75 (0.91)	93.80 (0.64)	92.80 (0.54)	.0066
QTc Interval (Fridericia), msec[i,j]	437.16 (13.53)	418.78 (1.85)	414.60 (0.64)	.0313	441.51 (6.76)	436.38 (4.99)	427.86 (1.33)	.0341
QTc Interval (Bazett), msec[i,j]	447.37 (14.00)	425.96 (2.11)	420.60 (0.82)l	.0109	453.17 (8.53)	447.92 (5.36)	436.79 (1.44)	.0140
QRS Amplitude, μV[i]	754.32 (26.18)	834.99 (15.62)	919.05 (10.71)	<.0001	801.28 (28.07)	853.63 (15.38)	941.49 (9.92)	<.0001
Systolic blood pressure, mm Hg[i]	137.58 (2.05)	131.93 (1.09)	127.27 (0.61)	<.0001	136.24 (1.72)	130.98 (1.27)	125.27 (0.46)	<.0001
Diastolic blood pressure, mm Hg[i]	79.89 (1.18)	79.78 (0.61)	78.12 (0.31)	.0130	75.56 (1.04)	75.54 (0.50)	73.81 (0.26)	.0024
Fasting blood glucose, mg/dl[i]	122.51 (4.66)	105.43 (1.81)	102.81 (0.68)	.0003	115.22 (3.97)	109.90 (2.74)	99.16 (0.81)	<.0001
High-density lipoprotein cholesterol, mg/dl[i]	45. 90 (2.19)	45.87 (0.99)	45.44 (0.56)	.8820	53.19 (1.38)	55.71 (0.94)	56.32 (0.62)	.0602
Triglycerides, mg/dl[i]	217.95 (25.79)	152.20 (5.48)	162.45 (5.53)	.0427	178.67 (15.71)	165.43 (9.94)	137.64 (5.38)	.0023
Waist circumference, cm[i]	101.46 (1.39)	97.88 (0.68)	99.10 (0.39)	.0786	95.79 (1.30)	92.21 (0.90)	96.16 (0.47)	.0016

[a]n (%).
[b]*p*-trend is provided from linear model.
[c]Participants who had systolic blood pressure >130 mm Hg, diastolic blood pressure >85 mm Hg blood pressure, and/or self-reported a diagnosis of hypertension or use of antihypertensive medications.
[d]Participants who had a fasting blood glucose >100 mg/dl and/or self-reported a diagnosis of diabetes or use of medication for diabetes.
[e]High-density lipoprotein (HDL) <40 mg/dl for males and HDL <50 mg/dl for females.
[f]Numbers may not add to total due to missing values.
[g]Elevated triglycerides >150 mg/dl.
[h]Waist circumferences >102 cm for males or >88 cm for females.
[i]Mean (*SE*).
[j]Corrected QT interval for heart rate using Fridericia's or Bazett's formula.

We used the following criteria to define the MetS components (NCHS, 1994): (a) Abdominal obesity: defined as a waist circumferences >102 cm for males or a waist circumference >88 cm for females (NHLBI, 2002). Waist circumference was measured during the examination (NCHS, 1994) (b) Elevated blood pressure: participants who had systolic blood pressure >130 mm Hg and/or diastolic blood pressure >85 mm Hg blood pressure were considered as individuals with elevated blood pressure (NHLBI, 2002). The blood pressure status was determined from the average blood pressure obtained during the interview and examination (NCHS, 1994). In addition, we considered those who self-reported a diagnosis of hypertension or used antihypertensive medications to have high blood pressure. (c) Impaired fasting blood glucose: if the participant had a fasting blood glucose > 100 mg/dl, had self-reported a diagnosis of diabetes, and/or self-reported use of medication for diabetes, he/she was considered as an individual with impaired blood glucose level (NHLBI, 2002; NCHS, 1994). We defined a fasting blood sample as a blood draw conducted at least 8 hours of fasting (NCHS, 1994). (d) Decreased HDL was defined as blood HDL < 40 mg/dl for males and < 50 mg/dl for females (NHLBI, 2002). (e) Elevated triglycerides were defined blood triglycerides as > 150 mg/dl (NHLBI, 2002). HDL and triglycerides were tested using the venous blood specimen drawn during the examination (NCHS, 1994).

