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ORIGINAL ARTICLE

Impact of pulmonary vein isolation on obstructive sleep apnea in patients with atrial fibrillation

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Abstract

Background: *Obstructive sleep apnea (OSA) has been identified as associated with the onset and propagation of atrial fibrillation (AF) and predicts recurrences of AF after pulmonary vein isolation (PVI). Vice versa, it has never been investigated whether PVI influences OSA. However, it has been controversial whether a restored atrial function can affect the course of OSA. Therefore, we have assessed whether PVI procedure modulates the prevalence and severity of OSA.*

Methods and Results: *We included 23 individuals with AF that were assigned to undergo PVI into this study. Patients were 65 ± 7 years old, obese (BMI 29.9 ± 5.4 kg/m^2), white (100%) and had a normal left ventricular function (LVEF 64 ± 9%). Polygraphic assessment was carried out before and 6 months after PVI. The prevalence of OSA, defined as an apnea-hypopnea index (AHI) ≥ 5 per hour of sleep, was 74% before PVI compared to 70% 6 months after the procedure (p > 0.05). Severity of OSA did not differ (AHI before vs. after: 18 ± 18/h vs. 15 ± 17/h, p > 0.05) as well as further polygraphic parameters did not differ before and after the procedure.*

Conclusions: *Prevalence and severity of OSA are not affected by PVI in patients suffering from AF.* (Cardiol J 2014; 21, 4: 392–396)

Key words: obstructive sleep apnea, pulmonary vein isolation, atrial fibrillation

Introduction

Atrial fibrillation (AF) remains the most frequent arrhythmia occurring in clinical practice [1]. Serious short- and long-term sequelae such as thrombembolic stroke, heart failure, reduced quality of life and increased overall mortality ask for further exploration of this disorder [2]. While several underlying disorders such as coronary artery disease and hypertension have been identified to be closely connected with the onset of this disease, there is still an enormous rate of AF that appears without co-existing classical cardiovascular conditions.

Therefore, further unknown instigating factors triggering and propagating AF have been assumed. One risk factor that has previously been shown to be independently associated with the onset of AF is obstructive sleep apnea (OSA) [3]. OSA is initiated by upper airway obstruction that is physiologically responded by augmented respiratory efforts, thereby increasing the intrathoracic pressure that finally leads to increased atrial vulnerability and atrial chamber enlargement. It has been suggested that these mechanisms also induce tissue remodeling at the pulmonary veins that are considered to provide arrhythmogenic areas inducing AF by electrical

avalanches [1]. Pulmonary vein isolation (PVI) diminishes the occurrence of AF by interrupting these electrical lines and usually leads to a significant impairment of AF burden [4–7]. Further, it can also induce reverse atrial remodeling [8]. Almost one-third of the patients undergoing PVI does not benefit from this procedure [5, 9]. Recently, we have shown that the prevalence and severity of OSA is particularly high in this group of patients that show resistance to PVI [10]. Our finding was recently corroborated by a study yielding that moderate to severe sleep-disordered breathing disturbances independently predict recurrences of AF after PVI as well [11]. To date, though various studies investigated the effects of OSA on AF, it has never been contemplated whether PVI might impact on the severity of OSA vice versa. However, it has been speculated that AF with subsequent increased left-atrial pressure can lead to pulmonary congestion and thereby might cause and aggravate OSA [12]. Interestingly, Garrigue et al. showed that atrial overdrive pacing diminished the amount of both central and OSA in patients with a permanent pacemaker implanted for sinus node dysfunction [13]. Given the vast number of studies concerning OSA and AF, this question should be addressed in order to unravel unknown factors possibly skewing the relation between OSA and PVI. Therefore, we conducted a pilot study to determine the prevalence and severity of OSA in patients with non-permanent AF before PVI and 6 months after this procedure.

Methods

Patients

Patients with non-permanent AF that were assigned to undergo PVI were consecutively enrolled in this study. Patients were excluded if they had reduced left ventricular ejection fraction, permanent AF, a history of poor compliance with drug treatment, evidence of the use of arrhythmogenic substances such as ethanol, cocaine and l-thyroxin, or known OSA with or without continuous positive airway pressure treatment. Twenty-three patients that were analyzed before and after PVI were generally late middle-aged (65 ± 7 years old), white (100%), and overweight 29.9 ± 5.4 kg/m^2 (Table 1). This study was approved by the local ethics committee and carried out in accordance with the declaration of Helsinki. Written informed consent was obtained from every individual.

Table 1. Baseline demographic and clinical characteristics of the patients.

