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Disturbances on Patients with Obstructive Sleep
Apnea: Clinical Implications and Technical
Solution

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Cardiac arrhythmia and conduction disturbances on patients with obstructive sleep apnea: Clinical implications and technical solution

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Abstract.*Background:* Obstructive sleep apnea (OSA) or sleep-disordered breathing (SDB) were commonly seen among patients with cardiac rhythm disorders, and OSA is then presumed to operate as triggers cardiac arrhythmias and conduction disorders (ACDs). In OSA, the drop of peripheral oxygen saturation (SpO₂) over a few seconds as a result of an apnea or hypopnea events making the SpO₂ an OSA screening parameter. Despite the potential link between OSA and ACDs have been suggested and discussed for long, there has scarcely been reports. *Methodology:* The study describes the possible association of some significant ACDs and OSA in patients hospitalized for cardiovascular and/or pulmonary disorders, and in those who had been presumed to have cardiorespiratory disorders and passed the specialized examination in hospital outpatient department. Respiratory or cardiorespiratory polygraphy (rPG/crPG) was performed when appropriate divided patients into with OSA and without OSA subgroups. The 24-hour ambulatory ECG was done thereafter to identify ACDs on both with- and without OSA subgroups. *Results:* Of total 48 patients, the current study showed in the subgroup of 26 patients with OSA a more prevalent presence of ACDs including premature atrial complexes, sinus bradycardia, sinus pauses, premature ventricular complexes and paroxysmal atrial fibrillation, compared to otherwise similar subgroup of 22 patients without OSA. *Conclusion and Discussion:* The possible association should be further assessed by the indication of ambulatory ECG recording and that of crPG on subjects with or suspected of cardiorespiratory disorders and/or SDB. By looking for technical solution allowing concurrent use of crPG and ambulatory ECG recording, the efforts to have crPG and ECG recording or, to a lesser extent, certain relevant parameters/channels of these integrated in a common command unit might be medically sound, engineeringly feasible and cost-effective.

Keywords: ACD, OSA, 24-hour-ECG-monitoring, crPG, SpO₂

1 Background

Obstructive sleep apnea (OSA) or sleep disordered breathing (SDB) in general have been identified as common abnormalities in adults, especially in elderly. This situation increases with rising speed of population aging and increasing global epidemic of overweight/obesity rates (both in adults and children), and is close and strongly associated with chronic respiratory, cardiovascular and metabolic diseases and complications.^[1-17]

Obstructive sleep apnea has a high incidence, critical health and socioeconomic impact and pressure on health systems. Sleep apnea has been identified in association with a number of cardiovascular diseases and complications, among which, arrhythmias and conduction disturbances can lead to major events that increase morbidity and mortality, manifest in subjects without common symptoms suggestive of sleep apnea.^[1,2,5-7,18-24] Also, cardio-metabolic diseases (such as coronary artery disease, heart valve problems, heart failure, high blood pressure, non-alcoholic fatty liver diseases, diabetes, overweight/obesity) and respiratory diseases, associated or not with peripheral oxygen desaturation, have been identified as common triggers for many arrhythmias.^[25,26]

Cardiac arrhythmias or conduction disturbances such as ectopic beats (atrial and ventricular), non-sustained ventricular tachycardia, sinus arrest, intermittent or prolonged atrial fibrillation, sinoatrial block, 2nd degree atrioventricular (AV) block were seen in more than one-third of cases with obstructive sleep apnea, increased with the density and duration of apnea episodes, and the severity of associated hypoxia. Along with hypertension, myocardial ischemia, arrhythmias and conduction disturbances, if undetected, identified, and treated will lead to or worsen heart failure and may lead to major adverse cardiac events.^[27-30] 24-hour ECG monitoring has a high diagnostic value on subjects at high risk, allowing the identification of many arrhythmias, conduction disorders or ischemic states, abnormalities that may be difficult or not found on the ECG recorded at times during the day.^[2,31] Although there still remains limitations or inconsistent opinion on effectiveness of pathogenesis-based interventions, the identification of arrhythmic or conduction disturbances will help clinicians to have an overall management attitude to reduce the incidence of important cardiovascular and/or neurological complications (MACNEs).^[2,32]