2.2.3 | Other covariates

Age, gender, race, and smoking status were self-reported during the household interview (NCHS, 1994). Age was indicated in years. Gender was categorized as male or female. Race was categorized as White or non-White. Smoking status was categorized as never smoker, current smoker, or former smoker. Heart rate was measured per a standardized protocol during the medical examination (NCHS, 1994). It was recorded in beats per minute. PR interval, QRS interval, QT interval, QRS amplitude, and left ventricular mass were assessed at the medical examination (NCHS, 1998). We corrected QT interval for heart rate using Fridericia's and Bazett's formulae. Fridericia's correction has been demonstrated to be most effective in minimizing the relation between QT interval and heart rate, while Bazett's correction is widely used in clinical settings (Faramawi, Wildman, Gustat, Rice, & Kareem, 2008; Vandenberk et al., 2016).

2.3 | Data analysis

We used SAS 9.4 software to conduct the statistical analysis. We used PROC SURVEY methods to account for the complex sampling design. We stratified by gender due to gender differences in QRS|T angle classification as well as gender differences in MetS status determination (NHLBI, 2002; Whang et al., 2012). We conducted univariate analysis to describe the weighted characteristics of the study population. Continuous variables were described using weighted means and standard error and categorical variables were described using weighted percentages. We conducted bivariate analysis to compare characteristics between normal, borderline, and abnormal spatial QRS|T angle as classified by Whang et al. (2012). For continuous variables, an independent weighted *t* test was used. For categorical variables, a weighted chi-square test was used. We conducted unadjusted weighted logistic regression to estimate the effect of MetS status, the number of MetS components, and other covariates on spatial QRS|T angle (reference set as normal). We conducted multivariate weighted logistic regression to assess the effect of MetS status on QRS|T angle after adjusting for the effect of age, race, smoking status, PR interval, QRS Interval, corrected QT interval (using Fridericia's formula), QRS amplitude, and heart rate. We repeated the analyses with the corrected QT interval using Bazett's instead of Fridericia's formula. We used Cochran–Armitage test to assess a dose-response effect for the number of MetS components on spatial QRS|T angle. We used Stata to conduct mediation analysis to determine the proportion of the total effect of MetS on spatial QRS|T angle mediated by left ventricular mass.

3 | RESULTS

This study included 6,249 participants: 44.4% males and 55.6% females. The mean age of males and females were 54.9 and 56.3 years, respectively. More than a third of the participants had MetS: 36.1% of males and 36.7% of females. For spatial QRS|T angle, about 5.1% of males and 5.7% of females had abnormally deviated QRS|T angle and 20.4% of males and 20.2% of females had a borderline spatial QRS|T angle orientation. For men, the following individuals had a positive association: African Americans and those with MetS (p = .0004 and p = .0200, respectively, Table 1). As the number of MetS components, age and heart rate increased, PR interval and corrected QT interval lengthened, and QRS amplitude decreased, the probability of having an abnormal spatial QRS|T angle increased. Men who had an impaired fasting blood glucose concentration, elevated blood pressure and a large waist circumference tended to have an abnormal spatial QRS|T angle. Among females, we observed similar relationships between the previously mentioned variables and the spatial QRS|T angle with a few exceptions (Table 1). Longer QRS interval rather than PR interval was associated with abnormal spatial QRS|T angle and women who had decreased HDL and elevated triglycerides tended to have an abnormal spatial QRS|T angle. We observed no apparent relation between smoking and the spatial QRS|T angle orientation among males or females (Table 1).

In the unadjusted logistic regression, the odds of having an abnormal spatial QRS|T angle orientation among males increased with MetS and the number of its components (Table 2). Elevated blood pressure, impaired fasting glucose, and abdominal obesity also increased the odds among males (Table 2). Among females, the spatial QRS|T angle orientation had a strong association with MetS and, similar to males, was associated with the number of its components, elevated blood pressure, impaired fasting glucose, and abdominal obesity (Table 2). Contrary to males, decreased HDL and elevated triglycerides were also positively associated with abnormal QRS|T angle in females (Table 2).

