THE FRONTAL PLANAR QRS/T ANGLE IN NEWLY DIAGNOSED OBSTRUCTIVE SLEEP APNEA PATIENTS

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ABSTRACT

Introduction: *Obstructive sleep apnea syndrome might have a deleterious effect on ventricular repolarization, reflected by an altered frontal planar QRS/T angle.*

Material and method*: We retrospectively analyzed the medical records of a total 120 patients underwent overnight polysomnography test. Patients were divided into 4 groups according to apnea hypopnea index (AHI) values (< 5/h, 5-15/h, 15-30/h, and > 30/h). The frontal planar QRS/T angle was defined as absolute difference between the frontal QRS wave axis and T-wave axis on resting 12-lead surface electrocardiography (ECG).*

Results*: The average frontal planar QRS-T angle of all participants was 42.79 ± 38.75°. The frontal planar QRS-T angle is increased with the severity of obstructive sleep apnea syndrome (OSAS) and significantly highest in severe OSAS group (AHI >30/h) (p< 0.001). In post hoc analysis, we found statistically significant differences as regard mean frontal planar QRS-T angle between normal (AHI 0-5/h) and severe OSAS (AHI > 30/h) (p = 0.002), and between mild OSAS (AHI 5-15/h) and severe OSAS (AHI > 30/h) (p = 0.002). Age, male sex, left ventricular ejection fraction and obstructive apnea index showed significant association with frontal planar QRS/T angle in multivariate linear regression analysis (for all, p < 0.005).*

Conclusion*: The frontal planar QRS/T angle is significantly widened in patients with newly diagnosed OSAS compared with controls and increased by the severity of the disease determined by AHI. This finding might help the underlying pathophysiological mechanism of life-threatening ventricular arrhythmic susceptibility in OSAS patients.*

Key words*: obstructive sleep apnea syndrome, apnea hypopnea index, frontal planar QRS/T angle, and arrhythmia.*

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Introduction

Obstructive sleep apnea syndrome (OSAS) is a common breathing disorder depicted by the cyclic partial (hypopnea) or complete (apnea) interruption of ventilation during sleep caused by the closure of the upper airway[1]. The prevalence of OSAS is presently affecting 2-4% of middle-aged adults and this rate is increasing with each passing day[2].

The apnea-hypopnea index (AHI) is commonly used to classify the severity of OSAS as the total number of apneas and hypopnea as per sleep hour.

Some large prospective studies have demonstrated that individuals suffering from OSAS might lead to higher incidence of cardiovascular disorders such coronary heart disease myocardial infarction, heart failure, cerebrovascular disease, hypertension and thereby, increased morbidity/mortality as com-

pared to the general population[3-6]. Also, patients with OSAS experience a variety of atrial and/or ventricular arrhythmias during episodes of disordered breathing[7]. Although the pathophysiological link between OSAS and fatal ventricular arrhythmias has not yet been completely recognized, an increase in the transmural dispersion of cardiac repolarization has been proposed as a hypothetical mechanism[7]. Numerous surface electrocardiography (ECG) markers provide information about the electrical heterogeneity of the ventricles during repolarization.

Recently popular of these ECG markers is frontal planar QRS/T angle defined as the angle between the mean QRS and T vectors, and shows the basic direction of electrical heart activity during ventricular depolarization and repolarization. Since frontal planar QRS/T angle is an easily measured, more robust and reproducible ECG parameter, it has newly grown rather more interest. A number of studies have demonstrated the predictive value and availability of frontal planar QRS/T angle in various patient groups (8-12). However, no report has examined the relationship between the frontal planar QRS/T angle and OSAS.

We assumed that episodes of disordered breathing in OSAS patients might have a deleterious effect on ventricular repolarization, reflected by an altered frontal planar QRS/T angle. To test this hypothesis, the present study was undertaken to investigate the frontal planar QRS/T angle in patients with OSAS according to the severity of the disease as determined by the AHI.

Material and methods

Study population

We retrospectively analyzed the medical records of a total 150 patient with nocturnal snoring and/or excessive daytime symptoms underwent overnight polysomnography (PSG) test at our institute between January 2007 and March 2010. Exclusion criteria were the following conditions that might have had an influence on the ECG parameters: drugs affecting cardiac conduction (such as beta blockers, digitalis, dihydropyridines or verapamil); arrhythmias during the sleep study such as chronic atrial fibrillation, second or third atrioventricular block, all bundle branch blocks (left, right, or complete), premature extra systoles (atrial or ventricular); presence of ventricular pacemaker; history of previous cardiac surgery; valvular heart disease; congenital heart disease and congestive heart failure. Also, patients with inadequate or incomplete ECG and PSG test data were excluded from study. A total of 30 patients who met the above criteria were excluded from the study. Ultimately, a total of 120 patients were included in the analysis.

