Journal of Advances in Medicine and Medical Research

26(11): 1-5, 2018; Article no.JAMMR.41277
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

QT Interval Variability in Patients with Obstructive Sleep Apnea

Mohammad Hashemi Jazi[1], Babak Amra[2], Khadijeh Miadi[1*], Mansour Jahangiri[3], Ali Gholamrezaei[4], Faezeh Tabesh[1] and Mohammad Reza Yazdchi[5]

[1]Department of Cardiology, Isfahan University of Medical Sciences, Isfahan, Iran.
[2]Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
[3]Department of Cardiology, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran.
[4]Department of Chronic Diseases, Translational Research Center for Gastrointestinal Disorders, Metabolism and Ageing, University of Leuven, Leuven, Belgium.
[5]Department of Biomedical Engineering, Isfahan University of Medical Sciences, Isfahan, Iran.

Authors' contributions

This work was carried out in collaboration between all authors. Authors MHJ, BA and KM designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MJ and AG managed the analyses of the study. Authors FT and MRY managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2018/41277
Editor(s):
(1) Pietro Scicchitano, Cardiology Department, Hospital "F. Perinei" Altamura (Ba), Italy.
Reviewers:
(1) Eva Libman, McGill University, Canada.
(2) Gaurav Nigam, Clay County Hospital, USA.
Complete Peer review History: http://www.sciencedomain.org/review-history/25180

Opinion Article

Received 27th March 2018
Accepted 9th June 2018
Published 18th June 2018

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

**Corresponding author: E-mail: kh.miadi@yahoo.com;*

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 is associated with prolongation of the QT interval [2]. However, others found no difference between OSA patients and controls in QT interval [9,10]. Baumert et al. [11] reported an association between severity of OSA and QTV, reflecting alterations in cardiac sympathetic activity. We evaluated QTV in patients with newly diagnosed OSA and compared it with healthy controls.

2. MATERIALS 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/meanQT2)/(RRvar/meanRR2)], 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

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

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).

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 [15-17]. 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. [18] showed daytime increase in rate-corrected QT in OSA patients. 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.

4. 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.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard written ethical permission has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A, et al. Sleep apnea and cardiovascular disease: An American Heart Association/American College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing. J Am Coll Cardiol. 2008;52:686-717.
2. Camen G, Clarenbach CF, Stowhas AC, Rossi VA, Sievi NA, Stradling JR, et al. The effects of simulated obstructive apnea and hypopnea on arrhythmic potential in healthy subjects. Eur J Appl Physiol. 2013;113:489-96.
3. Korcarz CE, Peppard PE, Young TB, Chapman CB, Hla KM, Barnet JH, et al. Effects of obstructive sleep apnea and obesity on cardiac remodeling: The Wisconsin sleep cohort study. Sleep. 2016;39:1187-95.
4. Dimitri H, Ng M, Brooks AG, Kuklik P, Stiles MK, Lau DH, et al. Atrial remodeling in obstructive sleep apnea: Implications for atrial fibrillation. Heart Rhythm. 2012;9: 321-7.
5. Horner RL. Pathophysiology of obstructive sleep apnea. Journal of Cardiopulmonary Rehabilitation and Prevention. 2008;28(5): 289-98.
6. Viigimae M, Karai D, Pirn P, Pilt K, Meigas K, Kaik J. QT interval variability index and QT interval duration in different sleep stages: Analysis of polysomnographic recordings in nonapneic male patients. BioMed Research International; 2015.
7. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: Update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8:597-619.
8. Gillis AM, Stoohs R, Guilleminault C. Changes in the QT interval during obstructive sleep apnea. Sleep. 1991;14: 346-50.
9. Kilicaslan F, Tokatli A, Ozdag F, Uzun M, Uz O, Isilak Z, et al. Tp-e interval, Tp-e/QT ratio, and Tp-e/QTc ratio are prolonged in patients with moderate and severe obstructive sleep apnea. Pacing Clin Electrophysiol. 2012;35:966-72.
10. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, Patil SP, 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.
11. Berger RD, Kasper EK, Baughman KL, Marban E, Calkins H, Tomaselli GF. Beat-to-beat QT interval variability: Novel evidence for repolarization lability in ischemic and nonischemic dilated cardiomyopathy. Circulation. 1997;96: 1557-65.
12. Park DH, Shin CJ, Hong SC, Yu J, Ryu SH, Kim EJ, Shin HB, Shin BH. Correlation between the severity of obstructive sleep apnea and heart rate variability indices. Journal of Korean Medical Science. 2008;23(2):226-31.
13. Dursunoglu D, Dursunoğlu N, Evrengül H, Özkurt S, Kılıç M, Fisekci F, Kuru Ö, Delen

Ö. QT interval dispersion in obstructive sleep apnoea syndrome patients without hypertension. European Respiratory Journal. 2005;25(4):677-81.
14. Bilal N, Dikmen N, Bozkus F, Sungur A, Sarica S, Orhan I, Samur A. Obstructive sleep apnea is associated with increased QT corrected interval dispersion: The effects of continuous positive airway pressure. Brazilian Journal of Otorhinolaryngology; 2017.
15. Baumert M, Smith J, Catcheside P, McEvoy RD, Abbott D, Sanders P, et al. Variability of QT interval duration in obstructive sleep apnea: An indicator of disease severity. Sleep. 2008;31:959-66.
16. Penzel T, Kantelhardt JW, Lo CC, Voigt K, Vogelmeier C. Dynamics of heart rate and sleep stages in normals and patients with sleep apnea. Neuropsychopharmacology. 2003;28(Suppl 1):S48-53.
17. Boudreau P, Yeh WH, Dumont GA, Boivin DB. Circadian variation of heart rate variability across sleep stages. Sleep. 2013;36:1919-1928.
18. Shamsuzzaman A, Amin RS, van der Walt C, Davison DE, Okcay A, Pressman GS, et al. Daytime cardiac repolarization in patients with obstructive sleep apnea. Sleep Breath. 2015;19:1135-40.
19. Nigam G, Camacho M, Riaz M. Rapid Eye Movement (REM) rebound on initial exposure to CPAP therapy: A systematic review and meta-analysis. Sleep Science and Practice. 2017;1(1):13.
20. Baumert M, Porta A, Vos MA, Malik M, Couderc JP, Laguna P, et al. QT interval variability in body surface ECG: Measurement, physiological basis, and clinical value: Position statement and consensus guidance endorsed by the European Heart Rhythm Association Jointly with the ESC Working Group on Cardiac Cellular Electrophysiology. Europace. 2016;18:925-44.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/25180