For the above reasons, screening and identification of sleep apnea and arrhythmia in subjects with chronic respiratory, cardio-metabolic conditions would be combined indications localized and highly effective.^[1,33] Ignoring the inconsistent views of the pathogenetic relationship between OSA and the metabolic disorders, simply consider OSA as a risk factor for cardiovascular problems, and cardiovascular problems with chronic respiratory pathologies (in a common complex of co-morbidities) amplifies further the risk of cardiovascular-metabolic complications that exacerbate the patient condition and increase mortality. To help physicians in this complex association to make indications appropriately and effectively in clinical practice, in this and some other studies otherwise, we proactively call respiratory polygraphy as cardio-respiratory polygraphy. Instead of paying attention to the symptoms considered as suggestive of OSA, doctors will focus on patient medical history of respiratory (1), cardiovascular (2) and/or metabolic (3) disorders.^[18,23]

In addition to the clinical significance, the implementation of these two techniques, cardio-respiratory polygraphy and 24-hour ECG monitoring in in- and outpatients allows studying the combination of multiple conditions and abnormalities including OSA and SDB that were directly linked in the pathogenesis or related as cardiovascular risk factors in complex manner.^[2,34] Since mid-2018, in Haiphong University Hospital, these techniques have been implemented in Department of Cardiovascular medicine and Pulmonology. In combination with sleep apnea study allows the overall risk assessment of a patient with determined or suspected chronic respiratory diseases and /or cardio-metabolic disorders.

This study was conducted with overall goal of describing a combination of cardiac arrhythmia and conduction disorders and sleep apnea in patients with respiratory or cardiovascular-metabolic diseases hospitalized or followed in hospital OPD.

Methodology

A prospective study was combined partly with retrospective eligible cases, conducted on adult patients followed-up in outpatient or hospitalized in Haiphong University Hospital for identified or suspected with respiratory diseases and/or cardiovascular conditions. When appropriated, cardiopulmonary polygraphy and 24-hour ECG monitoring were indicated and performed in enrolled patients. The study did not include patients who were taking antiarrhythmic medications or interferred for or carrying pacemakers for arrhythmia or conduction disturbances. The sleep apnea was diagnosed using Philips Respironics Alice Night One device and its software. The 24-hour ECG was monitored by using ASPEL ECG Holter recorder AsPEKT with accessories and analyzed using HolCARD 24W software. Research content is limited to a number of parameters: general information about patients (age, gender, height, weight, waist circumference) (1); special comorbidities of chronic respiratory, cardiovascular and/or metabolic diseases (2); results of cardiopulmonary polygraphy (3); and results of 24-hour ECG monitoring (4).

Results

Out of 48 patients (25 men, 23 women) with median age of 62,5 (range 37-85), the majority of studied subjects were overweight (BMI > 23) or obesity (BMI > 25) according to the weight status according to the scale reported by the World Health Organization in Asia-Pacific Region and the International Diabetes Research Institute (IDI).

Table 1: Some descriptive characteristics of subjects

	Both genders	Men	Women
Frequency	48	25	23
Age, <i>median (range)</i>	62,5 (37 – 85)	62 (37 – 79)	63 (42 – 85)
BMI, <i>mean (SD)</i>	26,3 (2,7)	27,2 (3,3)	25,5 (1,9)
Waist circumference, <i>mean (SD)</i>	90,1 (8,4)	95,7 (6,7)	84,9 (6,2)

Most patients involved have more than one health problem in their medical history. The metabolic syndrome (MetS) components such as overweight, obesity, dyslipidemia (increased total cholesterol, triglycerides, decreased HDL-cholesterol), hypertension, prediabetes, diabetes) got high percentages. Nearly half of subjects were eligible for the diagnosis of metabolic syndrome. More than half of studied subjects (37/48) have cardiovascular disorders such as chronic coronary artery disease, hypertension, heart failure associated or not with other pathologic conditions. Over a fourth of the target group (13/48) have chronic respiratory disease. In addition, there are co-morbidities or complications such as chronic kidney disease, stroke, other symptoms and health issues.