Variable	N = 23
Persistent AF	13 (57%)
Age [years]	65 ± 7
Male sex	16 (70%)
BMI [kg/m^2]	29.9 ± 5.4
LVEF [%]	64 ± 9
CAD	4 (7%)
Diabetes	3 (13%)
Hypertension	16 (70%)
Creatinin [mg/dL]	1.1 ± 0.4
ACEI	5 (22%)
Beta-blocker	17 (74%)
Statin	9 (39%)
Diuretic	5 (22%)
Amiodarone	2 (8%)
Dronedaron	5 (22%)
Class 1c	7 (30%)
Digitalis	4 (17%)
Ca^{2+}-antagonist	7 (30%)
Aspirin	4 (17%)
Marcumar	22 (96%)

AF — atrial fibrillation; BMI — body mass index; LVEF — left ventricular ejection fraction; CAD — coronary artery disease; ACEI — angiotensin converting enzyme inhibitor

Polygraphic assessment

All patients underwent an overnight polygraphic study the day before PVI was performed and 6 months after the procedure. Conventional polygraphic devices were used (Poly MESAM Device, ResMed). During the polygraphic examination, heart rhythm was determined using a precordial electrocardiograph. Thoraco-abdominal movements were assessed by a calibrated respiratory conductance phlethysmograph and oxygen saturation was measured by fingertip oximetry. The mean lowest oxygen saturation (SaO$_2$) during sleep was calculated by averaging the lowest SaO$_2$ for each 30 s episode during sleep. OSA was defined as an absence of airflow for at least 10 s and hypopneas were defined as a reduction in airflow for more than 50% from the baseline level for at least 10 s with 3% decrease in oxygen saturation while paradoxical thoraco-abdominal movements occurred. Subjects with more than 5 obstructive apneas and hypopneas were considered to suffer from OSA according to present guidelines [14, 15]. Analysis and interpretation of the obtained data

were performed blinded without knowledge about the patient's status.

Ablation procedure

PVI was performed by cryoballoon ablation technique as previously described [16]. Ablation success was controlled again 20 min after the last pulmonary vein was isolated. To prevent short-term recurrences of AF, patients were continued on prescribed anti-arrhythmic medication they had at the time of referral for PVI for further 3 months.

Follow-up

The follow-up period began immediately on the day after procedure and was continued at least until the second polygraphic study was performed. Patients were equipped with an event recorder and instructed to transmit one electrocardiogram (ECG) per day and to carry out additional measurements if they felt any symptoms of AF. Standard duration of all records was 1 min. Recording started 1 day after PVI and was continued for further 3 months. All recordings were analyzed for the occurrence of AF. The first month after the procedure was not included into the analysis and all episodes of AF within that month were therefore excluded. Patients were examined again 3 months after the procedure in our outpatients' department. Furthermore, a detailed medical history and a 12-lead ECG were taken. Patients were then followed up on a regular basis monthly. Routine and Holter ECG were performed regardless of symptoms. If asymptomatic AF was detected on conventional ECG or event recorder, patients were considered suffering from recurrent AF. If no episode of AF could be detected with the different applied instruments until the second polygraphic study was performed, patients were considered to be successfully treated by PVI.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation and categorial variables were expressed in percentages. Continuous data were analyzed by means of unpaired students' t-test and categorial variables were analyzed using χ^2 test. Statistical analysis was carried out with SPSS (Statistical Package for Social Sciences, Version 17, Chicago, IL, USA). $P < 0.05$ was considered to be statistically significant.

Results

Individuals suffering from AF (n = 23) were enrolled into this arm of the study. Polygraphic as-

sessment was performed before PVI and 6 months afterwards. OSA was detected in 74% of the patients before PVI was performed and in 70% of the patients 6 months after PVI (p > 0.05), indicating that PVI did not influence the prevalence of OSA in these patients. The overall severity of OSA in this population, as expressed by the apnea–hypopnea index (AHI), did not differ as well (AHI events/h: before 18 ± 18 vs. after 15 ± 17, p > 0.05) (Table 2). Assessment of the oxygen desaturation index (ODI) did not reveal any differences (ODI events/h: before 13 ± 12 vs. 13 ± 14, p > 0.05). Other polygraphic parameters did not differ before and after PVI as well.

Fifteen patients remained in sinus rhythm and were considered to be successfully treated by PVI while 8 patients suffered from recurrent AF after PVI during the follow-up period. Prevalence of OSA in patients that were cured from AF was 80% before PVI compared to 73% after PVI (before 80% vs. after 73%, p > 0.05). Again, we did not detect any differences with regards to the severity of OSA in successfully treated patients (AHI events/h: before 20 ± 18 vs. after 16 ± 12, p > 0.05). Assessment of the ODI did not reveal any differences as well (ODI events/h: before 14 ± 12 vs. 15 ± 11, p > 0.05). Relevant central sleep apnea was not detected in the study population.

