



ORIGINAL ARTICLE

Erectile dysfunction in obstructive sleep apnea syndrome—Prevalence and determinants[☆]

T. Santos^{a,*}, M. Drummond^{a,b}, F. Botelho^{c,d}

^a Faculdade de Medicina, Universidade do Porto, Porto, Portugal

^b Serviço de Pneumologia, Hospital de São João, Porto, Portugal

^c Serviço de Urologia, Hospital de S. João, Porto, Portugal

^d Departamento de Epidemiologia Clínica, Medicina Preditiva e Saúde Pública, Porto, Portugal

Received 8 July 2011; accepted 6 October 2011

KEYWORDS

Sleep apnea;
Obstructive;
Erectile dysfunction;
Aging;
Diabetes mellitus;
Hypertension

Abstract

Introduction: OSAS (obstructive sleep apnea syndrome) is defined by recurrent episodes of upper airway obstruction during sleep, causing multiple clinical consequences. Literature review suggests that OSAS induces a spectrum of abnormalities in neural, hormonal and vascular regulation that contribute to the development of ED (erectile dysfunction).

The aims of this study were to estimate the prevalence of ED in OSAS patients and evaluate its determinants.

Methods: 62 patients from Hospital S. João Sleep Laboratory with newly diagnosed OSAS were included in the study and answered the IIEF-5 (international index erectile function 5 item version) questionnaire.

Results: The prevalence of ED in OSAS patients was 64.4%. Age and diabetes constituted themselves as independent risk factors for more severe degrees of ED: OR = 1.226 (95% CI: 1.062–1.415) and OR = 31.205 (95% CI: 1.222–796.557), respectively. Compared with nonsmokers, ex-smokers group revealed a positive association with ED: OR = 4.32 (95% CI: 1.09–17.11). Hypertension and ACEI (angiotensin converting enzyme inhibitors) or ARB (angiotensin II receptor blockers) therapy were also correlated to ED symptoms: OR = 3.25 (95% CI: 1.09–9.65) and 7.39 (95% CI: 1.52–35.99), respectively.

No association was found relating BMI ($p = 0.254$), alcoholic habits ($p = 0.357$), acute myocardial infarction ($p = 0.315$), dyslipidemia ($p = 0.239$), metabolic syndrome ($p = 0.215$) and ED.

OSAS severity was not associated with ED in our sample.

Conclusions: The prevalence of ED in OSAS patients is high. ED determinants in our sample were age and diabetes. Past smoking habits, hypertension and ACEI/ARB therapy also revealed a statistically significant association with ED.

© 2011 Sociedade Portuguesa de Pneumologia. Published by Elsevier España, S.L. All rights reserved.

[☆] Please cite this article as: Santos T. Disfunção eréctil na síndrome de apneia obstrutiva do sono – Prevalência e determinantes. Rev Port Pneumol. 2011. doi:10.1016/j.rppneu.2011.10.004.

* Corresponding author.

E-mail address: med05101@med.up.pt (T. Santos).

PALAVRAS-CHAVE

Apneia obstrutiva do sono;
Disfunção erétil;
Envelhecimento;
Diabetes mellitus;
Hipertensão

Disfunção erétil na síndrome de apneia obstrutiva do sono – Prevalência e determinantes**Resumo**

Introdução: A SAOS (síndrome de apneia obstrutiva do sono) define-se pela ocorrência frequente de obstrução da via aérea superior durante o sono, com múltiplas consequências clínicas. Estudos anteriores sugerem que a SAOS provoca alterações na regulação neural, hormonal e vascular que contribuem para o desenvolvimento de DE (disfunção erétil).

Este estudo tem como principais objetivos estimar a prevalência da DE numa amostra de doentes com SAOS e avaliar os seus determinantes.

Métodos: Foram incluídos 62 doentes do Laboratório do Sono do Hospital S. João com diagnóstico recente de SAOS, que responderam ao questionário IIEF-5 (International Index Erectile Function-5 Item version).