TABLE 2 Logistic regression spatial QRS|T angle as classified by Whang et al. with MetS, stratified by gender

	Men				Women			
	Unadjusted Analysis *N* = 2,904		Adjusted Analysis[a] *N* = 2,904		Unadjusted Analysis *N* = 3,345		Adjusted Analysis[a] *N* = 3,345	
	Borderline (*n* = 639) versus normal (*n* = 2,079) OR (95% CI)	Abnormal (*n* = 186) versus normal (*n* = 2,079) OR (95% CI)	Borderline (*n* = 639) versus normal (*n* = 2,079) OR (95% CI)	Abnormal (*n* = 186) versus normal (*n* = 2,079) OR (95% CI)	Borderline (*n* = 690) versus normal (*n* = 2,420) OR (95% CI)	Abnormal (*n* = 235) versus normal (*n* = 2,420) OR (95% CI)	Borderline (*n* = 690) versus normal (*n* = 2,420) OR (95% CI)	Abnormal (*n* = 235) versus normal (*n* = 2,420) OR (95% CI)
Metabolic syndrome								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.11 (0.80–1.54)	2.48 (1.42–4.33)	1.01 (0.73–1.39)	1.83 (1.07–3.13)	1.64 (1.23–2.20)	3.00 (2.14–4.20)	1.42 (1.04–1.95)	2.30 (1.64–3.22)
Number components present								
0	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
1	0.96 (0.60–1.55)	1.56 (0.56–4.37)	0.90 (0.54–1.48)	1.14 (0.37–3.50)	1.14 (0.78–1.64)	1.74 (0.78–3.88)	1.06 (0.74–1.53)	1.39 (0.61–3.19)
2	0.94 (0.59–1.48)	1.69 (0.52–5.46)	0.79 (0.47–1.31)	0.99 (0.30–3.26)	1.19 (0.78–1.81)	1.43 (0.56–3.64)	1.04 (0.70–1.54)	1.09 (0.42–2.82)
3	1.01 (0.53–1.94)	3.14 (1.18–8.35)	0.83 (0.43–1.62)	1.63 (0.57–4.66)	1.59 (1.03–2.46)	3.81 (1.89–7.65)	1.35 (0.86–2.13)	2.51 (1.24–5.09)
4+	1.15 (0.68–1.93)	4.26 (1.53–11.83)	0.94 (0.53–1.67)	2.36 (0.77–7.21)	2.16 (1.37–3.39)	4.91 (2.62–9.21)	1.66 (1.04–2.66)	3.09 (1.57–6.08)
Number of Components Present	1.03 (0.91–1.17)	1.43 (1.16–1.78)	0.98 (0.86–1.12)	1.26 (1.02–1.60)	1.21 (1.08–1.35)	1.49 (1.34–1.66)	1.14 (1.01–1.28)	1.35 (1.20–1.51)
Elevated blood pressure[b]								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.34 (0.93–1.94)	2.73 (1.63–4.59)	1.26 (0.86–1.86)	1.86 (1.04–3.31)	1.48 (1.15–1.89)	2.88 (1.88–4.40)	1.35 (1.06–1.72)	2.21 (1.48–3.29)
Impaired fasting blood glucose[c]								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.24 (0.94–1.64)	2.57 (1.61–4.12)	1.21 (0.92–1.59)	2.40 (1.46–3.94)	1.51 (1.13–2.00)	1.92 (1.33–2.75)	1.38 (1.04–1.83)	1.62 (1.09–2.39)
Decreased high-density lipoprotein cholesterol[d]								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	1.06 (0.78–1.46)	1.35 (0.77–2.38)	0.99 (0.72–1.37)	1.15 (0.64–2.06)	1.31 (1.01–1.69)	1.94 (1.34–2.83)	1.17 (0.89–1.53)	1.61 (1.06–2.45)
Elevated triglycerides[e]								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.83 (0.64–1.06)	1.03 (0.71–1.51)	0.78 (0.59–1.03)	0.92 (0.58–1.45)	Ref1.59 (1.23–2.06)	1.53 (1.18–1.98)	1.40 (1.03–1.91)	1.28 (0.89–1.84)
Abdominal obesity[f]								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.86 (0.66–1.14)	1.87 (1.10–3.21)	0.73 (0.55–0.97)	1.18 (0.63–2.24)	1.23 (0.92–1.64)	2.11 (1.46–3.06)	1.04 (0.76–1.44)	1.72 (1.10–2.69)
Systolic blood pressure, 10 mm Hg	1.19 (1.10–1.30)	1.39 (1.25–1.56)	1.22 (1.10–1.35)	1.34 (1.17–1.53)	1.17 (1.10–1.23)	1.31 (1.21–1.42)	1.20 (1.14–1.26)	1.30 (1.16–1.45)
Diastolic blood pressure, 10 mm Hg	1.20 (1.06–1.36)	1.22 (0.95–1.56)	1.24 (1.06–1.44)	1.25 (0.95–1.63)	1.24 (1.09–1.40)	1.24 (0.97–1.58)	1.19 (1.04–1.37)	1.27 (0.98–1.65)
Fasting blood glucose, 10 mg/dl	1.03 (0.99–1.07)	1.11 (1.08–1.15)	1.02 (0.98–1.06)	1.10 (1.05–1.14)	1.07 (1.04–1.10)	1.09 (1.07–1.12)	1.06 (1.03–1.09)	1.08 (1.05–1.11)
High-density lipoprotein cholesterol, 10 mg/dl	1.02 (0.92–1.13)	1.02 (0.83–1.26)	1.05 (0.94–1.17)	1.09 (0.87–1.34)	0.98 (0.91–1.05)	0.88 (0.77–0.99)	1.01 (0.93–1.09)	0.93 (0.83–1.04)
Triglycerides, 10 mg/dl	0.99 (0.98–1.00)	0.99 (1.01–1.03)	0.99 (0.98–1.00)	1.02 (1.01–1.03)	1.01 (1.00–1.03)	1.02 (1.00–1.03)	1.01 (1.00–1.02)	1.01 (1.00–1.03)
Waist circumference, 10 cm	0.92 (0.82–1.03)	1.16 (0.97–1.39)	0.85 (0.75–0.96)	0.97 (0.75–1.26)	1.05 (0.96–1.15)	1.23 (1.10–1.36)	0.98 (0.88–1.09)	1.16 (1.02–1.31)

