Occurrence of sleep related breathing disorders in Egyptian patients with tachyarrhythmia without heart failure

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Received 26 July 2016; accepted 27 September 2016

Abstract Obstructive sleep apnea hypopnea syndrome (OSAHS) has been implicated in the pathogenesis of many cardiovascular diseases. Over the last decade, the association between OSAHS and cardiac rhythm disorders has garnered the attention of cardiologists and researchers from different clinical subspecialties.

Aim of the work: The aim of the study was to assess the occurrence of OSAHS in Egyptian patients with tachyarrhythmia, and to describe characteristics of patients with concomitant OSAHS and tachyarrhythmia.

Methods: We enrolled 32 patients with tachyarrhythmia. In addition to standard examination, investigations and echocardiography to exclude possible causes for arrhythmia all patients underwent an over-night sleep study (level III) to diagnose OSAHS. Manual scoring was performed by two specialists according to criteria established by the American Academy of Sleep Medicine 2012. We considered AHI of 15/h as a cutoff point for diagnosing OSAHS.

Results: Of the 32 patients: seventeen had rapid atrial fibrillation (AF), eight had premature ventricular contractions, five had persistent sinus tachycardia and three had paroxysmal supraventricular tachycardia. OSAHS was present in 27 patients (84.4%), three patients of them had obesity hypoventilation also. Dividing OSAHS patients according to the disease severity showed that moderate OSAHS in 29.6% patients, and severe OSAHS in 70.4% patients. Studying characteristics of patients with OSAHS revealed that the mean ± SD of neck circumference (NC) was 39.9 ± 2.47 cm, BMI was 36.3 ± 9.17 kg/m 2, Waist/hip ratio was 0.91 ± 0.08, Epworth Sleepiness Scale (ESS) was 10.85 ± 4.5, Mallampati score (MS) was 2.11 ± 0.84, clinical apnea score was 2.8 ± 1.5, and STOP BANG score was 4.03 ± 1.99. Apnea hypopnea index (AHI) was 49.3 ± 33.2, oxygen desaturation index [3%] (ODI) was 39.9 ± 31, mean O2 saturation was 93.6 ± 8.84 and minimal O2 saturation was 7.9 ± 14.49. Nocturnal bradytachyarrhythmia was found in most of patients, the minimal pulse rate during sleep ranges from 22 to 82/min while the maximal

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

http://dx.doi.org/10.1016/j.ejcdt.2016.09.005
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Introduction

Cardiac tachyarrhythmias are important epidemiological and public health problems as they are significantly associated with increased risks of cardiovascular complications and sudden death [1], consequently leading to decreased quality of life, disability, high mortality, and healthcare expense [2].

Obstructive sleep apnoea hypopnea syndrome (OSAHS) is the most common variant of SRBD. It affects 3–7% of men and 2–5% of women in the general adult population. Although OSAHS is a common disabling syndrome, yet it is still under-diagnosed [3].

Obstructive sleep apnoea hypopnea syndrome has been implicated in the pathogenesis of many cardiovascular diseases [4]. Over the last decade, the association between OSAHS and cardiac rhythm disorders has garnered the attention of cardiologists and researchers from different clinical subspecialties [5].

Tachyarrhythmias are presumed to be a common problem in patients with OSAHS. It is hypothesized that tachyarrhythmias can also occur in OSAHS even in the absence of heart failure and structural heart diseases [6]. The notion that OSAHS may originate tachyarrhythmia is attractive, but unfortunately the incidence and prevalence of SRBD in patients with tachyarrhythmia is poorly defined, in part due to smaller number of studies and also the fact that the two conditions share many of the same risk factors, such as age, obesity, male sex, hypertension, coronary disease, and heart failure, makes it difficult to control potential confounders and to establish a clear independent causal relationship between them [7].

Aim of the work

To study the occurrence of OSAHS in Egyptian patients with tachyarrhythmia, and to describe characteristics of patients with concomitant OSAHS and tachyarrhythmia.

Subjects and methods

Study population and subjects

Study population included thirty-two patients with tachyarrhythmia diagnosed on the basis of current American College of Cardiology, American Heart Association, and European Heart Society guidelines. Patients were enrolled over 18 months (April 2012–Sept 2013) from Maamoura Chest Hospital, Alexandria University Hospital, Kom Aishokafa Hospital and Alexandria petroleum Hospital.