Resultados: A prevalência da DE em pacientes com SAOS foi de 64,4%. A idade e a diabetes constituíram fatores de risco independentes para graus avançados de DE: OR = 1,226 (IC 95%:1,062–1,415) e OR = 31,205 (IC 95%:1,222–796,557), respetivamente. Comparados com pacientes fumadores, o grupo de pacientes ex-fumadores revelou associar-se à DE: OR = 4,32 (IC 95%:1,09–17,11). A hipertensão e o tratamento com IECAS (inibidores da enzima convertora da angiotensina) ou ARA (antagonistas dos recetores da angiotensina) evidenciaram uma associação com DE: OR = 3,25 (IC 95%:1,09–9,65) e 7,39 (IC 95%:1,52–35,99), respetivamente.

Não foi encontrada nenhuma relação no que diz respeito ao IMC ($p=0,254$), hábitos alcoólicos ($p=0,357$), enfarte agudo do miocárdio ($p=0,315$), dislipidemia ($p=0,239$), síndrome metabólico ($p=0,215$) e DE.

A gravidade da SAOS não se encontra associada a DE na amostra estudada.

Conclusões: A prevalência da DE em doentes com SAOS é elevada. Os determinantes da DE na amostra estudada foram a idade e a diabetes. Ex-fumadores, hipertensão e tratamento com ACEI/ARB também revelaram uma associação estatisticamente significativa com a DE.

© 2011 Sociedade Portuguesa de Pneumologia. Publicado por Elsevier España, S.L. Todos os direitos reservados.

Introduction

Erectile dysfunction (ED) is defined as the consistent inability to obtain and/or maintain a penile erection which is sufficient to permit satisfactory sexual intercourse.^{1,2} The prevalence of ED is estimated at 48% among Portuguese men aged 40–69 years old.³

Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive collapse of the upper airway due to the laxity of pharyngeal dilator muscles⁴ during sleep.

OSAS affects 4% of men between 30 and 60 years,⁵ but it is believed that the proportion of clinically diagnosed OSAS is underestimated.^{6–8} This is one of the most important medical conditions to have been identified in the last 50 years.⁹ It is related to increased morbidity and mortality due to clinical complications such as hypertension,¹⁰ congestive heart failure,¹¹ acute myocardial infarction,¹² stroke,¹³ diabetes,¹⁴ cognitive dysfunction¹⁵ and depression.¹⁶

In every REM sleep stage most men experience a sleep related erection (SRE),¹⁷ an event that ensures functional and morphological integrity to erectile tissue.¹⁸ In OSAS, intermittent hypoxic events and sleep fragmentation limit SRE, with serious consequences for erectile physiology.^{19–22} The literature review also defines hormonal,^{23–26} neural,^{27–30} endothelial^{31–35} and psychogenic¹⁶ mechanisms to explain ED complaints in OSAS.

OSAS and ED may also be connected through comorbidities such as hypertension and diabetes.²¹

As there are some inconsistencies in regard to the prevalence data,¹⁸ the main purpose of this study was to estimate the prevalence of ED in a population of OSAS patients sent to Hospital S. João for diagnosis and follow-up. Additionally, clinical and demographic information was collected to obtain the ED determinants in our population.

Methods**Study population**

Between 28 September and 31 December 2010, all men admitted ($n=207$) to S. João Hospital Sleep Laboratory for a first medical appointment because of suspected OSAS, were invited to participate in the present study. Each patient received written information about the study, an Informed Consent form and an IIEF-5 questionnaire for them to complete.

Ninety-five patients returned the completed questionnaire, 33 patients were excluded after sleep study as they did not present OSAS and one was excluded because of a previous diagnosis of ED.

Information about BMI, previous medical history (diabetes, hypertension, stroke, acute myocardial infarction) and usual pharmacological therapy was obtained from medical files.

This study was approved by S. João Hospital Ethics Committee.

