

Prevalence and characteristics of OSAFED syndrome in atrial fibrillation primary care patients

Jacek Wolf^{1*}, Tadeusz Dereziński^{2*}, Anna Szyndler¹, Krzysztof Narkiewicz¹

¹Department of Hypertension and Diabetology, Medical University of Gdansk, Gdansk, Poland

²NZOZ Eskulap Medical Centre, Gniewkowo, Poland

*Both authors (JW and TD) contributed equally to the manuscript.

Abstract

Background: Atrial fibrillation (AF) constitutes the most prevalent arrhythmia, affecting up-to 2% of the general population. Apart from well-established risk factors that increase the odds for the development of AF, e.g. age or arterial hypertension, recent analyses indicate that obstructive sleep apnoea (OSA) may independently, negatively modify the arrhythmia occurrence profile. Concurrently, erectile dysfunction (ED) is a commonly neglected, potent marker of cardiovascular risk, which considerably worsens men's psychological state. Unrecognised or untreated ED results in substantial deterioration of the patient's therapeutic programme adherence. Because AF, OSA, and ED share multiple risk factors and clinical consequences, in 2013 the concept of their frequent concurrence — OSAFED syndrome — was proposed.

Aim: The aim of the study was to evaluate the prevalence of OSAFED patients with AF in primary care practice.

Methods: Retrospective analysis was carried out of data from primary care physician charts (NZOZ Eskulap Gniewkowo, central Poland) including 1372 men aged 40–65 years. The primary goal was to determine the diagnosis of paroxysmal and/or permanent AF, which was followed by sleep apnoea screening (polygraphy) and erectile function evaluation (IIEF-5 questionnaire).

Results: Twenty-one (1.5%) patients with documented AF were identified. Based on the sleep-polygraphic studies, 14 (67%) of them had confirmation of OSA with mean apnoea–hypopnea index (AHI) equal to 27.5 ± 17.1 . Furthermore, 11 (52%) patients met the OSAFED syndrome criteria. Patients with OSAFED syndrome had a mean score in IIEF-5 of 11.6 ± 3.5 . The OSAFED-patients who were not diagnosed with all the of the syndrome components prior to the study-enrolment were characterised by substantially lower fat excess compared to their counterparts with already established OSAFED (body mass index: 30.1 ± 4.9 vs. 37.7 ± 3.9 kg/m², respectively, $p = 0.03$).

Conclusions: Frequently coexisting OSAFED syndrome components in all AF patients from the primary care setting should encourage a more active search for OSA and ED in patients with any documented form of AF. Most of the studied patients did not have the diagnosis of OSA nor ED done prior to participation in the study.

Key words: obstructive sleep apnoea, atrial fibrillation, erectile dysfunction, OSAFED, primary care

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INTRODUCTION

In 2013 a new concept of clinical syndrome, named OSAFED, constituting obstructive sleep apnoea (OSA), atrial fibrillation (AF) and erectile dysfunction (ED), was proposed by Szymański et al. [1]. The authors postulated wider use of screening methods in patients who present with any of the clinical elements of the syndrome. The rationale for

cross-screening was not only that OSA, AF, and ED share multiple risk factors and clinical consequences but also that they modify potentiated global cardiovascular (CV) risk in patients. From a clinical perspective, patients rarely present with only one risk factor [2]; in most of the cases there are a few coexisting conditions that altogether substantially potentiate CV risk.

Address for correspondence:

Jacek Wolf, MD, PhD, Department of Hypertension and Diabetology, Medical University of Gdańsk, ul. Dębinki 7C, 80–952 Gdańsk, Poland, tel: +48 58 3492527, fax: +48 58 3492601, e-mail: lupus@gumed.edu.pl

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Atrial fibrillation is one of the most common arrhythmias, with an estimated prevalence of 1–2% of the general population [2, 3]. AF is documented in < 1% of adults below the age of 50 years, whereas among 80-years-olds it is diagnosed in approximately 15%, implying that age is the strongest risk factor [2, 4]. As the mean life-span increases, partially as a function of more effective interventional procedures and preventive measures, AF prevalence consequently increases (it is expected to double in the next 50 years) [3, 4]. This phenomenon is especially evident in subjects at high CV risk [5] where screening for AF in patients with ischaemic stroke reveals arrhythmia in over 20% of cases [5, 6].

Obstructive sleep apnoea is one of the most prevalent sleep disturbances. Recent data updated from the Wisconsin cohort showed that moderate-to-severe disease affects 6% of adult women and 13% of men [7]. Importantly, the clear majority of affected patients remain without proper diagnosis, and thus OSA management. It should also be remembered that among patients with OSA syndrome the prevalence of cardiac arrhythmias including AF is higher compared to the general population [8–10].