Inclusion was not based on any clinical suspicion of underlying SRBD, patients were selected irrespective of age, gender or BMI. We excluded patients with structural heart diseases, LVEF < 50%, myocarditis, pericarditis and patients with acute coronary insult. We also excluded patients with arrhythmia due to a transient or reversible cause and drug induced tachyarrhythmia.

The study protocol was approved by the local ethics committee, and informed consents were obtained.

Study measurements

Critical care specialists had examined all patients as regards to clinical examination, ECG monitoring, echocardiography, plain chest x-rays and laboratory results. All patients were on anti-arrhythmic drugs.

All patients were subjected to the following

1. History taking including symptoms related to tachyarrhythmia and its possible causes, in addition to comprehensive sleep related complains and questionnaire including Epworth Sleepiness Scale [8], STOP BANG questionnaire: [9] and Clinical apnea score [10].

2. Full clinical examination including Mallampati score.

3. Anthropometric measurements including: Body mass index (BMI) [11], Neck circumference (NC), and Waist/hip ratio (WHR).

4. In addition to routine laboratory investigations arterial blood gases and lipid profile were assessed.

5. Sleep Study: Cardio respiratory screening (polygraph) using level 3 device (Sleep Test-Polymate YH-1000 Sleep Screener). We used a portable screener which helps to eliminate the first night fear and make the patient more comfortable.

The polymate sleep screener device evaluates: (a) Nasal airflow via a nasal cannula attached to a small case that houses a pressure transducer. (b) Arterial oxygen saturation and pulse rate measured using finger pulse sensor and pulse oximeter. (c) Snoring via a microphone attached to the device. (d) Body position through abdominal belt containing a built-in sensor for body position. (e) Chest and abdominal movement via two chest leads and two abdominal leads.
Manual scoring was performed for all patients. Apneas and hypopneas scored using criteria established by the American Academy of Sleep Medicine 2012. [12] Apnea was considered when there is drop in the flow excursion by ≥90% of baseline for at least ten seconds and hypopnea was defined when there is drop by ≥30% of baseline and associated with ≥3% desaturation from pre-event baseline for at least 10 s. Obstructive apnea was scored if apnea is associated with continued inspiratory effort throughout the entire period of absent airflow and Central apnea was scored if it is associated with absent inspiratory effort throughout the entire period of absent airflow while Mixed apnea is considered if the apnea starts as a central event and then becomes obstructive during the latter portion of the same episode. Obstructive hypopnea was considered if associated with either of snoring, flow limitation or paradoxical movement of the respiratory muscles while central hypopnea is considered if all of the three criteria were absent. Hypoventilation was considered when there was sustained decrease of SpO2 as detected by the oximeter (sagging of the oximetric tracing) while the patient is on room air and not receiving any supplemental oxygen [13].

The following parameters were calculated: Apnea hypopnea index (AHI), baseline O2 saturation, mean O2 saturation, minimal O2 saturation, oxygen desaturation index 3% (ODI 3%), 90%, and snoring index. Also minimal pulse rate, maximum pulse rate and average pulse rate.

Clinically, OSAHS is defined by the occurrence of daytime sleepiness, loud snoring, witnessed breathing interruptions, or awakenings due to gasping or choking in the presence of at least 5 obstructive respiratory events (apneas, hypopneas or respiratory effort related arousals) per hour of sleep. The presence of 15 or more obstructive respiratory events per hour of sleep while Mixed apnea is considered if the apnea starts as a central event and then becomes obstructive during the latter portion of the same episode. Obstructive hypopnea was considered if associated with either of snoring, flow limitation or paradoxical movement of the respiratory muscles while central hypopnea is considered if all of the three criteria were absent. Hypoventilation was considered when there was sustained decrease of SpO2 as detected by the oximeter (sagging of the oximetric tracing) while the patient is on room air and not receiving any supplemental oxygen [13].

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Statistical analysis

The raw data were coded and transformed into coding sheets. The results were checked. Then, the data were entered into SPSS system files (SPSS package version 18) using personal computer. Analysis and interpretation of data were conducted. Exploration of the data yielded:

(a) Complete descriptive statistics including the minimum and maximum, range, mean, median and inter-quartile range for each variable.

(b) Normality test was performed and as all variables resulted in insignificant Kolmogorov–Smirnov (KS) so, normally distributed variables were analyzed using parametric analysis.

- Data were described using minimum, maximum, mean and standard deviation.
- Box and Whiskers graph was used in all variables regardless of normality.
- Parametric correlation using Pearson’s correlation was used.