[a]Adjusted for age, race, heart rate, smoking, PR interval, corrected QT interval (Fridericia formula), QRS interval, and QRS amplitude.
[b]Participants who had systolic blood pressure >130 mm Hg, diastolic blood pressure >85 mm Hg blood pressure, and/or self-reported a diagnosis of hypertension or use of antihypertensive medications.
[c]Participants who had a fasting blood glucose >100 mg/dl and/or self-reported a diagnosis of diabetes or use of medication for diabetes.
[d]High-density lipoprotein (HDL) <40 mg/dl for males and HDL <50 mg/dl for females.
[e]Elevated triglycerides >150 mg/dl.
[f]Waist circumferences >102 cm for males or >88 cm for females.

After we controlled for the effects of age, race, heart rate, smoking, PR interval, QRS interval, corrected QT interval (Fridericia's formula) spatial QRS|T angle orientation remained positively associated with MetS as well as its number of components; however, effect sizes were slightly attenuated (Table 2). Among those with MetS, the odds of abnormal spatial QRS|T angle relative to normal was 83% higher for men and 130% higher for women compared to those without MetS (95% CI: 1.07–3.13 and 1.64–3.22, respectively). Among men and women, individual components previously mentioned to be associated remained associated with spatial QRS|T angle, with the exception of abdominal obesity among men and elevated triglycerides among women (Table 2). Repeated analyses adjusting for corrected QT interval using Bazett's formula yielded the same conclusions.

In unadjusted mediation analysis, left ventricular mass mediated 77.00% of the total effect of MetS on spatial QRS|T angle. After adjusting for the effects of age, gender, race, heart rate, and smoking status, the proportion of the total effect of MetS on spatial QRS|T angle mediated by left ventricular mass was reduced to 58.05%.

4 | DISCUSSION

In this study, we observed a positive relationship between the MetS as well as the number of its components with the abnormal deviation of the spatial QRS|T angle: the odds of having QRS|T angle deviation increased with MetS and its component. The effect of MetS and its components among women was higher than that among males. In women, four of the five components of MetS—elevated blood pressure, impaired blood glucose concentration, low HDL, and abdominal obesity—had an association with the spatial QRS|T angle. In men, elevated blood pressure and impaired fasting blood glucose were the only components that had an association with the angle. Therefore, we can conclude that the gender may modify the effect of MetS on spatial QRS|T angle. However, the overlying confidence bounds of MetS in Table 2 do not exclude similar values of odds for females and males. The QRS|T angle is an important ECG predictor for cardiovascular events such as ventricular arrhythmia (Narayanan & Chugh, 2016; Oehler et al., 2014; Voulgari et al., 2013; Zhang et al., 2015). Hence, we can conclude that men and women, with MetS have higher odds for ventricular arrhythmias.

Individuals with MetS had higher odds for having an abnormally deviated angle. MetS is an established risk factor of an increase in the left ventricular mass (Cuspidi et al., 2017). Thus, in this study MetS might have increased the risk of the deviation of spatial QRS|T angle by increasing the left ventricular mass. Our analysis revealed that about 56% of the effect of MetS on the QRS|T angle was mediated by the left ventricular mass. An increase in the left ventricular mass is associated with abnormal QRS|T angle (Voulgari et al., 2013).

