Opinion Article

QT interval variability in patients with obstructive sleep apnea

ABSTRACT

Aims:
Obstructive sleep apnea (OSA) increases the risk of cardiac arrhythmias. We investigated QT interval variability among OSA patients.

Study design: It is a descriptive-cross-sectional study.

Methodology: Newly diagnosed OSA patients and healthy controls were studied. Inter-heartbeat and QT intervals were extracted from electrocardiography (for 1 hour at 3 AM). QT interval metrics including duration and variability indexes were compared between patients and controls.

Results: 35 patients and 13 controls were studied. There was no difference between patients and controls, neither between mild/moderate OSA versus severe OSA patients, in the measured QT interval variables. No significant correlation was found between apnea severity and the measured QT interval variables.

Conclusion: We found no difference between OSA patients and controls in QT variability. Also, no clear association between OSA severity and QT variability was observed.

Keywords: Sleep apnea, arrhythmia, cardiovascular, cardiac electrophysiology

1. INTRODUCTION

Obstructive sleep apnea (OSA) is associated with cardiac arrhythmias.[1] Obstructive episodes during sleep increase cardiac load which can induce cardiac remodeling and structural changes contributing to arrhythmias.[2-4] Given that the renin-angiotensin-aldosterone system's stimulation and sympathetic activity can be increased in OSA patients, the higher risk of cardiac arrhythmias and sudden death can be expected for this group of patients. [5,6] Characteristics of the QT interval, including QT variability (QTV), can provide information regarding cardiac electrical activity in OSA patients. Abnormalities of the QT interval can indicate abnormal repolarization during which cardiac vulnerability is heightened toward the development of arrhythmias. The QTV index (QTVi) assesses repolarization lability and is a predictor of cardiac arrhythmias and mortality. [7] QT interval variation may happen during and after sleep apnea episodes due to increased vagal activity and subsequent increased sympathetic tone and/or vagal withdrawal.[8] Camen et al. showed that simulated obstructive hypopnea/apnea are associated with prolongation of the QT interval.[2] However, others found no difference between OSA patients and controls in QT interval.[9] Baumert et al. reported an association between severity of OSA and QTV, reflecting alterations in cardiac sympathetic activity.[11] We evaluated QTV in patients with newly diagnosed OSA and compared it with healthy controls.

2. MATERIAL AND METHODS

This is a descriptive analytic study in which all patients presenting with symptoms of sleep apnea, loud and frequent snoring at night, severe obesity, and enlarged adenoids at Bamdad sleep clinic in

2017 were considered as candidates for polysomnography (PSG) of which 50 persons were selected through convenience sampling.

The inclusion criteria were patients aged at least 18 years, with OSA diagnosed by PSG. Those with cardiovascular, kidney, or pulmonary diseases or diabetes were excluded (2 cases with indications of diabetes). Thus, a sample size of 48 was considered. The study was approved by local committee of Isfahan University of Medical Sciences. A written informed consent was obtained from each participant undergoing PSG. Apnea–hypopnea index (AHI) of ≥5 events/hour was considered diagnostic.[6] Patients were categorized to mild (5≤AHI<15), moderate (15≤AHI≤30), severe (AHI>30) OSA.[7] and controls (AHI<5). [10] On a separate day, Holter electrocardiography was performed using a digital Holter recorder with three channels (I, II, and III) and sampling rate of 200 Hz (H200 recorder, Kavoshgaran Teb Kharazmi Co., Iran). Software was developed by the Department of Biomedical Engineering (Isfahan University) for signal processing. The QT and inter-heartbeat (RR) intervals were extracted from the channel II and were inspected by a cardiologist for errors. The QTV analyses were performed for an hour of sleeping period at night (3-4 AM). The QTVi was calculated as $\log[(QTvar/meanQT^2)/(RRvar/meanRR^2)]$, where QTvar contains the variance of all QT intervals and RRvar contains the variance of all RR intervals during an hour.[11]

2.1 Statistical analysis:

Data analysis was performed using SPSS software (version 16.0, SPSS Inc., Chicago, IL). Continuous variables were compared between the groups using Independent sample t-Test or Mann-Whitney U test. Categorical data were compared using the Chi-square test. Pearson and Spearman correlation analyses were used to estimate the relationship between variables. A *P* value <0.05 was considered significant in all analyses.

3. RESULTS AND DISCUSSION

35 patients and 13 controls were included into the study. The two groups were not different regarding age, gender, or BMI (*P*>0.05). The QT interval metrics are summarized in Table 1. There was no significant difference between patients and controls, neither between mild/moderate OSA versus severe OSA patients, in QT interval variables (*P*>0.05). No significant correlation was found between AHI and QT interval variables (*P*>0.05).