Polysomnography (PSG)

All study participants underwent PSG at our sleep laboratory using a computerized PSG device. Polygraphic sleep recording with breathing and superficial leg electromyogram recording accompanied by video monitoring were made in all patients during spontaneous night sleep. Arterial oxygen saturation (SpO_2) was monitored continuously with a pulse oximeter. Respirational actions were recorded as follows: apnea was defined as a interruption of airflow for more than 10 sec. Hypopnea was defined as a decrease of at least 50% of the oronasal flow amplitude during 10 sec (accompanied by ≤ 3% desaturation from baseline) or at least 30% of the oronasal flow amplitude during 10 sec (accompanied by ≤ 4% desaturation from baseline)[13]. The AHI was calculated by dividing the number of apneic and hypopneic events by the number of hours of sleep. AHI values were categorized as normal (AHI < 5), mild sleep apnea (5 ≤ AHI < 15), moderate sleep apnea (15 ≤ AHI < 30), and severe sleep apnea (AHI ≥ 30). The oxygen desaturation event index was calculated as the number of oxygen desaturation events per hour of sleep. Nocturnal heart rate was also recorded as mean, minimal and maximal. All digitally stored parameters were analyzed retrospectively.

Measurement of frontal planar QRS/T angle

A resting 12-lead surface ECG with a paper speed of 50 mm/s and a signal size of 10 mm/mV was recorded in the morning period of the PSG test. Frontal plane QRS-axis and T-wave axis were included in the reports of the automated ECG machine. The absolute difference between the frontal QRS wave axis and T-wave axis was defined as frontal planar QRS/T angle. If such a difference exceeded 180 degrees, the difference was calculated by subtracting from 180 degrees[14]. Two investigators unaware of the study hypothesis, blinded to the patients' clinical and PSG data analyzed the ECGs.

Statistical analysis

The data were tested for normal distributions using the Kolmogorov-Smirnov test. Categorical variables are expressed as numbers and percentages, and continuous variables as the mean ± standard deviation (SD). Chi-square test was used to compare categorical data. The one-way analysis of variance (ANOVA) was used to determine whether there are any significant differences between the means of four groups. Spearman's and Pearson's correlation coefficients were used to perform univariate correlation between patients' data and frontal planar QRS/T angle. Following univariate correlations, a linear regression analysis model was used to explain the parameters, which may have an independent effect on frontal planar QRS/T angle in OSAS patients. Differences were considered significant at $p < 0.05$. The Statistical Package for Social Sciences (SPSS, Chicago, IL, USA) version 20 was used to perform all statistical analyses and calculations.

The study was in compliance with the principles outlined in the Declaration of Helsinki, and the local ethics committee of our institute approved the study protocol.