(c) Logistic regression analysis was done to predict patients with tachyarrhythmia and OSAHS. Different studied parameters were measured. All predictor variables were initially entered into this analysis as continuous variables then the backward conditional analysis was performed.

Results

The present study was carried out on randomly selected (irrespective of age and gender) thirty-two patients with tachyarrhythmia of unknown etiology.

Electrocardiogram characteristics

According to ACC/AHA guidelines [15] the following types of arrhythmia have been encountered: Seventeen patients had rapid atrial fibrillation. (2 had paroxysmal, 1 had persistent and 14 had permanent AF), eight patients had premature ventricular contractions (one had bigeminy and 7 had multifocal), five patients had persistent sinus tachycardia and three patients had paroxysmal supraventricular tachycardia (case 14 had both rapid AF and multifocal PVCs).

According to symptoms and sleep study the patients were divided into two groups (Fig. 1)

Group I: OSAHS patients

27 patients with AHI ≥15/hr. (84.4%): Eight patients had moderate OSAHS and nineteen patients had severe OSAHS; three of those patients had OHS in addition.

Group II: Five patients did not fulfill the criteria of OSAHS diagnosis

Two had AHI <5/hr and three had AHI from 5–15/hr in the absence of sleep related complaints.

Due to the very small sample size of group II patients (n = 5) which implies low statistical significance, comparison and parametric correlations were done in group I patients only.

Table 1 shows the results of demographic, anthropometric data, different scores and scales examined, presence or absence of related cardiovascular and metabolic disorders and laboratory investigations in the studied patients.

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Table 1 shows the results of demographic, anthropometric data, different scores and scales examined, presence or absence of related cardiovascular and metabolic disorders and laboratory investigations in the studied patients.

Regarding types of tachyarrhythmias in patients of group I, thirteen patients were admitted due to AF; eleven of them were having permanent AF, one persistent and one paroxysmal AF. Five patients suffer from sinus tachycardia, seven patients suffer from multifocal premature ventricular contractions and three patients suffer from paroxysmal supraventricular tachycardia. Patient number 14 was suffering from both Paroxysmal AF and M.PVCs.

Table 2 shows the sleep study and arterial blood gases data in both groups. Apnea hypopnea index and ODI3% values were presented in box plot diagram (Fig. 2). Also minimal, mean and maximal heart rates during sleep are presented in Fig. 3. Using the OSAHS severity classification which is defined as mild for AHI ≥5/h and <5/h, moderate for AHI ≥15/h and ≤30/h, severe for AHI >30/h. [24] None was diagnosed as having mild OSAHS, eight had moderate OSAHS (29.6%), 19 had severe OSAHS (70.4%), (Fig. 1) three
of the patients with severe OSAHS had obesity hypoventilation syndrome in addition. None of the included patients had central sleep apnea.

Linear correlation between different studied parameters measured for patients of group I revealed the following statistically significant correlations:

Both body mass index and neck circumference were correlated directly with each of apnea hypopnea index, (AHI) \( p = 0.018 \) and \( < 0.0001 \) (Figs. 4 and 5 respectively), oxygen desaturation index (ODI) \( p = 0.011 \) and \( < 0.0001 \), baseline oxygen saturation \( p = 0.009 \) and 0.045, mean oxygen saturation \( p = 0.008 \) and 0.014, minimal oxygen saturation \( p = 0.004 \) and 0.010, and 190 \( p = < 0.0001 \) and 0.002.

AHI was correlated directly with each of mean pulse rate during sleep \( p = 0.002 \), serum cholesterol \( p = 0.004 \), triglycerides \( p < 0.0001 \) (Fig. 6), and fasting blood glucose \( p < 0.0001 \).