Table 1: Comparison of demographic data between the patients and controls

	Mild/Moderate OSA AHI 5 to 30, n = 19	Severe OSA AHI >30, n = 16	Controls AHI <5, n = 13	*P* *	*P* **
Age, year	47.5 ± 6.7	48.1 ± 7.6	47.7 ± 6.5	0.969†	0.805†
Male gender	9 (47.4)	8 (50)	7 (53.8)	0.500‡	0.937‡
BMI, kg/m^2	28.0 ± 4.2	29.9 ± 6.6	27.2 ± 1.9	0.294†	0.311†
AHI, /h	19.0 ± 6.4	56.4 ± 22.5	2.4 ± 1.2	<0.001†	<0.001†
QT, ms	406.6±30.2	396.1±23.3	407.5±27.9	0.524†	0.266†
QTSD, ms	12.7±6.0	12.4±4.0	12.0±5.0	0.733†	0.875†
QTvar, ms^2	197.8 [49.7]	171.0 [31.5]	168.9 [40.7]	0.539‡	0.832ǂ
logQTvar, ms^2	2.13±0.36	2.15±0.25	2.09±0.34	0.767†	0.666†
QTVi, nu	0.30± [0.10]	0.18± [0.05]	0.33± [0.09]	0.143‡	0.193 ǂ
logQTVi, nu	-0.74 ± 0.40	-0.89 ± 0.37	-0.63 ± 0.38	0.167†	0.152†

Data are presented as mean ± standard deviation [or standard of error] and number (%)
OSA: Obstructive sleep apnea; BMI: Body mass index; AHI: Apnea/hypopnea index (/h); QTSD: Standard deviation of QT interval; QTvar: Variance of QT interval; QTVi: QT variability index
* Patients vs. controls
** Mild/moderate OSA vs. severe OSA
† Independent sample *t*-Test
‡ Chi-square test
ǂ Mann-Whitney U Test

3.1 DISCUSSION

The cardiovascular disease is of importance particularly among OSA patients. [12] Electrocardiogram (ECG) parameters including QT interval (QT) and QT dispersion (QTd) are usually applied to evaluate myocardial repolarization. [13, 14]

Based on results of the current study, we found no difference between OSA patients and controls in the measured QT interval metrics, neither an association between OSA severity and QT dynamicity.

We analyzed cardiac activity of only one hour of sleeping time (3-4 AM). In contrast, Baumert et al.[15] analyzed all consecutive 5-min ECG segments throughout the night which provides quasi-stationary conditions of RR and QT time series for all sleeping time. QTV may be affected by sleep stages due to sleep-related variations in autonomic function.[15-16] Baumert et al. also found that QT variability was elevated in 5-min epochs that contained sleep apnea events.[15] Therefore, it is important for the future studies to perform cardiac monitoring at the same time as polysomnography to be able to analyze QTV in different sleep stages and to evaluate temporal association between apnea/hypopnea events and QT variations. Shamsuzzaman et al. showed daytime increase in rate-corrected QT in OSA patients.[18] Accordingly, daytime monitoring will provide more comprehensive information about diurnal variation of QT in OSA patients.

Due to potential restrictions of the device, some of limitations in the study were unavoidable such as measuring RR interval (60 / heart rate) which is required to rate correction. This was a time-limited study. Therefore, it could not be carried out in a longer period of time.

REM sleep duration and REM density could affect both AHI and arrhythmic activity. However, this issue can be considered as a limitation of this study. [19]

Our results might also be affected by some technical aspects. ECG acquisition sampling rate in our study was lower than what is recommended for QTV analysis (≥500 Hz).[20] Measurement of QT interval, either manually or automatically by a software, is challenging. Most of the available systems utilize simple tangent and threshold methods and our method was also detection of each of the Q, R, S, and T points based a gradient-based algorithm. These techniques may be less efficient compared to techniques that use ECG waveforms with pre-defined templates.[20] There are still controversial issues such as necessity for excluding ectopic and subsequent beats, the preferred lead for QT measurement, necessity for rate correction, and increasing reproducibility by random sampling across long-term monitoring which requires further investigations.

CONCLUSION:

In summary, we found no significant difference between OSA patients and controls in QT variability. Studies with cardiac monitoring during various sleep stages as well as monitoring diurnal variations of QT interval are still required to better investigate QTV as a possible index of cardiac vulnerability toward arrhythmias in OSA patients.

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