	All population	AHI 0-5 (n= 22)	AHI 5-15 (n= 39)	AHI 15-30 (n= 21)	AHI > 30 (n= 38)	P value
Male, n (%)	97 (80.8)	14 (63.6)	28 (71.8)	21 (100)	34 (89.5)	0.004
Smoke, (n (%)	48 (40.7)	5 (25)	16 (41)	9 (42.9)	18 (47.4)	0.426
Diabetes, n (%)	33 (28)	4 (20)	8 (20.5)	7 (33.3)	14 (36.8)	0.436
Hypertension, n (%)	66 (55.9)	9 (45)	20 (51.3)	11 (52.4)	26 (68.4)	0.36
Age, years	55.33 ± 12.12	52.81 ± 11.20	53.41 ± 11.93	54.66 ± 12.56	59.13 (12.12)	0.125
Body Mass Index, (kg/m2)	30.60 ± 5.03	29.44 ± 4.95	31.25 ± 3.76	32.27 ± 3.86	32.27 ± 3.86	0.034
Fasting Glucose, (mg/dL)	110.92 ± 33.32	105.38 ± 23.11	111.76 ± 41.03	105.95 ± 16.32	115.89 ± 36.57	0.595
eGFR ($mL/min/1.73m^2$)	80.89 ± 16.92	85.73 ± 16.13	80.78 ± 17.81	82.56 ± 16.13	77.28 ± 16.66	0.293
Low Density Lipoprotein, (mg/dL)	129.70 ± 38.99	122.85 ± 30.70	128.13 ± 44.70	140.85 ± 36.33	128.86 ± 38.53	0.49
High Density Lipoprotein, (mg/dL)	47.56 ± 11.15	51.85 ± 10.55	45.62 ± 12.20	45.52 ± 9.36	48.27 ± 10.91	0.163
Total Cholesterol, (mg/dL)	210.19 ± 42.33	203.33 ± 37.23	208.65 ± 47.75	219.19 ± 35.87	210.56 ± 43.24	0.676
Triglyceride, (mg/dL)	167.54 ± 90.54	141.42 ± 59.75	174.68 ± 87.64	188.71 ± 148.62	163.02 ± 59.43	0.362
Heart Rate, (bpm)	72.44 ± 12.91	74.18 ± 14.53	68.84 ± 11.26	76.90 ± 14.00	72.65 ± 12.38	0.113
QTc, (msc)	413.00 ± 33.62	415.72 ± 26.73	406.35 ± 28.68	408.80 ± 32.29	420.52 ± 41.26	0.274
Frontal Planar QRS/T angle, (O)	42.79 ± 38.75	27.31 ± 24.02	33.23 ± 28.31	38.90 ± 26.88	63.71 ± 50.90	<0.001
Left Ventricular Ejection Fraction, (%)	62.31 ± 6.96	62.17 ± 7.55	63.94 ± 5.37	60.09 ± 8.80	62.02 ± 6.76	0.245

Table 1: Basal demographic, clinical and characteristics and laboratory findings.

Results

The ratio of male to female was about 4 to 1 ($p = 0.004$) and mean age was 55.33 ± 12.12 years. The mean body mass index (BMI) of all patients was 30.60 ± 5.03 kg/m^2. In relation to the fact that OSAS patients have been associated with obesity, a gradual increase in BMI was observed between groups regarding severity of OSAS ($p = 0.034$). No association was found for other baseline demographic and clinical data (Table 1).

In comparison of OSAS subgroups regarding PSG test results, as expected, there were statistically significant differences for AHI, obstructive apnea index, mixed apnea index, hypopnea index oxygen desaturation event index, mean O_2 saturation, the percentage sleep time with SaO_2<90%, periodic leg movements sequences and limb movements between OSAS subgroups regarding severity of disease ($p < 0.005$ for all) (Table 2).

The average frontal planar QRS-T angle of all participants was 42.79 ± 38.75°. The frontal planar QRS-T angle was increased with the severity of OSAS and was significantly highest in severe OSAS group (AHI >30/h) ($p< 0.001$). We also performed a post hoc Tukey test to evaluate intergroup differences in detail. We found statistically significant differences as regard mean frontal planar QRS-T angle between normal (AHI 0-5/h) and severe OSAS (AHI > 30/h) ($p = 0.002$), and between mild OSAS (AHI 5-15/h) and severe OSAS (AHI > 30/h) ($p = 0.002$) (Figure 1).

In univariate correlation analysis, age, sex, left ventricular ejection fraction, AHI, obstructive apnea index, mixed apnea index, hypopnea index, mean oxygen saturation, oxygen desaturation event index, the percentage sleep time with SaO2 <90%, periodic leg movements sequences and limb movements were found significantly correlated with frontal planar QRS/T angle (for all, $p < 0.05$). Then, we performed a backward multivariate linear regression analysis to determine the independent variables likely to affect the frontal planar QRS/T angle

including variables, which were found significant in univariate correlation analysis. Age, male sex, left ventricular ejection fraction and obstructive apnea index continued significant association with frontal planar QRS/T angle in multivariate linear regression analysis (for all, $p < 0.005$) (Table 3).