Table 1 Demographic, anthropometric data, different scores and scales examined, presence of related cardiovascular and metabolic disorders and laboratory investigations in the studied patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>44.2 ± 10</td>
<td>33 ± 6.63</td>
</tr>
<tr>
<td>Sex (Male: Female) (ratio)</td>
<td>1:2</td>
<td>2:3</td>
</tr>
<tr>
<td>BMI</td>
<td>36.39 ± 9.1</td>
<td>27.2 ± 6.01</td>
</tr>
<tr>
<td>Neck circumference</td>
<td>39.9 ± 2.47</td>
<td>35.4 ± 1.67</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>0.92 ± 0.08</td>
<td>0.78 ± 0.076</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ex-smoker (n)</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Non smoker (n)</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>Mallampati score</td>
<td>2.11 ± 0.84</td>
<td>5.6 ± 1.67</td>
</tr>
<tr>
<td>Epworth Sleepiness Scale</td>
<td>10.85 ± 4.528</td>
<td>0.4 ± 0.54</td>
</tr>
<tr>
<td>Clinical Apnea Score</td>
<td>2.11 ± 0.847</td>
<td>0.6 ± 0.54</td>
</tr>
<tr>
<td>STOP BANG</td>
<td>4.03 ± 1.992</td>
<td>4.03 ± 1.992</td>
</tr>
<tr>
<td>Other related disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (n)</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Ischemic heart disease (n)</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Pulmonary hypertension (n)</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Diabetes Mellitus (n)</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Metabolic syndrome (n)</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td>Serum Cholesterol</td>
<td>181.9 ± 31.1</td>
<td>127.6 ± 40.7</td>
</tr>
<tr>
<td>Serum Triglycerides</td>
<td>169.7 ± 47.3</td>
<td>115 ± 14.8</td>
</tr>
<tr>
<td>Fasting Blood Glucose</td>
<td>155.5 ± 94.6</td>
<td>86.6 ± 11.8</td>
</tr>
</tbody>
</table>

M: male; F: female; NS: never-smoker; XS: ex-smoker; BMI: body mass index; NC: Neck circumference; W/H ratio: waist/hip ratio; n: number of patients.

Linear regression analysis of potential predictors of increased apnea hypopnea index in the studied patients with tachyarrhythmia

Stepwise regression analysis was performed. Predictors entered in model are age, BMI, NC, Serum TG, Diastolic BP, Mini-
Occurrence of sleep related breathing disorders in Egyptian patients with tachyarrhythmia without heart failure.

Table 2: The sleep study and arterial blood gases data in studied patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean ± SD</td>
<td>Min–Max</td>
</tr>
<tr>
<td>AHI n/h</td>
<td>49.3 ± 33.2</td>
<td>15–133</td>
</tr>
<tr>
<td>Baseline O₂ saturation (%)</td>
<td>93.6 ± 6.36</td>
<td>65–99%</td>
</tr>
<tr>
<td>Mean O₂ saturation (%)</td>
<td>93.6 ± 8.84</td>
<td>65–97%</td>
</tr>
<tr>
<td>Minimal O₂ saturation (%)</td>
<td>77.9 ± 14.49</td>
<td>31–93%</td>
</tr>
<tr>
<td>ODI (4%) n/h</td>
<td>28.4 ± 32.13</td>
<td>2.4–110</td>
</tr>
<tr>
<td>ODI (3%)</td>
<td>39.9 ± 31</td>
<td>8–120</td>
</tr>
<tr>
<td>T90% (%)</td>
<td>11.1 ± 26.7</td>
<td>0–100%</td>
</tr>
<tr>
<td>Snoring index</td>
<td>247.3 ± 294</td>
<td>5–927</td>
</tr>
<tr>
<td>Minimum pulse rate</td>
<td>43.3 ± 13.9</td>
<td>22–82</td>
</tr>
<tr>
<td>Maximum pulse rate</td>
<td>115.7 ± 37.8</td>
<td>77–254</td>
</tr>
<tr>
<td>Mean pulse rate</td>
<td>77.7 ± 15.3</td>
<td>45–111</td>
</tr>
<tr>
<td>pH</td>
<td>7.37.6 ± 0.02</td>
<td>7.32–7.42</td>
</tr>
<tr>
<td>PaCO₂ mmHg</td>
<td>42.8 ± 7.2</td>
<td>37–68</td>
</tr>
<tr>
<td>PaO₂ mmHg</td>
<td>88.8 ± 12.9</td>
<td>46–99</td>
</tr>
<tr>
<td>HCO₃ mEq/L</td>
<td>25 ± 3.3</td>
<td>22–36</td>
</tr>
</tbody>
</table>

Figure 2: Box plot: apnea hypopnea index and oxygen desaturation Index 3% in OSAHS patients.

Figure 3: Maximum, mean and minimum pulse rate during sleep in OSAHS patients.

Figure 4: Correlation between Body mass index and apnea hypopnea index in OSAHS patients.

Figure 5: Correlation between neck circumference and apnea hypopnea index in OSAHS patients.

Mean pulse rate, Mean pulse rate. Three models were carried out and we adopted model “3”. Partial correlation proved there is no multicollinearity (r never exceed 0.85). Residual errors proved to be independent (Durbin Watson = 2.104).