Table2: Arrhythmia and conduction disturbances on 24-hour ECG monitoring

Subjects with sleep apnea	AHI (5-15]	AHI (15-30]	AHI > 30
Frequency (%)	6 (12,5)	16 (33,3)	4 (8,3)
Arrhythmia and conduction disturbances			
First degree AV blocks(<i>AVB1</i>)	0	0	1
Second degree AV blocks, Mobitz I (<i>AVB2-I</i>)	0	1	0
Bundle branch blocks	1	3	1
Disturbed cardiac repolarization	1	3	2
Cardiopause	0	2	1
Atrial fibrillation(<i>AFib/AF</i>)	1	3	1
Sinus/junctional bradycardia(<i>SVB</i>)	1	3	1
Paroxysmal supraventricular tachycardia(<i>PSVT</i>)	0	1	0
Supraventricular tachycardia(<i>SVT</i>)	0	2	1
Supraventricular premature complexes (<i>SVPC</i>)	1	3	1
Ventricular tachycardia(<i>VT</i>)	0	1	0
Junctional escape beats(<i>JEB/TVR</i>)	0	0	0
Prematured ventricular contractions(<i>PVC</i>)	1	5	2
PVC - Segments of bigeminy	1	2	2
PVC - Segments of trigeminy	1	2	1
PVC - Salvo events	0	1	1

24-hour ECG recording on patients with sleep apnea results in significant higher frequency of cases with arrhythmias and conduction disturbances compared to that observed in patients with out sleep apnea (15/26 vs 5/22). Nearly a half of patients with sleep apnea have more than one abnormalities on results of ECG monitoring, of which, there are abnormalities that need to be identified and appropriately managed. Typically, cases of SA block with ventricular depolarisation absence, of 1st degree atrioventricular (AV) block associated with a bradycardia that accounts for almost 100% of time monitored (average frequency is 42 bpm, lowest is 26 bpm, with many sinus arrests of above 3 seconds; of conduction disturbance and repolarization suspected of type I Brugada syndrome; other cases had multiple prolonged sinus arrest; cases of atrial fibrillation, some with sinus rhythm switching; cases of prematured ventricular contractions (PVCs) with dangerous R/T pattern, segments of bigeminy/trigeminy or of salvo events.