	All population	AHI 0-5 (n= 22)	AHI 5-15 (n= 39)	AHI 15-30 (n= 21)	AHI > 30 (n= 38)	P value
Apnea hypopnea index, (/hour)	24.99 ± 23.71	2.05 ± 1.46	9.60 ± 3.06	23.63 ± 3.78	54.80 ± 17.73	< 0.001
Obstructive apnea index, (/hour)	9.25 ± 13.58	0.47 ± 0.55	1.57 ± 2.09	6.51 ± 4.36	23.77 ± 16.06	< 0.001
Central apnea index, (/hour)	0.76 ± 2.83	0.16 ± 0.57	0.19 ± 0.39	0.64 ± 1.45	1.77 ± 4.80	0.078
Mixed apnea index, (/hour)	1.20 ± 5.17	0.21 ± 0.63	0.13 ± 0.42	0.46 ± 1.32	3.36 ± 8.80	0.024
Hypopnea index, (/hour)	14.63 ± 14.16	2.81 ± 5.46	7.60 ± 2.77	15.98 ± 4.10	27.28 ± 17.55	< 0.001
Oxygen desaturation event index (/hour)	26.41 ± 23.83	3.97 ± 2.95	10.25 ± 5.62	23.49 ± 9.13	54.12 ± 18.48	< 0.001
Mean O_2 saturation, (%)	92.05 ± 2.30	92.91 ± 1.81	93.20 ± 1.54	91.76 ± 1.62	90.73 ± 2.71	< 0.001
The percentage sleep time with SaO^2 <90%	13.37 ± 18.28	4.70 ± 8.79	4.81 ± .8.78	13.62 ± 13.86	24.54 ± 23.31	< 0.001
Periodic leg movements sequences	17.19 ± 23.96	4.67 ± 7.74	12.42 ± 20.27	15.75 ± 25.16	29.32 ± 27.53	0.001
Limb movements	28.34 ± 26.44	13.08 ± 10.32	21.80 ± 22.45	30.96 ± 30.52	41.37 ± 27.99	< 0.001
Snoring Time (minute)	18.49 ± 19.78	16.18 ± 14.98	15.95 ± 19.88	18.23 ± 17.95	21.62 ± 22.42	0.669
The percentage of supine position	33.92 ± 30.12	37.95 ± 31.35	28.85 ± 23.14	29.71 ± 21.39	38.92 ± 38.15	0.444
The percentage of left-sided sleeping position	27.70 ± 19.94	24.27 ± 20.44	30.09 ± 23.51	27.89 ± 17.39	27.01 ± 17.62	0.787
The percentage of right-sided sleeping position	36.46 ± 21.95	33.21 ± 20.13	36.13 ± 22.02	39.52 ± 21.92	36.79 ± 23.36	0.858
The percentage of prone position	2.38 ± 7.83	2.37 ± 5.05	2.93 ± 10.21	1.84 ± 7.59	2.20 ± 6.67	0.969
Mean heart rate, bpm	65.54 ± 8.49	65.94 ± 8.61	60.93 ± 5.88	68.20 ± 8.79	68.45 ± 8.79	< 0.001
Minimum heart rate, bpm	48.21 ± 9.63	52.50 ± 11.23	47.83 ± 7.79	48.38 ± 8.33	46.32 ± 10.89	0.174
Maximum heart rate, bpm	90.08 ± 15.92	91.22 ± 14.68	85.91 ± 17.85	95.42 ± 12.87	90.68 ± 15.47	0.169

Table 2: Polysomnographic results.

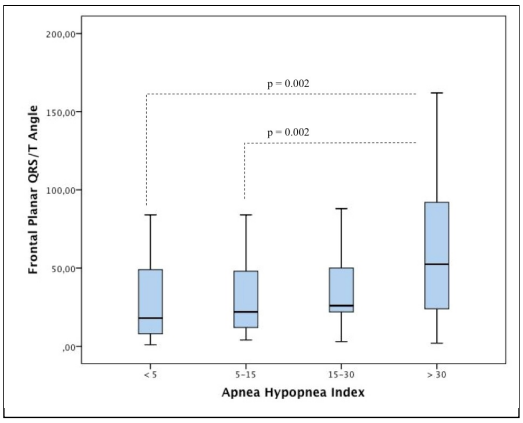

Figure 1: Frontal planar QRS/T angles of subjects according to the apnea hypopnea index. Significant results of post hoc Tukey test.

Discussion

In this retrospective study, we found that frontal planar QRS/T angle, which reflects the increased heterogeneity of ventricular repolarization is significantly widened in patients with newly diagnosed OSAS compared with controls. Nonetheless, the frontal planar QRS/T angle is increased by the severity of the disease determined by AHI.