Multiple regression analysis was used to develop a model to predict the presence of OSAHS in patients with tachyarrhythmia. Each of the predictor variables entered in the multiple regression analysis had a significance of $p < 0.01$. We adopted three models of which model “3” (BMI + NC + serum triglycercides) yielded the highest predictive value ($r^2 = 0.886$, adjusted $r^2 = 0.871$, std error = 9.83). Multiple regression analysis results suggest that patients with tachyarrhythmia...
who have higher BMI, NC and triglycerides values are more likely to have underlying OSAHS (Table 3).

Discussion

In the present study we examined 32 patients, admitted to the hospital due to tachyarrhythmia, for presence of obstructive sleep apnea. Only 5 patients (15.6%) didn’t fulfill the criteria for diagnosing OSAHS, while 27 patients (84.4%) were diagnosed as having OSAHS.

Other studies have evaluated the potential independent relationship between OSAHS and cardiac tachyarrhythmia. The first report was published in 2004 by Porthan et al. [16] who studied the prevalence of sleep apnea syndrome in 59 patients with lone AF. They found that the prevalence of sleep apnea syndrome in the AF group was 32%, which did not differ much from that in the control subjects (29%, p = 0.67).

The previous study was soon contradicted by Gami et al. [17] who prospectively assessed the risk of OSAHS (using Berlin questionnaire) in 2 groups of patients, group I included 151 patients with AF who were referred for cardioversion, while group II is the general cardiology group (with no past or current AF) and those included 373 patients. Both groups had statistically similar gender distribution, age, body mass index, and rates of diabetes, hypertension, and congestive heart failure. OSAHS was significantly higher in the AF group than in the general cardiology group (49% versus 32%, P = 0.0004).

Braga et al. [18] evaluated SRBD – using polysomnography – in 52 chronic AF patients 32 control. Considering a cut-off value for AHI ≥10/h of sleep, the AF group had a higher frequency of OSAHS compared to the control group (81.6% versus 60%, p = 0.03).

Stevenson et al. [19] investigated the prevalence of SRBD in 90 patients with paroxysmal or permanent AF and compared this with 45 control patients who had cardiac arrhythmia other than atrial fibrillation. The proportion of patients with significant SRBD (AHI >15/h) was significantly higher in the AF group than in the control population (62% versus 38% respectively, P = 0.01). Apnea hypopnea index in AF patients was higher than in controls (23.19 ± 19.26 versus 14.66 ± 12.43, P = 0.01) [19].

In 2009, Bitter et al. [20] investigated the prevalence of sleep disordered breathing in 150 patients with AF and normal systolic left ventricular function. SRBD was documented in 74% of all patients with AF (43% had OSAHS and 31% had CSA/CSB) [20].

Comparing our results with the results of the previously mentioned studies, we find that the prevalence of OSAHS in patients with tachyarrhythmia is higher in the present study. This may be related to higher BMI values in our patients or because we included all types of tachyarrhythmia. However, if we excluded non-AF patients and included only patients with AF, the proportion of patients with OSAHS would be 76% (13 out of 17 patients) which is comparable with Stevenson, Bitter and Braga et al. results.

Another explanation for the higher prevalence of OSAHS in the present study may be related to the new rules of manual scoring we used [12]. We considered hypopnea when there was only ≥3% desaturation in association with ≥30% decrease in the amplitude of the airflow which may lead to increase in hypopnea index.

Although Porthan et al. results showed no difference between AF group and control group, yet results did find a high prevalence of sleep apnea syndrome in patients with lone AF (32% had sleep apnea syndrome). One would presume that our results are higher because we did not exclude patients with hypertension, ischemic heart disease nor diabetes. This assumption was taken into consideration, and we found that if we excluded patients who were either hypertensive, ischemic or diabetic, 10 patients out of 14 (71%) have OSAHS. Also a limitation in Porthan et al. study is that the control group was derived from respondents to a letter, 43% of which were not answered. As other authors point out [19]; this raises the possibility of bias in the control group toward those with symptoms.

In 2015, Lavergne et al. concluded that inclusion of SDB recognition and management strategies as part of AF management appears to have the potential to reduce the impact of this arrhythmia at both the individual and societal levels, and it should be recognized as important in recent guidelines [21].

In the present study, sixteen patients had tachyarrhythmia other than AF; fifteen of those patients (93.7%) had OSAHS; seven out of eight patients with PVCs had OSAHS, all patients with chronic sinus tachycardia and paroxysmal supraventricular tachycardia were diagnosed as having OSAHS.