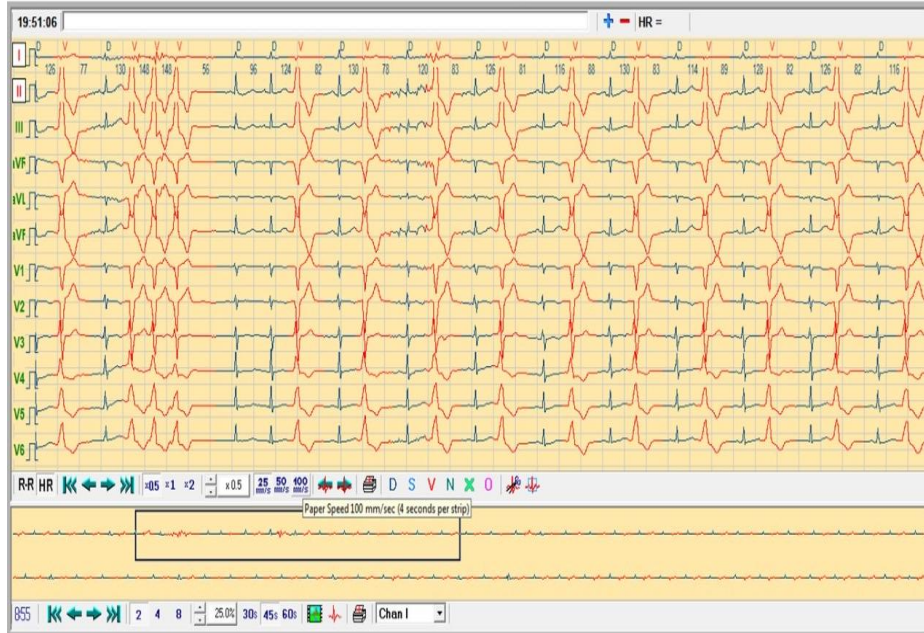


Fig. 1. Illustration of PVC: Segments of trigeminy/bigeminy with *salvo events*

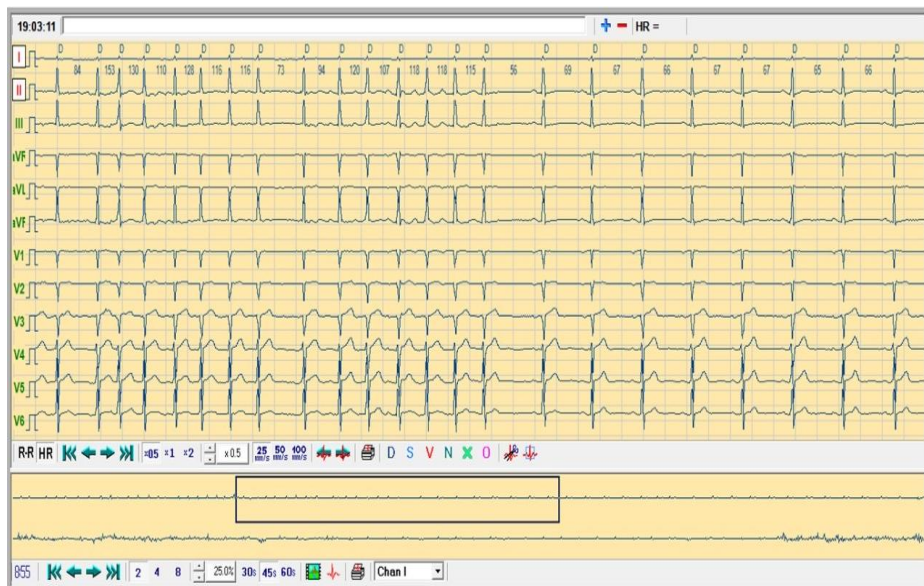


Fig. 2. Illustration of restoration of sinus rhythm in a patient with atrial fibrillation