IIEF-5 (International Index Erectile dysfunction – 5 item version)

IIEF-5 is a simple and useful questionnaire for screening patients with ED.³⁶ Designed as a simplified version of IIEF, it consists of 5 questions regarding erectile function and satisfaction³⁷ (Appendix A). The possible scores for IIEF-5 range from 5 to 25, and ED was classified into five categories based on the scores obtained: absent (22–25), mild (17–21), mild to moderate (12–16), moderate (8–11), and severe (5–7).

It was validated to be used in Portuguese.³⁸

Polygraphic cardiorespiratory sleep study (PCSS)

OSAS is defined by the presence of at least 5 obstructive respiratory events (apneas, hypopneas or respiratory effort related arousals) per hour of sleep in association with daytime sleepiness, loud snoring, witnessed breathing interruptions or waking up due to gasping or choking.³⁹ The presence of 15 or more obstructive respiratory events in the absence of sleep related symptoms is also sufficient for the diagnosis.³⁹

Polysomnography is routinely indicated for the diagnosis of sleep related breathing disorders,^{39–42,44,43} but its use is limited by high costs and waiting lists.⁴⁵

An overnight PCSS is an alternative to Polysomnography when there is high pre-test probability.³⁹ PCSS is made up of a portable monitor device⁴⁶ that records oronasal airflow (measured by nasal cannula), arterial oxygen saturation (measured by finger pulse oximetry), pulse rate, upper limb, abdominal and thoracic movements, body position and snoring.⁴⁷

All participants underwent PCSS with ApneaLink®, AlphaScreen Pro®, EMBLETTA® or Stardust® devices, which calculate the number of apneas (episodes of $\leq 20\%$ of previous airflow with at least 10 s of duration) and hypopneas (episodes showing 20–50% of the previous airflow, with at least 10 s of duration joined with a 4% dip in oxygen saturation) per hour of estimated sleep time. It also provides information on desaturations $>4\%$ per hour of estimated sleep time (oxygen desaturation index).

Our analysis focused on apnea–hypopnea index (AHI), oxygen desaturation index (ODI), minimum and medium oxygen saturation.

According to established criteria,³⁹ the severity OSAS was stratified according to AHI value: mild (5–15), moderate (16–29) and severe (≥ 30).

Statistical analysis

Data analysis was performed with SPSS® (Statistical Package for Social Sciences), 18.0 version.

A frequency analysis was used to describe the population. The Chi-square test was used to determine the association between categorical variables and Kruskal–Wallis test to define any association between continuous and categorical

variables. Multivariate logistic regression was used to evaluate the effect of each variable adjusted to other possible confounding factors.

Every association with $p < 0.05$ was considered statistically significant.

Results

The general characteristics of the population are described in Table 1. The mean age was 52 years. Of 62 patients studied, 28 (45.1%) were obese, 23 (37.1%) had dyslipidemia, 11 (17.7%) metabolic syndrome (MS), 36 (58.1%) arterial hypertension, 10 (16.1%) diabetes and 4 (6.5%) heart failure. Previous acute myocardial infarction, stroke and pelvic surgery were identified in 2 (3.2%), 6 (9.7%) and 2 (3.2%) participants, respectively. Mild OSAS was diagnosed in 30 (48.4%), moderate OSAS in 14 (22.6%) and severe OSAS in 17 (27.4%) individuals. The ED prevalence was 64.4%, it was mild in 24 (38.7%), mild to moderate in 12 (19.3%), moderate in 1 (1.6%) and severe in 3 (4.8%) participants.

Univariate analysis results are shown in Table 2. Aging was found to be significantly related to ED: OR (95% CI) of 3.90 (1.00–15.28); 5.50 (1.16–26.14); and 6.00 (1.00–35.91) in categories 46–55, 56–65 and >65 years, respectively. Past smoking habits were associated with ED (OR 4.32 (1.09–17.11)). Hypertension and ACEI (Angiotensin Converting Enzyme Inhibitors) or ARB (Angiotensin II Receptor Blockers) therapy revealed a statistically significant association with ED (OR 3.25 (1.09–9.65) and 7.39 (1.52–35.99)).