The current study confirms the results of the previous studies that concluded that MetS increases the risk for cardiac arrhythmias (Elffers et al., 2017; Faramawi, Sall, et al., 2008; Faramawi, Wildman, et al., 2008). However, herein we used a superior ECG parameter, that is, spatial QRS|T angle, to conventional ECG parameters that are associated with cardiac arrhythmias such as the T-wave deviation and QT interval (Elffers et al., 2017; Faramawi, Sall, et al., 2008; Faramawi, Wildman, et al., 2008). When we adjusted for other ECG parameters: PR interval, corrected QT interval, QRS interval, and QRS amplitude, MetS remained associated with abnormal QRS|T angle. In our study, we excluded participants with ischemic heart diseases, heart failure, and prolonged QRS duration, to minimize the effect of symptomatic cardiac diseases on the reported measures. We also stratified the analysis by gender because the distribution of the QRS|T angle of males differs from that of females. The results of the current analysis should be interpreted in the context of the following limitations. First, our study was cross-sectional; therefore, we had no opportunity to prove a temporal causation between MetS or its components. Second, we had no echocardiographic measures of left ventricular function to adjust for their effects in our models. Third, we used a self-report measure to exclude those with congestive heart failure which may have resulted in some persons with unreported congestive heart failure being included in the sample. Fourth, we had no chance to evaluate if abnormal QRS|T can predict cardiovascular outcomes because NHANES did not collect specific nonfatal cardiovascular outcomes especially ventricular arrhythmias, which have been associated with abnormal QRS|T angle in previous studies; additionally, the study was cross-sectional.

Nevertheless, this study has several points of strength. First, to our knowledge, this is the first study to explore the relationship of MetS and the number of its components with QRS|T angle—an important risk factor for ventricular arrhythmias—in a nationally representative sample of US adults. Second, we used a superior ECG parameter to quantify the mean difference between cardiac depolarization and repolarization: the spatial QRS|T angle. Third, the data of the study were collected according to comprehensive protocols and thorough quality control measures. Fourth, the datasets had information on important covariates, which allowed us to adjust for important confounders while conducting the statistical analysis. Finally, our results might have a clinical implication because they confirm that individuals who have MetS without known heart disease may need frequent clinical evaluation and careful medical management to decrease their cardiac morbidity and mortality.

5 | CONCLUSIONS

In summary, among women and men, there is an association between MetS as well as its components with spatial QRS|T angle. Those who have MetS without symptomatic heart disease could be at risk for ventricular arrhythmias because of their impaired ventricular depolarization and repolarization. The results of the current analysis need to be validated in future prospective studies.

CONFLICT OF INTEREST

None.

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REFERENCES

Aguilar, M., Bhuket, T., Torres, S., Liu, B., & Wong, R. J. (2015). Prevalence of the metabolic syndrome in the United States, 2003–2012. *JAMA*, *313*(19), 1973–1974. https://doi.org/10.1001/jama.2015.4260

Blackburn, H., Keys, A., Simonson, E., Rautaharju, P., & Punsar, S. (1960). The electrocardiogram in population studies: A classification system. *Circulation*, *21*(6), 1160–1175. https://doi.org/10.1161/01.CIR.21.6.1160

Cuspidi, C., Quarti, F., Dell'Oro, R., Facchetti, R., Bombelli, M., Sala, C., … Mancia, G. (2017). Long-term changes in left ventricular mass echocardiographic findings from a general population. *Journal of Hypertension*, *35*(11), 2303–2309. https://doi.org/10.1097/HJH.0000000000001453

Elffers, T. W., de Mutsert, R., Lamb, H. J., Maan, A. C., Macfarlane, P. W., Willems van Dijk, K. O., … Trompet, S. (2017). Association of metabolic syndrome and electrocardiographic markers of subclinical cardiovascular disease. *Diabetology & Metabolic Syndrome*, *9*(1), 40. https://doi.org/10.1186/s13098-017-0238-9

Faramawi, M. F., Sall, M., & Kareem, M. Y. A. (2008). The association of the metabolic syndrome with T-wave axis deviation in NHANES III. *Annals of Epidemiology*, *18*(9), 702–707. https://doi.org/10.1016/j.annepidem.2008.06.002

Faramawi, M. F., Wildman, R. P., Gustat, J., Rice, J., & Kareem, M. Y. A. (2008). The association of the metabolic syndrome with QTc interval in NHANES III. *European Journal of Epidemiology*, *23*(7), 459. https://doi.org/10.1007/s10654-008-9252-4

Heart and Lung and Blood Institute (2002). Third report of the national cholesterol education program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III) final report. *Circulation*, *106*(25), 3143.