Although it is known that OSAS is likely to exert adverse effects on hemodynamics (6), a controversy still remains as to whether OSAS is an independent etiologic risk factor for arrhythmias. In several studies, cardiac arrhythmias during sleep were reported to occur more commonly in OSAS patients[15]. On the other hand, some studies did not demonstrate any or barely a feeble association[16]. Rhythm disturbances, such as sinus bradycardia, sinus arrest, asystole and atrioventricular block are regarded as typical features of OSAS[17]. Nonetheless, a significant set of evidence denotes cardiovascular mortality (especially, sudden cardiac death at night) might occur due to an increased incidence of lethal ventricular arrhythmias in OSAS patients[18].

The increased susceptibility to ventricular arrhythmias in OSAS patients may be explained by structural remodeling (resultant formation of an arrhythmogenic substrate), electrical remodeling (exhibiting as repolarization abnormality), sympathetic overstimulation, hemodynamic, humoral, neuroendocrine and mechanical changes (e.g. cardiac stretch)[19-23]. Apnea- and hypopnea-related repetitive hypoxemia during sleep may result in insufficient delivery of oxygen to the myocardium leading to nocturnal angina and arrhythmias[18]. Intermittent hypoxia to nocturnal hypopnea or apnea episodes and arousal reactions is related to surges in sympathetic activity and decreases in parasympathetic activity, and thereby, may facilitate arrhythmogenesis by a re-entrant mechanism and triggered activity[18, 24-27].

Also, large negative intra-thoracic pressure (60-80 mmHg) due to repeated enforced inspiration against the closed upper airway throughout each obstructive apnea or hypopnea episodes might enhance transmural pressure of ventricles and lead to increases in ventricular wall stretch and myocar-

	Univariate analysis		Multivariate analysis	
	r	P value	Unstandardized Coefficients B (95% CI)	P value
Age	0.226	0.013	0.654 [(0.121) – (1.187)]	0.017
Male sex	0.217	0.017	19.122 [(2.340) – (35.903)]	0.026
Left Ventricular Ejection Fraction	-0.192	0.047	-1.092 [(-2.077) – (-0.106)]	0.03
Apnea hypopnea index	0.423	< 0.001	-3.98 [(-1.965) – (1.170)]	0.615
Obstructive apnea index	0.426	< 0.001	0.959 [(0.459) – (1.459)]	< 0.001
Mixed apnea index	0.23	0.014	10.393 [(-6.914) – (27.700)]	0.236
Hypopnea index	0.236	0.011	0.315 [(-1.161) – (0.790)]	0.192
Mean oxygen saturation	-0.361	< 0.001	-0.721 [(-4.094) – (2.652)]	0.672
Oxygen desaturation event index	0.437	< 0.001	0.358 [(-0.783) – (1.500)]	0.534
The percentage sleep time with SaO2 <90%	0.341	< 0.001	-0.251 [(-1.020) – (0.518)]	0.518
Periodic leg movements sequences	0.243	0.008	0.021 [(-0.762) – (0.804)]	0.958
Limb movements	0.254	0.006	-0.043 [(-0.355) – (0.269)]	0.784

Table 3: The variables significantly correlated with frontal planar QRS/T angle in univariate and multivariate analyses.

dial oxygen consumption[28, 29]. These abnormal physiologic events may result in increased heterogeneity in ventricular repolarization, which may serve as a major determinant of fatal arrhythmias and predispose OSAS individuals to life-threatening ventricular arrhythmias[19, 30].

Ventricular depolarization or repolarization abnormalities are important in arrhythmia provocation and have been shown to carry prognostic value for various patient groups. In literature, most of the studies demonstrating the disruption of ventricular repolarization in OSAS patients are related to increased QT or QTc dispersion, which have been associated with increased risk of cardiac morbidity and mortality[31, 32]. Dursunoglu et al.[33] showed that increased QTc dispersion is well correlated with the severity of OSAS as determined by AHI. Nakamura et al.[34] reported that nocturnal QTc dispersion was longer during sleep than before sleep in patients with OSAS and was decreased with CPAP therapy independently of cardiac sympathetic function.

The QRS axis reflects the main orientation of electrical activity of the heart during ventricular depolarization, whereas the T axis reflects it during ventricular repolarization[35]. Consequently, the QRS-T angle has been regarded as a merged measurement of ventricular depolarization and repolarization. Normally, as a result of the balanced regulation of electric activity of the heart, the direction of the ventricular depolarization and repolarization axes is in a similar course, which results in a narrow QRS-T angle[36]. When the spread of electrical forces through the myocardial wall is distorted with structural and functional myocardial changes, ventricular repolarization heterogeneity occurs and the QRS-T angle widens[37].