No association was found between dyslipidemia ($p = 0.239$), metabolic syndrome ($p = 0.215$), chronic therapy with beta blockers ($p = 0.217$), calcium antagonists ($p = 0.827$) and serotonin-selective reuptake inhibitors ($p = 0.250$) and ED.

All patients with diabetes, stroke, cardiac failure and previous pelvic surgery referred to ED on questionnaire, so it was not possible to calculate odds ratio (OR) for these variables.

PCSS parameter analysis is described in Table 3. No association was verified between ED and OSAS severity measured by ODI, minimum and medium oxygen saturation and AHI ($p = 0.494$, $p = 0.657$, $p = 0.498$ and $p = 0.403$, respectively).

Multivariate analysis results are shown in Table 4. Age and diabetes were independent risk factors for more severe degrees of ED: OR (95% CI) of 1.226 (1.062–1.415) and 31.205 (1.222–796.557), respectively. There was no evidence that BMI ($p = 0.932$), smoking habits ($p = 0.853$), alcohol consumption ($p = 0.683$), hypertension ($p = 0.077$) and OSAS severity ($p = 0.661$) were independent risk factors for ED.

Discussion

In 1981, Schmidt and Wise were the first to describe a relationship between ED and sleep disorders.⁴⁸ After that, several studies confirmed the increased prevalence of ED in OSAS patients^{51–54}: Guilleminault et al. reported ejaculatory dysfunction and decreased libido in 48% men with OSAS⁴⁹; Hirshkowitz et al. verified that 91.3% patients with ED symptoms also had OSAS⁵⁰; Seftel et al. concluded that 40% OSAS patients had ED.⁵¹ However, the association was rejected by Schiavi et al.⁵² In the present study, a 64.4% ED prevalence

Table 1 Population general description (n = 62).

Variables	Frequencies
Age	
Mean (years)	52.16
≤45	20 (32.3%)
46–55	18 (29%)
56–65	14 (22%)
>65	10 (16%)
BMI	
Mean	29.69
20–24.9	11 (17.7%)
25–29.9	23 (37.1%)
30–34.9	19 (30.6%)
>35	9 (14.5%)
Smoking habits	
Current	18 (29%)
Pack-years (mean)	25.16
Past	23 (37.1%)
Pack-years (mean)	34.12
Nonsmokers	21 (33.9%)
Alcohol consumption	
Absent	29 (46.8%)
≤60 g/day	23 (37.1%)
>60 g/day	10 (16.1%)
Comorbidities	
Dyslipidemia	23 (37.1%)
Hypertension	36 (58.1%)
Diabetes	10 (16.1%)
Metabolic syndrome	11 (17.7%)
Heart failure	4 (6.5%)
Medical history	
Stroke	2 (3.2%)
Myocardial infarction	6 (9.7%)
Pelvic surgery	2 (3.2%)
OSAS severity	
Mild	30 (48.4%)
Moderate	14 (22.6%)
Severe	17 (27.4%)
Erectile dysfunction	
Absent	22 (35.5%)
Mild	24 (38.7%)
Mild to moderate	12 (19.3%)
Moderate	1 (1.6%)
Severe	3 (4.8%)

BMI (body mass index); OSAS (obstructive sleep apnea syndrome); ED (erectile dysfunction) classification: absent (IIEF-5 22–25); mild (IIEF-5 17–21); mild to moderate (IIEF-5 12–16); moderate (IIEF-5 8–11); severe (IIEF-5 5–7).

was found, which is consistent with most published material on the subject.

In our sample, ED was not associated with severity of OSAS. However it can be seen that the group with severe OSAS did have a higher ED prevalence (Table 2) and patients who reported severe ED had the worst results in sleep study (Table 3), which indicates that studies with higher sample size are needed to support the association Margel

Table 2 ED prevalence and association with clinical and demographic variables.