McCullough, A. J. (2011). Epidemiology of the metabolic syndrome in the USA. *Journal of Digestive Diseases*, *12*(5), 333–340. https://doi.org/10.1111/j.1751-2980.2010.00469.x

Mottillo, S., Filion, K. B., Genest, J., Joseph, L., Pilote, L., Poirier, P., … Eisenberg, M. J. (2010). The metabolic syndrome and cardiovascular risk: A systematic review and meta-analysis. *Journal of the American College of Cardiology*, *56*(14), 1113–1132. https://doi.org/10.1016/j.jacc.2010.05.034

Narayanan, K., & Chugh, S. S. (2016). The 12-lead electrocardiogram and risk of sudden death: Current utility and future prospects. Ep. *Europace*, *17*(suppl_2), ii7–ii13. https://doi.org/10.1093/europace/euv121

National Center for Health Statistics (1994). Plan and operation of the third national health and nutrition examination survey, 1988–94. *Vital Health Statistics*, *32*, 1–407.

National Center for Health Statistics (1998). *Third National Health and Nutrition Examination Survey (NHANES III), 1988–94: NHANES III electrocardiography data file documentation*. Series 11, No. 2A. Retrieved Sep 17, 2017 from https://wwwn.cdc.gov/nchs/data/nhanes3/2a/NH3ECG-acc.pdf.

Oehler, A., Feldman, T., Henrikson, C. A., & Tereshchenko, L. G. (2014). QRS-T angle: A review. *Annals of Noninvasive Electrocardiology*, *19*(6), 534–542. https://doi.org/10.1111/anec.12206

Rautaharju, P. M., MacInnis, P. J., Warren, J. W., Wolf, H. K., Rykers, P. M., & Calhoun, H. P. (1990). Methodology of ECG interpretation in the Dalhousie program; NOVACODE ECG classification procedures for clinical trials and population health surveys. *Methods of Information in Medicine*, *29*(04), 362–374. https://doi.org/10.1055/s-0038-1634798

Rautaharju, P. M., Prineas, R. J., & Zhang, Z. M. (2007). A simple procedure for estimation of the spatial QRS/T angle from the standard 12-lead electrocardiogram. *Journal of Electrocardiology*, *40*(3), 300–304. https://doi.org/10.1016/j.jelectrocard.2006.11.003

Schreurs, C. A., Algra, A. M., Man, S.-C., Cannegieter, S. C., van der Wall, E. E., Schalij, M. J., … Swenne, C. A. (2010). The spatial QRS-T angle in the Frank vectorcardiogram: Accuracy of estimates derived from the 12-lead electrocardiogram. *Journal of Electrocardiology*, *43*(4), 294–301. https://doi.org/10.1016/j.jelectrocard.2010.03.009

Vandenberk, B., Vandael, E., Robyns, T., Vandenberghe, J., Garweg, C., Foulon, V., … Willems, R. (2016). Which QT correction formulae to use for QT monitoring? *Journal of the American Heart Association*, *5*(6), e003264. https://doi.org/10.1161/JAHA.116.003264

Voulgari, C., Pagoni, S., Tesfaye, S., & Tentolouris, N. (2013). The spatial QRS-T angle: Implications in clinical practice. *Current Cardiology Reviews*, *9*(3), 197–210. https://doi.org/10.2174/1573403X113099990031

Whang, W., Shimbo, D., Levitan, E. B., Newman, J. D., Rautaharju, P. M., Davidson, K. W., & Muntner, P. (2012). Relations between QRS| T angle, cardiac risk factors, and mortality in the third national health and nutrition examination survey (NHANES III). *The American Journal of Cardiology*, *109*(7), 981–987. https://doi.org/10.1016/j.amjcard.2011.11.027

Zhang, X., Zhu, Q., Zhu, L., Jiang, H., Xie, J., Huang, W., & Xu, B. (2015). Spatial/frontal QRS-T angle predicts all-cause mortality and cardiac mortality: A meta-analysis. *PLoS ONE*, *10*(8), e0136174. https://doi.org/10.1371/journal.pone.0136174

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