The concept of the QRS-T angle has been known for a long time. Recent studies has been shown that a wider QRS-T angle > 90° results is a powerful predictor of fatal and non-fatal cardiovascular disease events, independently of other clinical and ECG predictors in the general population[8, 38, 39] and in various patient groups[9-12, 14, 40]. Despite many studies about this new parameter on several cardiac disorders, we cannot find any paper in the literature about the role of QRS/T angle in patients with OSAS. To the best of our knowledge, our study is the first study in this era. We found that frontal planar QRS/T angle significantly widened in OSAS patients. We proposed that repetitive partial or complete interruption of ventilation during sleep might affect the electrical activity of the heart and predispose to development of malignant ventricular arrhythmias in subjects with OSAS. However, the pathophysiological mechanisms underlying ventricular repolarization abnormalities were not investigated in our study. Patients suffering from OSAS are commonly obese[41]. Most of the previous studies concluded that obesity might cause ventricular repolarization abnormalities as determined by QT dispersion[42]. We found a significant correlation between BMI and AHI ($r= 0.313$, $p < 0.001$), between BMI and obstructive apnea index ($r=0.188$, $p=0.048$), and between BMI and hypopnea index ($r=0.317$, $p=0.001$). However, we did not find a relationship between BMI and frontal planar QRS/T angle ($r=0.115$, $p=0.210$). In the previous studies, patients were morbidly obese; while our subjects' mean BMI was only $30.60 \pm 5.03 kg/m^2$.

Study limitations

The present study has a number of inherent limitations. The main limitation of the present study is its retrospective design, with a relatively small sample size. In addition, our single center registry used here may not reflect the findings in the general community, and the results should be further confirmed with several longitudinal studies. Although the measurement of frontal planar QRS/T angle is a basic and relatively rough method of measuring heterogeneity of ventricular repolarization, it has been shown that the spatial QRS/T angle has superior role for cardiac risk prediction than frontal planar QRS/T angle[43]. Measurement of the spatial QRS/T angle is very complicated and necessitates studious electrophysiological knowledge, and a dedicated computer program, which is not generally available in most centers. On the other hand, the measurement of frontal planar QRS-T angle exhibits less methodological limitations and most current ECG machines report automatic QRS and T axes. Therefore, we measured the frontal planar QRS-T angle, not the spatial QRS-T angle. Finally, since it is beyond the scope of this study, we did not focused on the question as to which pathophysiological mechanisms underpin the association between OSAS and the widened frontal planar QRS/T angle in this investigation.

In conclusion, the present observations suggest that the heterogeneity of ventricular repolarization as determined by wider frontal planar QRS/T angle is associated with the severity of the OSAS as determined by AHI. Our study can give inspiration for understanding the predisposing of the OSAS patients to life-threatening ventricular arrhythmic susceptibility. Further large, prospective studies are needed to confirm its predictive value and elucidate the reasons for wider frontal planar QRS/T angle in patients with OSAS.