Discussion

We have analyzed the effects of PVI procedure in patients with AF on the course of OSA. The possibility that OSA can be affected by PVI has not been ruled out yet, though it is conceivable that successfully treating AF associated with a restored atrial function might also modulate the prevalence and severity of OSA in these patients. Here, we provide first evidence demonstrating that PVI does neither affect the prevalence nor the severity of OSA in patients undergoing PVI. Considering the large number of investigations studying the effects of OSA on AF [17], this finding is an important contribution to the scientific community that is necessary for a better interpretation of the association of OSA and AF. It has recently been demonstrated that renal sympathetic denervation does not only lower blood pressure but is also accompanied by an improvement of OSA indicated by a diminishment in AHI in patients suffering from therapy-resistant hypertension [18]. Although the exact mechanism has not been identified in this study, it is conceivable that the reduced sympathetic tonus and reduced fluid overload are responsible for the observed improvement in OSA.

Table 2. Results of polygraphic assessment. Prevalence of obstructive sleep apnea (OSA) and mean apnea–hypopnea index (AHI) — before and 6 months after pulmonary vein isolation (PVI). Results of all individuals (n = 23) are shown in the upper part. Results of patients (n = 15) that were successfully treated by PVI are shown in the lower part.

All	Before PVI (n = 23)	After PVI (n = 23)	P
Prevalence OSA	74%	70%	0.67
AHI [events/h]	18 ± 18	15 ± 17	0.63
ODI [events/h]	13 ± 12	13 ± 14	0.97
Mean SaO$_2$ [%]	92 ± 4	93 ± 4	0.49
Minimal SaO$_2$ [%]	74 ± 24	81 ± 17	0.26
ESS score	8 ± 3	9 ± 5	0.40
Heart rate [bpm]	75 ± 25	66 ± 10	0.49
AF-free group	**Before PVI (n = 15)**	**After PVI (n = 15)**	**P**
Prevalence OSA	80%	73%	0.74
AHI [events/h]	20 ± 18	16 ± 12	0.53
ODI [events/h]	14 ± 12	15 ± 11	0.91
Mean SaO$_2$ [%]	92 ± 3	93 ± 3	0.40
Minimal SaO$_2$ [%]	75 ± 22	83 ± 8	0.23
ESS score	8 ± 3	11 ± 5	0.12
Heart rate [bpm]	77 ± 30	66 ± 10	0.19

Chi-square test and unpaired t-test were used for statistical analysis. Data are mean ± standard deviation; AF — atrial fibrillation; ODI — oxygen-desaturation index; SaO$_2$ — oxygen saturation; ESS — Epworth Sleepiness Scale

There have been controversial studies investigating the effects of atrial function on OSA. Garrigue et al. reported a reduction of sleep-disordered breathing in patients that received a pacemaker with atrial overdrive pacing in order to reduce the incidence of atrial tachyarrhythmias [13]. Interestingly, the authors did not only report a reduction of central sleep apnea but — unexpectedly — also of OSA. However, the mechanism implicated in that improvement remained unclear. In our study, we investigated the effect of therapeutic PVI on OSA.

Although the majority of individuals was cured from AF burden and remained in sinus rhythm after PVI, we did not detect any improvements pertaining to AHI. If there was an effect of PVI on OSA, one would expect an improvement of OSA especially in patients that were cured from AF. However, we detected sleep profile differences neither in the overall study population nor selectively in the group of patients that were cured after PVI. Although the prevalence of OSA was relatively high in patients that were successfully treated via PVI, one may speculate that these individuals are less prone to OSA-induced recurrent AF. On the other hand, it has recently been shown that electrical remodeling particularly occurs in patients with more severe forms of OSA (AHI > 30 events/h) [19] while our population suffered from moderate OSA. Nonetheless, our finding suggests that neither a restored left atrial function nor PVI, respectively, impact on OSA. Another study is in line with our finding. Krahn's study showed that temporary atrial pacing does not appear to improve respiratory manifestations of OSA [13].

Limitations of the study

This study has several limitations that should be considered. (1) The number of patients involved in this study is low. Larger trials have to corroborate the results obtained in this analysis. (2) PVI can influence left atrial remodeling and even induce reverse atrial remodeling [8] that can be assessed via echocardiography. For this study we did not obtain any echocardiographic parameters of the left atrium. However, echocardiography would allow a better assessment of atrial function and several atrial parameters. (3) Further, no electrical assessment of atrial remodeling, such as signal-averaged p-wave duration, was obtained. Therefore, further studies are needed to selectively correlate the course of OSA after PVI with features of structural and electrical atrial remodeling. (4) We have ana-

lyzed patients with non-permanent AF that were scheduled to undergo PVI. It has to be mentioned that the effect of PVI on restoring atrial function is less in this population compared to patients suffering from long lasting AF. (5) Finally, our population suffered from moderate OSA. However, it has been shown that particularly severe forms of OSA influence atrial remodeling. Thus, if PVI influences sleep parameters, it is conceivable that these effects are only detectable in more severe forms of OSA in which atrial remodeling is farther progressed before PVI is performed.

Conclusions

PVI in patients suffering from AF does not influence the prevalence and severity of OSA.

Acknowledgements

Conflict of interest: none declared

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