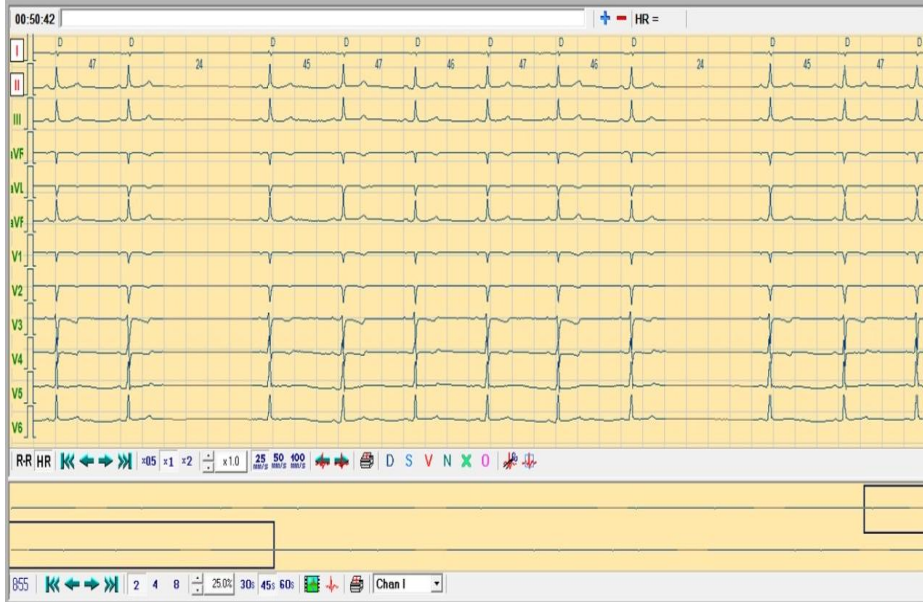


Fig. 3. Illustration of sinoatrial (SA) block

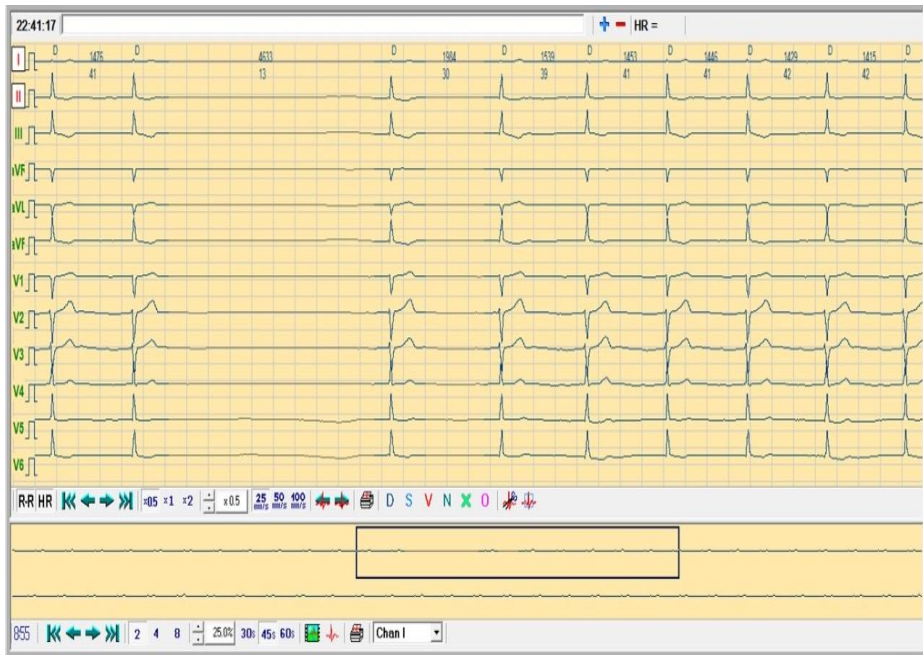


Fig. 4. Sinus bradycardia with prolonged sinus arrest

Discussions

This study illustrated the frequent arrhythmias and conduction disturbances on patients with OSA. A number of studies in the world about the combination of OSA and arrhythmia and sudden death during sleep show that patients with sleep apnea have an increased risk of arrhythmia during sleep time. The risk increases 2 to 4 times (or more) with bradycardic patterns are among the most common, seen more frequently during the period of dreaming when oxygen saturation may drop. A case-crossover study even showed an associated 18 fold-increased risk of nocturnal arrhythmia within 90 seconds of apneic or hypopneic events.^[10] Asystole can also occur at this stage in subjects who do not actually have atrioventricular conduction disturbances. Research literature showed that ventricular ectopic beats were very common in subjects with obstructive sleep apnea and often occur in apneic episodes. Continuous positive airway pressure (CPAP) ventilation support is determined to be effectively preventive. Beside OSA, central sleep apnea (CSA) was showed to be associated with increased risk for development of atrial fibrillation.^[2] Other studies in the elderly showed that the rate of atrial fibrillation (AFib) and premature ventricular contractions (PVCs) increased with the level (severity) of apnea.^[11,21,23]