Lastly, ED, described as an inability to attain and/or maintain erection sufficient to perform full sexual intercourse, affects 18–40% of men above 20 years of age [11]. The prevalence of ED increases with age, and predisposing factors are hypertension, diabetes, coronary artery disease, sedentary life style, smoking, depression, and low economic status [12]. ED is considered as an independent CV risk factor and an early diagnostic marker for subclinical and overt target organ damage. It is estimated that it precedes CV complication development for three to five years [13]. The frequent coincidence of ED and OSA (especially severe), has been confirmed in numerous cross-sectional, case-control, as well as interventional studies, and it is estimated that ED may affect up to 60% of OSA patients [12, 14, 15].

The aim of our work was the assessment of the coexisting elements of OSAFED syndrome among male patients diagnosed with AF in a primary care centre.

METHODS

Into our observational study, we included all men between the age of 40–65 years, who regularly attended a primary care centre (NZOZ Eskulap, Gniewkowo, Kuyavian-Pomeranian Voivodeship) over the previous five-years. None of the coexisting diseases was an excluding criterion at the enrolment. Clinical characteristics, including anthropometrics (body weight, height, body mass index [BMI]), prescribed drugs, and comorbidities were extracted from the patients' records.

The regular patients' files were revised to identify men with paroxysmal or chronic AF (AF+). AF was identified based on an electrocardiogram (ECG) tracing or medical records of any documented form of AF in the past five years (ICD-based classification as I48).

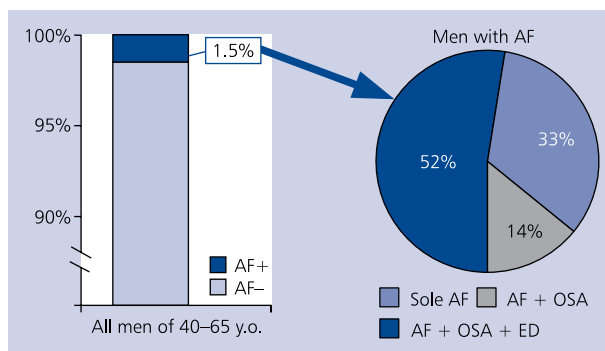


Figure 1. Prevalence of OSAFED syndrome in primary health care (n = 1372); AF — atrial fibrillation; ED — erectile dysfunction; OSA — obstructive sleep apnoea

Next, all AF+ men were asked individually to complete a standard questionnaire focusing on their erectile status over the period of the last three months (International Index of Erectile Function [IIEF-5]) [16]. Following the instructions, the patients were handed a copy of a questionnaire and asked to complete it individually at home. During the next visit, the doctor in charge (TD) discussed the results with the patient. The total score less than 21 points in IIEF-5 classified patients as having been diagnosed with erectile dysfunction (ED+).

Finally, all identified AF+ patients underwent ambulatory overnight polygraphic examination with a portable monitor (ApneaLink™, ResMed), which recorded nasal pressure via a cannula, respiratory effort, and pulse oximetry. A positive sleep study was based on oxygen desaturation index equal to or greater than 5.

All identified patients gave their informed consent to participate in the study, including statistical data processing and anonymous dissemination. The subjects were instructed about scheduled procedures and they were free to withdraw at any time without consequences. The procedures were conducted by suitably qualified medical personnel. The study conformed to the standards set by the Declaration of Helsinki.

Statistical analysis

All data were tabulated and calculated in MS Excel spreadsheet and MedCalc®, respectively. Continuous variables were expressed as mean ± standard deviation, and categorical variables as medians (Q1, Q3) or absolute numbers (+ percentage). Statistical comparisons between groups were made using t-test or Mann-Whitney test, where appropriate. A p-value less than 0.05 was considered valid for all tests.

RESULTS

Investigation of patients' records revealed 1372 men of 40–65 years of age, and identified 21 (1.5%) men with documented paroxysmal or chronic/persistent AF (Fig. 1).