References

1) *Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research*. The Report of an American Academy of Sleep Medicine Task Force. Sleep, 1999; 22: *667-89*.
2) Young T, Palta M, Dempsey J, Peppard PE, Nieto FJ, et al. *Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort study*. WMJ, 2009; 108: *246-9*.
3) Sorajja D, Gami AS, Somers VK, Behrenbeck TR, Garcia-Touchard A, et al. *Independent association between obstructive sleep apnea and subclinical coronary artery disease*. Chest, 2008; 133: *927-33*.
4) Hung J, Whitford EG, Parsons RW, Hillman DR. *Association of sleep apnoea with myocardial infarction in men*. Lancet, 1990; 336: *261-4*.
5) Kasai T, Bradley TD. *Obstructive sleep apnea and heart failure: pathophysiologic and therapeutic implications*. J Am Coll Cardiol, 2011; 57: *119-27*.
6) Butt M, Dwivedi G, Khair O, Lip GY. *Obstructive sleep apnea and cardiovascular disease*. Int J Cardiol, 2010; 139: *7-16*.
7) Voigt L, Haq SA, Mitre CA, Lombardo G, Kassotis J. *Effect of obstructive sleep apnea on QT dispersion: a potential mechanism of sudden cardiac death*. Cardiology, 2011; 118: *68-73*.
8) Aro AL, Huikuri HV, Tikkanen JT, Junttila MJ, Rissanen HA, et al. *QRS-T angle as a predictor of sudden cardiac death in a middle-aged general population*. Europace, 2012; 14: *872-6*.
9) Cardoso CR, Leite NC, Salles GF. *Factors associated with abnormal T-wave axis and increased QRS-T angle in type 2 diabetes*. Acta Diabetol, 2013; 50: *919-25*.
10) Dilaveris P, Gialafos E, Pantazis A, Synetos A, Triposkiadis F, et al. *The spatial QRS-T angle as a marker of ventricular repolarisation in hypertension*. J Hum Hypertens, 2001; 15: *63-70*.
11) Li YH, Ren XJ, Han ZH, Wang YL, Wang Y, et al. *Value of the frontal planar QRS-T angle on cardiac dysfunction in patients with old myocardial infarction*. Int J Clin Exp Med, 2013; 6: *688-92*.
12) Selvaraj S, Ilkhanoff L, Burke MA, Freed BH, Lang RM, et al. *Association of the frontal QRS-T angle with adverse cardiac remodeling, impaired left and right ventricular function, and worse outcomes in heart failure with preserved ejection fraction*. J Am Soc Echocardiogr, 2014; 27: *74-82 e2*.
13) Epstein LJ, Kristo D, Strollo PJ, Jr., Friedman N, Malhotra A, et al. *Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults*. J Clin Sleep Med, 2009; 5: *263-76*.
14) Raposeiras-Roubin S, Virgos-Lamela A, Bouzas-Cruz N, Lopez-Lopez A, Castineira-Busto M, et al. *Usefulness of the QRS-T angle to improve long-term risk stratification of patients with acute myocardial infarction and depressed left ventricular ejection fraction*. Am J Cardiol, 2014; 113: *1312-9*.
15) Hoffstein V, Mateika S. *Cardiac arrhythmias, snoring, and sleep apnea*. Chest, 1994; 106: *466-71*.
16) Alonso-Fernandez A, Garcia-Rio F, Racionero MA, Pino JM, Ortuno F, et al. *Cardiac rhythm disturbances and ST-segment depression episodes in patients with obstructive sleep apnea-hypopnea syndrome and its mechanisms*. Chest, 2005; 127: *15-22*.
17) Namtvedt SK, Randby A, Einvik G, Hrubos-Strom H, Somers VK, et al. *Cardiac arrhythmias in obstructive sleep apnea (from the Akershus Sleep Apnea Project)*. Am J Cardiol, 2011; 108: *1141-6*.
18) Monahan K, Storfer-Isser A, Mehra R, Shahar E, Mittleman M, et al. *Triggering of nocturnal arrhythmias by sleep-disordered breathing events*. J Am Coll Cardiol, 2009; 54: *1797-804*.