<table>
<thead>
<tr>
<th>Model 3</th>
<th>Unstandardized coefficients</th>
<th>95% Confidence interval for B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B</td>
<td>Std. Error</td>
</tr>
<tr>
<td>(Constant)</td>
<td>−194.884</td>
<td>42.6594</td>
</tr>
<tr>
<td>TG</td>
<td>0.325</td>
<td>0.0</td>
</tr>
<tr>
<td>NC</td>
<td>5.137</td>
<td>1.436</td>
</tr>
<tr>
<td>BMI</td>
<td>−0.633</td>
<td>0.285</td>
</tr>
</tbody>
</table>
Likewise, Stevenson et al. [22] conducted a study to evaluate the prevalence of SRBD in patients with severe ventricular arrhythmias and normal LV systolic function. They found that 60% had SRBD with AHI ≥ 10/h, and 34% had moderate to severe SRBD, with an average AHI of 33.6 ± 16.6/h. Central dominant sleep apnea was evident in 3 patients with SRBD.

The results of the present study suggest a link between OSAHS and both AF and non AF tachyarrhythmia. Some authors speculated that oxygen desaturation accompanied by surge in arterial blood pressure and sympathetic nerve activity, which attain levels observed during waking is responsible for these arrhythmias. [23,24]. In a previous study [25] we found that urinary norepinephrine was significantly higher in early morning samples than sample derived before sleep in OSAHS patients suffering from cardiac arrhythmia, and that norepinephrine levels were decreased significantly in samples derived while the patients were using CPAP.

Whether it is the acute effects of respiratory events or the chronic structural changes resulting from OSA that cause recurrent atrial fibrillation may have important therapeutic implications. If it is the former, specific treatment of OSA with CPAP or any other effective therapy may be needed to reduce risk of recurrence. While if it is the autonomic effects of acute apneic events that trigger recurrent atrial fibrillation, there may be effective alternatives to prevent OSA-related recurrence using pharmacologic modalities, renal sympathetic denervation, or modification of the ablation procedure.

Many studies – in a reverse way – have investigated the occurrence of cardiac arrhythmia in patients with OSAHS [26,27]. As early as 1983, Guilleminault et al. [26] studied the occurrence of cardiac arrhythmia in 400 patients with OSAHS. Results showed that 19% of OSAHS patients had the occurrence of cardiac arrhythmia in 400 patients with OSAHS patients suffering from cardiac arrhythmia, and that norepinephrine levels were decreased significantly in samples derived while the patients were using CPAP.

None of the patients included in the present study had central sleep apnea (CSA), this is mostly due to the prior exclusion of congestive heart failure as a potential cause for arrhythmia. Likewise, Stevenson et al. [19] who studied SRBD in AF with normal LVEF and found that CSA was zero%.

However, Bitter et al. results [20] showed an increased prevalence of CSA/CSB (31.3%) in patients with AF and normal global systolic LVF. Also Koshino et al. [22] found evidenced CSA in 3 out of 35 patients with ventricular tachyarrhythmia and normal LVF.

“Is sleep apnea a primary etiologic factor for the development of arrhythmia?” This question is fundamental in the field of “sleep apnea-related cardiovascular diseases”. In the present study, the former question motivated us to exclude – so did previously mentioned studies - possible cofounders that might cause arrhythmia. Yet, it is difficult to control common risk factors particularly obesity. These practical constraints had led to more rigorous study of the assumed “independent” relationship between OSAHS and tachyarrhythmia, directly and indirectly (by studying the effect of OSAHS treatment on cardiac arrhythmia).

Camen et al. [28] examined the effects of “simulated” obstructive apnea and hypopnea on arrhythmic potential in 41 healthy volunteers. ECG was continuously recorded prior, during and after simulated obstructive hypopnea (inspiration through a threshold load), simulated apnea (Mueller maneuver), end-expiratory central apnea and normal breathing in randomized order. The number of subjects with premature beats was significantly higher during inspiration through a threshold load (n = 7), and the Mueller maneuver (n = 7) compared to normal breathing (n = 0) (p = 0.008 for all comparisons), but not during end-expiratory central apnea (n = 3, p = 0.125) [28].