Table 1. Selected clinical characteristic of studied patients with OSAFED syndrome

Patient No.	Age [years]	BMI [kg/m ²]	AHI [#/h]	ODI [#/h]	SpO ₂ [%]	CPAP	HTN	T2DM	OAT	CHA ₂ DS ₂ - -VASc
1	59	27.7	7	12	91	No	Yes	Yes	Yes	3
2	60	31.9	22	25	93	No	Yes	No	Yes	1
3	59	39.8	30	32	93	No	Yes	Yes	Yes	4
4	53	22.7	39	28	93	No	No	No	Yes	0
5	59	37	25	24	93	No	Yes	Yes	Yes	4
6	65	26	20	26	93	No	Yes	Yes	Yes	3
7	62	31.5	6.1	9	91	No	Yes	No	No	1
8	48	33.1	22	24	94	No	No	No	Yes	2
9	57	38.6	35	25	93	Yes	Yes	Yes	Yes	6
10	56	33	27	30	95	No	Yes	No	Yes	2
11	53	40.4	69	66	92	Yes	No	Yes	No	0

AHI — apnoea-hypopnoea index; BMI — body mass index; CPAP — continuous positive airway pressure; HTN — hypertension; OAT — oral anticoagulant treatment; ODI — oxygen desaturation index; SpO₂ — mean sleep-time blood oxygen; T2DM — type 2 diabetes mellitus

Polygraphic sleep study confirmed sleep disordered breathing in 14 (67%) screened men, and seven had undisturbed breathing during sleep. Among patients with coexisting AF and OSA, 11 patients scored less than 21 points on the IIEF-5 questionnaire, which was consistent with the diagnosis of ED, thus meeting OSAFED syndrome definition (Fig. 1). Patients with OSAFED syndrome had a mean score in IIEF-5 of 11.6 ± 3.5 . Additionally, the OSAFED-patients who were not diagnosed with all of the of the syndrome components prior to the study-enrolment were characterised by substantially lower fat excess denoted by BMI compared to their counterparts with already established OSAFED (30.1 ± 4.9 vs. 37.7 ± 3.9 kg/m², respectively, $p = 0.03$).

Four patients classified to the OSAFED+ group had established OSA diagnosis before the initiation of the trial; however, only two were chronically treated with nasal continuous positive airway pressure (nCPAP). In the remaining two patients, treatment with nCPAP was postponed due to low left ventricular ejection fraction (LVEF < 45%) and coexisting central apnoea [17].

Selected clinical characteristics of identified cases are presented in Table 1 and 2.

DISCUSSION

In the studied population of 1372 men 40–65 years of age we identified 21 (1.5%) patients with either paroxysmal or persistent/chronic AF. In this group, we found 14 patients with OSA syndrome, which was latent before enrolment into the study in most cases. Among them, 11 (52%) were diagnosed with newly postulated OSAFED syndrome, constituting AF, OSA, and ED coexistence (Fig. 1).

Table 2. Clinical characteristics of patients with OSAFED syndrome vs. patients who did not meet syndrome diagnostic criteria

	OSAFED (+)	OSAFED (–)	p
Age [year]	57.4 ± 4.7	55.0 ± 5.1	0.35
BMI [kg/m ²]	32.9 ± 5.8	30.4 ± 3.6	0.36
AHI [#/hr]	27.5 ± 17.1	2.2 ± 0.6	< 0.01
ODI [#/hr]	27.4 ± 14.6	3.6 ± 1.1	0.001
SpO ₂ [%]	92.8 ± 1.2	95.0 ± 0.6	< 0.001
CHA ₂ DS ₂ -VASc	2.0 (1.0; 3.75)	1.0 (1.0; 2.0)	0.26

AHI — apnoea-hypopnoea index; BMI — body mass index; ODI — oxygen desaturation index; SpO₂ — mean sleep-time blood oxygen

Sleep disordered breathing detection and OSA-patient management is unacceptably low in Poland, which partially results from limited availability of in-clinic diagnostic polysomnography, and thus long waiting lists. Another factor that influences such a low effectiveness is insufficient patient and physician awareness of untreated-OSA CV consequences. Those facts may, to some extent, explain why the clear majority of the OSA patients remain undiagnosed. However, in our cohort four out of 11 patients had previously established OSA diagnosis, which accounts for ~36% of the target population. This relatively high percentage may result from the fact that consequent and extensive CV-risk factor screening is standard in the primary-care practice subjected to our analysis. In general, both in Poland as well as in most neighbouring countries, OSA detection is largely based on the confirmation of a diagnosis in patients with

full-blown phenotype, predominantly suffering from excessive daytime sleepiness. Rarely, it constitutes a regular work-up of CV-patients. Interestingly, seven patients diagnosed during the present study had unlike phenotype compared to patients with OSA diagnosis made before the enrolment (BMI equalled 30.1 ± 4.9 vs. 37.7 ± 3.9 kg/m², respectively, $p = 0.03$). We noted the differences in anthropometrics, sleep-study indices, and comorbidities, which is partially consistent with previous reports in which patients with coexisting AF and OSA vs. those without OSA diagnosis were characterised with higher BMI, neck and waist circumference, older age, and positive stroke/transient ischaemic attack history [18, 19].