19) Chan KH, Wilcox I. *Obstructive sleep apnea: novel trigger and potential therapeutic target for cardiac arrhythmias*. Expert Rev Cardiovasc Ther, 2010; 8: *981-94*.
20) Rossi VA, Stoewhas AC, Camen G, Steffel J, Bloch KE, et al. *The effects of continuous positive airway pressure therapy withdrawal on cardiac repolarization: data from a randomized controlled trial*. Eur Heart J, 2012; 33: *2206-12*.
21) Mehra R, Benjamin EJ, Shahar E, Gottlieb DJ, Nawabit R, et al. *Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study*. Am J Respir Crit Care Med, 2006; 173: *910-6*.
22) Hersi AS. *Obstructive sleep apnea and cardiac arrhythmias*. Ann Thorac Med, 2010; 5: *10-7*.
23) Mehra R, Stone KL, Varosy PD, Hoffman AR, Marcus GM, et al. *Nocturnal Arrhythmias across a spectrum of obstructive and central sleep-disordered breathing in older men: outcomes of sleep disorders in older men (MrOS sleep) study*. Arch Intern Med, 2009; 169: *1147-55*.
24) Leung RS. *Sleep-disordered breathing: autonomic mechanisms and arrhythmias*. Prog Cardiovasc Dis, 2009; 51: *324-38*.
25) Aytemir K, Deniz A, Yavuz B, Ugur Demir A, Sahiner L, et al. *Increased myocardial vulnerability and autonomic nervous system imbalance in obstructive sleep apnea syndrome*. Respir Med, 2007; 101: *1277-82*.
26) Vanninen E, Tuunainen A, Kansanen M, Uusitupa M, Lansimies E. Cardiac sympathovagal balance during sleep apnea episodes. Clin Physiol, 1996; 16: 209-16
27) Zwillich CW. Sleep apnoea and autonomic function. Thorax, 1998; 53 Suppl 3: S20-4
28) Virolainen J, Ventila M, Turto H, Kupari M. *Effect of negative intrathoracic pressure on left ventricular pressure dynamics and relaxation*. J Appl Physiol (1985), 1995; 79: *455-60*.
29) Koshino Y, Villarraga HR, Orban M, Bruce CJ, Pressman GS, et al. *Changes in left and right ventricular mechanics during the Mueller maneuver in healthy adults: a possible mechanism for abnormal cardiac function in patients with obstructive sleep apnea*. Circ Cardiovasc Imaging, 2010; 3: *282-9*.
30) Wolf J, Lewicka J, Narkiewicz K. *Obstructive sleep apnea: an update on mechanisms and cardiovascular consequences*. Nutr Metab Cardiovasc Dis, 2007; 17: *233-40*.
31) Yamashita J, Nomura M, Uehara K, Nakaya Y, Uemura E, et al. *Influence of sleep apnea on autonomic nervous activity and QT dispersion in patients with essential hypertension and old myocardial infarction*. J Electrocardiol, 2004; 37: *31-40*.
32) Dursunoglu D, Dursunoglu N. *Effect of CPAP on QT interval dispersion in obstructive sleep apnea patients without hypertension*. Sleep Med, 2007; 8: *478-83*.
33) Dursunoglu D, Dursunoglu N, Evrengul H, Ozkurt S, Kilic M, et al. *QT interval dispersion in obstructive sleep apnoea syndrome patients without hypertension*. Eur Respir J, 2005; 25: *677-81*.
34) Nakamura T, Chin K, Hosokawa R, Takahashi K, Sumi K, et al. *Corrected QT dispersion and cardiac sympathetic function in patients with obstructive sleep apnea-hypopnea syndrome*. Chest, 2004; 125: *2107-14*.
35) Karabacak K, Celik M, Gokoglan Y, Kadan M, Kaya E, et al. *Frontal planar QRS/T angle can be a prognostic factor in the early postoperative period of patients undergoing coronary bypass surgery*. Heart Surg Forum, 2014; 17: *E288-92*.
36) Scherptong RW, Henkens IR, Man SC, Le Cessie S, Vliegen HW, et al. *Normal limits of the spatial QRS-T angle and ventricular gradient in 12-lead electrocardiograms of young adults: dependence on sex and heart rate*. J Electrocardiol, 2008; 41: *648-55*.
37) Rautaharju PM, Kooperberg C, Larson JC, LaCroix A. *Electrocardiographic abnormalities that predict coronary heart disease events and mortality in postmenopausal women: the Women's Health Initiative*. Circulation, 2006; 113: *473-80*.
38) Kardys I, Kors JA, van der Meer IM, Hofman A, van der Kuip DA, et al. *Spatial QRS-T angle predicts cardiac death in a general population*. Eur Heart J, 2003; 24: *1357-64*.
39) Yamazaki T, Froelicher VF, Myers J, Chun S, Wang P. *Spatial QRS-T angle predicts cardiac death in a clinical population*. Heart Rhythm, 2005; 2: *73-8*.
40) Rautaharju PM, Ge S, Nelson JC, Marino Larsen EK, Psaty BM, et al. *Comparison of mortality risk for electrocardiographic abnormalities in men and women with and without coronary heart disease (from the Cardiovascular Health Study)*. Am J Cardiol, 2006; 97: *309-15*.
41) Grimm W, Becker HF. *Obesity, sleep apnea syndrome, and rhythmogenic risk*. Herz, 2006; 31: 213-8; quiz 219
42) Khositseth A, Nantarakchaikul P, Kuptanon T, Preutthipan A. QT dispersion in childhood obstructive sleep apnoea syndrome. Cardiol Young, 2011; 21: *130-5*.
43) Voulgari C, Pagoni S, Tesfaye S, Tentolouris N. *The spatial QRS-T angle: implications in clinical practice*. Curr Cardiol Rev, 2013; 9: *197-210*.

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