Also, Monahan et al. [29] evaluated respiratory disturbances as potential triggers for arrhythmia in those with SRBD. Overnight polysomnograms from the Sleep Heart Health Study (n = 2816) were screened for paroxysmal atrial fibrillation and non sustained ventricular tachycardia (NSVT). The main finding of this study is the nearly 18-fold increase in the relative risk of nocturnal arrhythmia following a respiratory disturbance in individuals with a broad range of SRBD severity (OR 17.5; 95% CI 5.3–58.4) compared to the odds of an arrhythmia occurring following normal breathing. These results support a direct temporal link between SRBD events and the development of these arrhythmias [29].

Likewise, in an indirect way, the effect of CPAP treatment on cardiac rhythm disturbance had been studied. In a previous study [25] we found that nocturnal supraventricular and ventricular ectopics were evident in patients with OSAHS which were abolished almost completely while using CPAP therapy. Also CPAP increased the minimal heart rate while the maximal heart rate decreased significantly than patients without CPAP, this showed that the bradytachyarrhythmias usually associating respiratory events decreased or abolished while using CPAP.

Neilan et al. [30] found that therapy with CPAP is associated with lower blood pressure, atrial size, and ventricular mass, and a lower risk of AF recurrence after pulmonary vein isolation. Sumi et al. [31] in his study found that CPAP decreases heart rate in OSAHS patients and Kanagala et al. [32] found that the recurrence rate of AF at 12 months after cardioversion was 82% in untreated OSAHS compared to 42% in treated OSAHS patients and 53% in patients without OSAHS (control group) (p = 0.013).

On 2015 a meta-analysis study systematically reviewed the published reports on CPAP use and risk of AF. A total of 8 studies on OSA were identified with 698 CPAP users and 549 non-CPAP users. In metaregression analysis, benefits of CPAP were stronger for younger, obese, and male patients (p < 0.05). An inverse relationship between CPAP therapy and AF recurrence was observed. Results suggest that more patients with AF should be tested for OSA [33].

In the present study, all OSAHS patients were moderate to severe, 8 patients (29.5%) had AHI of 15–30/h, 12 patients (44.5%) had AHI of 30–60/h and 7 patients (26%) had AHI > 60/h. three of the patients with severe OSAHS had obesity hypoventilation syndrome in addition. In accordance with our results, Mehra et al. [34] found that increasing severity of sleep-disordered breathing, as determined by increasing quartiles of the respiratory disturbance index (RDI), was associated with increased odds of AF (OR 2.15) and complex ventricular ectopy (CVE) (OR 1.43) compared with the lowest quartile. Mehra et al. also discovered that different types of sleep apnea were associated with distinct kinds of arrhythmias: an increasing obstructive sleep apnea quartile was significantly associated with increasing CVE but not AF while central sleep apnea was more strongly associated with AF (OR 2.69) than CVE (OR 1.27) [34].
Also, Hoffstein et al. [35] found that the associated rate of cardiac arrhythmias rose along with the increase in AHI. These results advance our understanding of the relationship between daytime tachyarrhythmia and severity of OSAHS. Some researchers found that arrhythmias caused by mild sleep disordered breathing are rare, even among patients with other potentially arrhythmogenic factors such as disabling angina, and that the prevalence of tachyarrhythmias increases as OSAHS indices worsen [36]. We can explain this by the persistence of sympathetic overdrive during the day in subjects having severe OSAHS. Narkiewicz and Somers [37] postulated that several neural and humoral mechanisms may contribute to maintenance of higher sympathetic activity and blood pressure. These mechanisms include chemoreflex and baroreflex dysfunction, altered cardiovascular variability, vasoconstrictor effects of nocturnal endothelin release and endothelial dysfunction.

The body mass index (BMI) of OSAHS patients in the present study was quite elevated and the obesity had a central distribution; the waist-hip ratio had a mean ± SD value of 0.91 ± 0.08. Also, elevated body mass indices in patients with tachyarrhythmia and OSAHS had been reported in many studies [27].

We found that, both BMI and waist-hip ratio showed statistically significant direct correlation with the severity of OSAHS as assessed by AHI and oxygen desaturation index (ODI 3%). Similarly, Peppard and colleagues [38] demonstrated that BMI is a significant independent predictor of the degree of oxygen desaturation during obstructive events. Oxygen desaturation (as a consequence of obesity and sleep apnea), directly or indirectly (by promoting ischemia, sympathetic activation, and inflammation) may be an important mechanistic link to cardiac rhythm disturbance [27].

Frost et al. [39] and Dublin et al. [40] found that risk of AF rises for about 8% per BMI unit increment. Rosengren et al. [41] found that BMI gain between age 20 and midlife was strongly related to subsequent AF occurrence in men.