Both sleep apnoea and ED are characterised by a high prevalence in the general adult population, which is chiefly explained by the fact that they share the same risk factors where obesity and obesity-ascribed complications play a major role. Based on the epidemiological reports that show increasing overweight and obesity rates, one may assume that also the number of patients fulfilling the criteria for OSAFED syndrome will grow in the near future. From the clinical perspective, AF has the highest rates of diagnosis and proper management among all three elements of OSAFED syndrome. While there is a small but consequent increase in the awareness of OSA-related morbidity and mortality, the problem with ED is largely neglected and vastly underdiagnosed in general practices in Poland. Part of this problem may be simply ascribed to socially-driven obstacles; however, considering current evidence-based knowledge on the role of ED in the prediction of cardiac events, it should be no longer ignored. This is especially important because ED screening is a rapid and low-cost procedure that initially consists of the completion of a five-item questionnaire focusing on erectile function (IIEF-5).

Anticoagulant therapy

There are several clinical conditions that imply the requirement of chronic oral anticoagulation therapy, and it is estimated that patients with AF constitute up to 70% of people receiving such treatment as standard [20]. Using commonly accepted scales the risks of thromboembolic vs. haemorrhagic complications should be assessed in every AF-patient. Apparently, comparisons of CHADS₂ scale of OSA patients vs. their counterparts who are free of sleep disordered breathing consistently showed that OSA is associated with higher stroke risk, and the risk profile corresponds with OSA severity [19]. In line with these findings, a previously published meta-analysis showed that OSA patients, similarly to patients with AF, have substantially higher stroke risk [21–23]. Additionally, the prevalence of OSA among patients hospitalised for AF ablation is estimated at approximately 45% [18]. It is then justified to include untreated sleep apnoea in stroke prediction models as proposed by Yazdan-Ashoori and Baranchuk [24], who postulated that OSA should be awarded an additional point

on the modified CHADS₂ scale (CHADSS₂) in AF patients. In our cohort we compared CHA₂DS₂-VASC score between OSAFED(+) and OSAFED(–) groups, and the difference did not meet statistical significance (Table 2). This, however, may be contributed to by the fact that the OSAFED(–) group included a subset of patients with AF, who were also positive on the sleep study but scored more than 21 points on the IIEF-5 questionnaire (Fig. 1).

The role of CPAP treatment

Nasal CPAP has been the therapy of choice for sleep apnoea treatment for more than 30 years [25]. It stabilises the upper airways, preventing their collapse, which ensures a free passage of air. The effectiveness of nCPAP in OSA symptom withdrawal has been well documented. Interestingly, more recent analyses also point at the role of nCPAP in cardiac arrhythmia management, especially for recurrent AF [26]. In fact, cardiac arrhythmias have been described very early on while the definition of sleep-apnoea syndrome was emerging [27]. Additionally, several observations also suggested a possible favourable role of CPAP therapy on the course of ED in men affected with coexisting OSA and ED [28, 29]. A common problem with CPAP treatment is related to its relatively poor long-term adherence, which is estimated to be as low as approximately 50% of all eligible patients after one year of scheduled treatment [30]. Although there are available studies analysing the spectrum of confounders that potentially influence CPAP-therapy adherence such as excessive daytime somnolence or sleep study-derived indices, none of them take into account the possible role of erectile status changes along with the treatment [31]. In fact, underlining this aspect could further enhance patients' counselling in persistent nCPAP use, which could conceivably translate into additional CV benefits for OSAFED patients.

Strengths and limitations of the study

We performed the analysis on a rather limited group of patients, including subjects solely from one general practice (n = 1372). Therefore, the conclusions should be generalised with caution. To mitigate, we would like to underline that the prevalence of both AF and OSA corresponded moderately well with the rates observed in larger studies. Additionally, we performed the analysis of the whole eligible population records without a single exemption.

In our study the ED assessment was performed utilising a shortened IIEF-5 questionnaire to focus on this aspect of men's sexual health. Our study did not aim at assessment of all possible men's sexual health problems, which could be better addressed with extended queries such as IIEF-15. We found it irrelevant because the OSAFED syndrome definition actually considers only men's erectile status.