The combination of arrhythmias and conduction disturbances with sleep apnea is very meaningful both for clinical practice and research and development activities in the field of sleep medicine. However, the direct correlation between cardiac arrhythmias and conduction abnormalities and sleep apnea could only be seen well when inputs from these two systems is recorded simultaneously as on polysomnographic systems (currently not yet widely equipped and deployed). In order to benefit from the simultaneous evaluation of respiratory and cardiovascular information, when clinical suspicion of at least one of the two conditions is warranted, analytical models on apnea or hypopnea from the ECG information recorded during sleep should be evaluated.^[35]

A characteristic feature associated with sleep apnea is the drop of peripheral oxygen saturation, leading to the idea of integrating minimally of an oxymetry channel into an ECG monitoring device to form combined device of ECG holter-oximetry to evaluate indirectly episodes of sleep apnea. Combined with the above systemic analytic model, it is possible to hope for an reliable assessment of sleep apnea at acceptable sensitivity and specificity by using both soft- and hardware solutions developed locally for reasonable first-set screening with benefits and cost-effectiveness in medical practice.^[36]

Reference

- [1] W. Randerath, C. L. Bassetti, M. R. Bonsignore, R. Farre, L. Ferini-Strambi, L. Grote, J. Hedner, M. Kohler, M. A. Martinez-Garcia, S. Mihaicuta, J. Montserrat, J. L. Pepin, D. Pevernagie, F. Pizza, O. Polo, R. Riha, S. Ryan, J. Verbraecken, and W. T. McNicholas, Challenges and perspectives in obstructive sleep apnoea: Report by an ad hoc working group of the Sleep Disordered Breathing Group of the European Respiratory Society and the European Sleep Research Society, *Eur. Respir. J.*, 52 (2018).
- [2] R. Mehra, Sleep apnea and the heart, *Cleve. Clin. J. Med.*, 86 (2019) 10-18.

- [3] A. N. Vgontzas, J. Gaines, S. Ryan, and W. T. McNicholas, CrossTalk proposal: Metabolic syndrome causes sleep apnoea, *J. Physiol*, 594 (2016) 4687-4690.
- [4] P. Levy, M. Kohler, W. T. McNicholas, F. Barbe, R. D. McEvoy, V. K. Somers, L. Lavie, and J. L. Pepin, Obstructive sleep apnoea syndrome, *Nat. Rev. Dis. Primers.*, 1 (2015) 15015.
- [5] R. S. Leung and T. D. Bradley, Sleep apnea and cardiovascular disease, *Am. J. Respir. Crit Care Med.*, 164 (2001) 2147-2165.
- [6] H. Schafer, U. Koehler, S. Ewig, E. Hasper, S. Tasci, and B. Luderitz, Obstructive sleep apnea as a risk marker in coronary artery disease, *Cardiology*, 92 (1999) 79-84.
- [7] T. Moore, T. Rabben, U. Wiklund, K. A. Franklin, and P. Eriksson, Sleep-disordered breathing in men with coronary artery disease, *Chest*, 109 (1996) 659-663.
- [8] X. Soler, E. Gaio, F. L. Powell, J. W. Ramsdell, J. S. Lored, A. Malhotra, and A. L. Ries, High Prevalence of Obstructive Sleep Apnea in Patients with Moderate to Severe Chronic Obstructive Pulmonary Disease, *Ann. Am. Thorac. Soc.*, 12 (2015) 1219-1225.
- [9] F. Dalgaard, R. North, K. Pieper, G. C. Fonarow, P. R. Kowey, B. J. Gersh, K. W. Mahaffey, S. Pokorney, B. A. Steinberg, G. Naccarrelli, L. A. Allen, J. A. Reiffel, M. Ezekowitz, D. E. Singer, P. S. Chan, E. D. Peterson, and J. P. Piccini, Risk of major cardiovascular and neurologic events with obstructive sleep apnea among patients with atrial fibrillation, *Am. Heart J.*, 223 (2020) 65-71.
- [10] K. Monahan, A. Storfer-Isser, R. Mehra, E. Shahar, M. Mittleman, J. Rottman, N. Punjabi, M. Sanders, S. F. Quan, H. Resnick, and S. Redline, Triggering of nocturnal arrhythmias by sleep-disordered breathing events, *J. Am. Coll. Cardiol.*, 54 (2009) 1797-1804.
- [11] A. S. Hersi, Obstructive sleep apnea and cardiac arrhythmias, *Ann. Thorac. Med.*, 5 (2010) 10-17.
- [12] S. Ancoli-Israel, D. F. Kripke, M. R. Klauber, W. J. Mason, R. Fell, and O. Kaplan, Sleep-disordered breathing in community-dwelling elderly, *Sleep*, 14 (1991) 486-495.
- [13] C. Cuspidi, M. Tadic, C. Sala, E. Gherbesi, G. Grassi, and G. Mancia, Blood Pressure Non-Dipping and Obstructive Sleep Apnea Syndrome: A Meta-Analysis, *J. Clin. Med.*, 8 (2019).