In the present study, BMI had statistically significant direct correlation with systolic blood pressure and fasting blood glucose level ($r = 0.486$, $p = 0.010$, $r = 0.489$, $p = 0.009$ respectively). Also it showed statistically significant direct correlation with serum total cholesterol and serum triglycerides levels ($r = 0.537$, $p = 0.002$, $r = 0.517$, $p = 0.003$ respectively). In accordance with our findings, many other studies emphasized that obesity is highly correlated with the other four components of metabolic syndrome [42].

In the present study, neck circumference (NC) showed statistically significant direct correlation with the severity of OSAHS assessed by AHI ($r = 0.749$, $p < 0.0001$). Considerable amount of published studies have shown that, from all clinical predictors, neck circumference is the strongest anthropometric predictor of OSAHS severity followed by waist circumference or W–H ratio as an indicator of central distribution of obesity. Neck Circumference-Height Ratio (NHR) was suggested recently to be included as a simple screening tool for OSA in children and adults, which along with other predictors, may improve the ability of clinicians to triage children and adults at risk for OSA for further evaluation with PSG [43].

In the present study, dyslipidemia was a common finding in OSAHS patients. 18 out of 27 patients (60%) had hypercholesterolemia and 21 (70%) had hypertriglyceridemia. Total cholesterol and triglyceride showed statistically significant direct correlation with the severity of OSAHS as assessed by AHI. Dyslipidemia may indirectly promote AF due to its atherogenic complications. [6] Hypercholesterolemia could lead to temporal, and then permanent, changes in cell membranes of atrial myocytes by provoking injury of endothelium cells of atrial muscle microcirculation. These mechanisms may cause electric remodeling and AF paroxysms. Yet there is no firm proof of direct interdependence [6]. In a study by Watanabe et al. [44] low HDL-cholesterol level ( < 40 mg/dl in men and < 50 mg/dl in women) was found to be a risk factor for AF (HR = 1.52; 95% CI = 1.09–2.14). No significant relationship was observed for other atherogenic lipid disturbances. Similarly, neither dyslipidemia nor any of its components were identified as AF risk factors in the Framingham population [45].

Combining the components of metabolic syndrome (Met. S), in the present study, 19 patients (63.3%) had Met.S. Another finding is that OSAHS patients with Met.S were found to have AHI mean ± SD value of 64.4 ± 35.4 comparing to 27.3 ± 9 in OSAHS patients without Met.S.

Trombetta et al. [46] examined how the presence of OSAHS in patients with metabolic syndrome affected hemodynamic and autonomic variables associated with poor cardiovascular outcome and they found that patients with Met.S and comorbid OSAHS have higher BP, higher sympathetic drive, and diminished baroreceptor reflex, compared with patients with Met.S without OSAHS. These adverse cardiovascular and autonomic consequences of OSAHS may be associated with poorer outcomes in these patients [46].

Watanabe et al. [44] concluded that metabolic syndrome is associated with increased risk of AF. The mechanisms by which Met.S increases the risk of AF are multifactorial including inflammation and oxidative stress (C-reactive proteins) have been implicated in the pathogenesis of AF [44–46]. Low HDL cholesterol was strongly associated with the risk of AF [44]. Mechanical stress including structural remodeling and electrophysiological remodeling are critical for AF to perpetuate [44,46].

Finally, the present study offers some important insights about the importance of considering sleep study for patients with tachyarrhythmia. Multiple regression analysis was used to develop a model to predict the presence of OSAHS in patients with tachyarrhythmia. Each of the predictor variables entered in the multiple regression analysis had a significance of $p < 0.01$. We adopted three models of which model “3” (BMI + NC + serum triglycerides) yielded the highest predictive value ($r^2 = 0.886$, adjusted $r^2 = 0.871$, std error = 9.83). Multiple regression analysis results suggest that patients with tachyarrhythmia who have higher BMI, NC and triglycerides values are more likely to have underlying OSAHS.

**Conclusion**

OSAHS is highly prevalent in patients with tachyarrhythmia. High triglyceride, NC and BMI are the most predictors of presence of OSAHS. AF is the most common form of the arrhythmia in patients with OSAHS. OSAHS should be considered as part of the workup of patients with tachyarrhythmia. Both clinical apnea score and STOP BANG are good screening questionnaire to choose patients who need sleep study.
Disclosure statement

The authors have indicated no conflicts of interest.

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