Lastly, several studies documented a close relationship between worsening of erectile status and different psycho-

somatic problems, e.g. coronary artery disease, heart failure, diabetes mellitus, or depression, to name a few. Although it was not our primary goal, it would be interesting to see the analysis of interdependences between ED and CV disease, target organ damage, hormonal abnormalities, drug regimen, diet, or smoking habit in our patients. We have tabulated selected clinical characteristic of the OSAFED patients; however, the number of patients with identified OSAFED syndrome did not allow for reliable multivariable analysis.

CONCLUSIONS

Our analysis showed high prevalence of OSAFED syndrome in the setting of AF patients from primary care. It is therefore highly advisable to screen for the remaining OSAFED syndrome elements in all patients with identified AF.

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Conflict of interest: none declared

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Występowanie zespołu OSAFED wśród chorych z migotaniem przedsionków w praktyce podstawowej opieki zdrowotnej

Jacek Wolf^{1*}, Tadeusz Dereziński^{2*}, Anna Szyndler¹, Krzysztof Narkiewicz¹

¹Klinika Nadciśnienia Tętniczego i Diabetologii, Gdański Uniwersytet Medyczny, Gdańsk

²NZOZ Eskulap Centrum Medyczne, Gniewkowo

*Obaj autorzy (J.W. i T.D.) mają jednakowy wkład w powstanie niniejszego artykułu.

Streszczenie

Wstęp: Migotanie przedsionków (AF) stanowi jedną z najczęściej występujących form zaburzenia rytmu serca, które może dotyczyć do 2% dorosłego społeczeństwa. Niezależnie od klasycznych czynników ryzyka występowania nadkomorowych zaburzeń rytmu serca, takich jak np. nadciśnienie tętnicze czy wiek pacjentów, coraz częściej postuluje się konieczność diagnostyki osób z AF w kierunku obturacyjnego bezdechu sennego (OSA). Wyniki badań przeprowadzonych w ostatnich czterech dekadach dotyczące współwystępowania AF i bezdechu wykazały, że OSA może istotnie zwiększać ryzyko wystąpienia różnych form tej arytmii. W ostatnich latach zwrócono także uwagę na istotę nieleczonych zaburzeń erekcji (ED) u mężczyzn w kontekście ryzyka chorób układu sercowo-naczyniowego. Wykazano, że nieleczone problemy sfery seksualnej mężczyzn negatywnie modyfikują poziom współpracy z chorym, wtórnie pogarszając profil ryzyka sercowo-naczyniowego. Ze względu na fakt, że AF, bezdech senny i zaburzenia wzwodu łączy wiele wspólnych czynników ryzyka, z czego może wynikać ich częste współwystępowanie, Szymański i wsp. uzasadnili koncepcję diagnozowania zespołu klinicznego, który w swojej istocie obejmuje trzy omówione patologie (OSAFED).

Cel: Celem niniejszej pracy była ocena częstości występowania i charakterystyki klinicznej pacjentów z zespołem OSAFED pozostających pod stałą opieką lekarza rodzinnego.

Metody: Badanie obejmowało retrospektywną analizę dokumentacji medycznej 1372 pacjentów pozostających pod stałą opieką lekarza rodzinnego w NZOZ Eskulap w Gniewkowie w województwie kujawsko-pomorskim. Analiza dotyczyła mężczyzn w wieku 40–65 lat i obejmowała ustalenie rozpoznania AF. Następnie w tej grupie oszacowano ilościowo i jakościowo zaburzenia oddechu w czasie snu i funkcje erekcyjne (kwestionariusz IIEF-5).

Wyniki: U 21 (1.5%) pacjentów rozpoznano AF, z czego 14 chorych charakteryzowało się współwystępującymi zaburzeniami oddechu w czasie snu. W tej grupie 11 (52%) pacjentów spełniało kryteria rozpoznania zespołu OSAFED.

Wnioski: Występowanie zespołu OSAFED jest częste w grupie osób z AF pozostających pod stałą opieką lekarza rodzinnego. Pacjenci z AF w większości nie mają dostatecznej świadomości dotyczącej pozostałych składowych zespołu OSAFED.

Słowa kluczowe: obturacyjny bezdech senny, migotanie przedsionków, zaburzenia erekcji, OSAFED, podstawowa opieka lekarska

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Adres do korespondencji:

dr n. med. Jacek Wolf, Klinika Nadciśnienia Tętniczego i Diabetologii, Gdański Uniwersytet Medyczny, ul. Dębinki 7C, 80–952 Gdańsk, tel: +48 58 3492527, faks: +48 58 3492601, e-mail: lupus@gumed.edu.pl

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