- [14] S. J. Crinion, S. Ryan, J. Kleinerova, B. D. Kent, J. Gallagher, M. Ledwidge, K. McDonald, and W. T. McNicholas, Nondipping Nocturnal Blood Pressure Predicts Sleep Apnea in Patients With Hypertension, *J. Clin. Sleep Med.*, 15 (2019) 957-963.
- [15] E. O'Brien and E. Dolan, Ambulatory Blood Pressure Measurement in the Elderly, Hypertension, 73 (2019) 961-964.
- [16] F. Roche, Arrhythmias and conduction disturbances in obstructive sleep apnoea: the heart of the problem?, *Eur. Respir. J.*, 41 (2013) 1244-1246.
- [17] K. Todd, W. F. McIntyre, and A. Baranchuk, Obstructive sleep apnea and atrial fibrillation, *Nat. Sci. Sleep*, 2 (2010) 39-45.
- [18] B. Ustun, M. B. Westover, C. Rudin, and M. T. Bianchi, Clinical Prediction Models for Sleep Apnea: The Importance of Medical History over Symptoms, *J. Clin. Sleep Med.*, 12 (2016) 161-168.
- [19] X. Soler, S. Y. Liao, J. M. Marin, G. Lorenzi-Filho, R. Jen, P. DeYoung, R. L. Owens, A. L. Ries, and A. Malhotra, Age, gender, neck circumference, and Epworth sleepiness scale do not predict obstructive sleep apnea (OSA) in moderate to severe chronic obstructive pulmonary disease (COPD): The challenge to predict OSA in advanced COPD, *PLoS. One.*, 12 (2017) e0177289.
- [20] J. Shen, J. Barbera, and C. M. Shapiro, Distinguishing sleepiness and fatigue: focus on definition and measurement, *Sleep Med. Rev.*, 10 (2006) 63-76.
- [21] K. Kadhim, M. E. Middeldorp, A. D. Elliott, D. Jones, J. M. L. Hendriks, C. Gallagher, M. Arzt, R. D. McEvoy, N. A. Antic, R. Mahajan, D. H. Lau, C. Nalliah, J. M. Kalman, P. Sanders, and D. Linz, Self-Reported Daytime Sleepiness and Sleep-Disordered Breathing in Patients With Atrial Fibrillation: SNOozE-AF, *Can. J. Cardiol.*, 35 (2019) 1457-1464.
- [22] P. E. Peppard, T. Young, J. H. Barnet, M. Palta, E. W. Hagen, and K. M. Hla, Increased prevalence of sleep-disordered breathing in adults, *Am. J. Epidemiol.*, 177 (2013) 1006-1014.
- [23] K. Kadhim, D. H. Lau, P. Sanders, and D. Linz, Sleep apnea in atrial fibrillation - Highly prevalent, highly relevant, but most patients are not somnolent!, *Int. J. Cardiol. Heart Vasc.*, 26 (2020) 100463.
- [24] M. W. Johns, A new method for measuring daytime sleepiness: the Epworth sleepiness scale, *Sleep*, 14 (1991) 540-545.
- [25] A. J. Thomas and P. Valabhji, Arrhythmia and tachycardia in pulmonary heart disease, *Br. Heart J.*, 31 (1969) 491-495.

- [26] Y. Kusunoki, T. Nakamura, K. Hattori, T. Motegi, T. Ishii, A. Gemma, and K. Kida, Atrial and Ventricular Arrhythmia-Associated Factors in Stable Patients with Chronic Obstructive Pulmonary Disease, *Respiration*, 91 (2016) 34-42.
- [27] C. Viljoen, R. Smith, and A. Chin, Reviewing the causes of electrocardiographic pauses, *Cardiovasc. J. Afr.*, 28 (2017) 257-260.
- [28] G. R. Geovanini and G. Lorenzi-Filho, Cardiac rhythm disorders in obstructive sleep apnea, *J. Thorac. Dis.*, 10 (2018) S4221-S4230.
- [29] A. R. Patel, A. R. Patel, S. Singh, S. Singh, and I. Khawaja, The Association Between Obstructive Sleep Apnea and Arrhythmias, *Cureus.*, 11 (2019) e4429.
- [30] N. Patel, C. Donahue, A. Shenoy, A. Patel, and N. El-Sherif, Obstructive sleep apnea and arrhythmia: A systemic review, *Int. J. Cardiol.*, 228 (2017) 967-970.
- [31] P. Hanly, Z. Sasson, N. Zuberi, and K. Lunn, ST-segment depression during sleep in obstructive sleep apnea, *Am. J. Cardiol.*, 71 (1993) 1341-1345.
- [32] S. A. Di Fusco, C. Pignalberi, L. Santini, F. Colivicchi, and M. Santini, Arrhythmias and sleep apnea: physiopathologic link and clinical implications, *J. Interv. Card Electrophysiol.*, 57 (2020) 387-397.
- [33] K. Bibbins-Domingo, D. C. Grossman, S. J. Curry, K. W. Davidson, J. W. Epling, Jr., F. A. Garcia, J. Herzstein, A. R. Kemper, A. H. Krist, A. E. Kurth, C. S. Landefeld, C. M. Mangione, W. R. Phillips, M. G. Phipps, M. P. Pignone, M. Silverstein, and C. W. Tseng, Screening for Obstructive Sleep Apnea in Adults: US Preventive Services Task Force Recommendation Statement, *JAMA*, 317 (2017) 407-414.
- [34] J. R. Tietjens, D. Claman, E. J. Kezirian, M. T. De, A. Mirzayan, B. Sadroonri, A. N. Goldberg, C. Long, E. P. Gerstenfeld, and Y. Yeghiazarians, Obstructive Sleep Apnea in Cardiovascular Disease: A Review of the Literature and Proposed Multidisciplinary Clinical Management Strategy, *J. Am. Heart Assoc.*, 8 (2019) e010440.
- [35] T. Penzel, J. McNames, A. Murray, C. P. de, G. Moody, and B. Raymond, Systematic comparison of different algorithms for apnoea detection based on electrocardiogram recordings, *Med. Biol. Eng Comput.*, 40 (2002) 402-407.
- [36] C. P. de, C. Heneghan, and W. T. McNicholas, Multimodal detection of sleep apnoea using electrocardiogram and oximetry signals, *Philos. Trans. A Math. Phys. Eng. Sci.*, 367 (2009) 369-389.