Variable	ED (%) ^a	OR (95% CI) ^b	p
Age			
≤45	40.0	1	0.011
46–55	72.5	3.90 (1.00–15.28)	
56–65	78.6	5.50 (1.16–26.14)	
>65	80	6.00 (1.00–35.91)	
BMI			
20–24.9	63.6	1	0.254
25–29.9	78.3	2.06 (0.42–9.97)	
30–34.9	52.6	0.64 (0.14–2.91)	
>35	55.6	0.71 (0.12–4.32)	
OSAS severity			
Mild	66.7	1	0.723
Moderate	50.0	0.50 (0.14–1.82)	
Severe	76.5	1.63 (0.42–6.29)	
Metabolic syndrome			
Absent	60.4	2.4 (0.59–9.76)	0.215
Present	78.6		
Hypertension			
Absent	48.0	3.25 (1.09–9.65)	0.032
Present	75.0		
Dyslipidemia			
Absent	59.0	1.97 (0.64–6.09)	0.239
Present	73.9		
Myocardial infarction			
Absent	62.5	3.00 (0.32–27.46)	0.215
Present	83.3		
Alcohol consumption			
Absent	69.0	1	0.357
≤60 g/day	65.2	0.84 (0.26–2.70)	
>60 g/day	50.0	0.45 (0.10–1.95)	
Smoking habits			
Nonsmokers	52.4	1	0.719
Past	82.6	4.32 (1.09–17.11)	
Current	55.6	1.14 (0.32–4.02)	
ACEI/ARA therapy			
Absent	53.5	7.39 (1.52–35.99)	0.007
Present	89.5		

^a Erectile dysfunction (ED): IIEF ≤ 21.

^b 95% confidence interval.

et al. concluded that ED is associated exclusively with severe OSAS.⁵³ Furthermore, trials evaluating OSAS treatment found improvements in ED,^{54–58} which shows that there may be an association between both disorders, which is understandable given that patients on CPAP treatment show decreased hypoxia, improved endothelial function, decreased blood pressure and sympathetic hyperactivity, all of which can improve erectile function.

In this study, age proved to be an independent risk factor for ED, as suggested by the literature.⁵⁹ It was also confirmed that the risk of ED increases with aging. It is already

Table 3 PCSS study parameter analysis according to ED severity.

ED	ODI	Min _{O₂Sat}	Med _{O₂Sat}	AHI	
Absent	Median	13.3	81.0	94.6	16.3
	Min–Max	1.8–85.0	63.0–94.0	91.0–96.7	8.2–48.8
Mild	Median	7.75	83.0	95.0	13.6
	Min–Max	0.6–70.0	24.0–91.0	88.0–98.0	5.3–76.0
Mild to moderate	Median	13.20	82.0	94.0	30.0
	Min–Max	1.4–67.2	22.0–92.0	77.0–97.0	6.3–91.0
Severe	Median	24.0	76.0	89.0	24.9
	Min–Max	9.0–81.3	50.0–84.0	84.4–96.4	9.9–83.2
<i>p</i>		0.494	0.657	0.498	0.403

It was not possible to analyze the category “moderate DE” because it was composed only by one subject.

ED (erectile dysfunction) classification: absent (IIEF-5 22–25); mild (IIEF-5 17–21); mild to moderate (IIEF-5 12–16); moderate (IIEF-5 8–11); severe (IIEF-5 5–7).

ODI (oxygen desaturation index); Min_{O₂Sat} (minimum O₂ saturation); Med_{O₂Sat} (medium O₂ saturation); AHI (apnea–hypopnea index); Min–Max (minimum–maximum).

established that age has more impact on erectile function than the severity of OSAS.⁶⁰

In addition, the data confirmed that Diabetes is an independent risk factor for ED. It can be seen that diabetic patients have a 31 times higher risk for more severe ED, which is supported by the effect of hyperglycemia on penile neurovascular structure.⁶¹

Arterial hypertension was associated with ED in the univariate analysis. However, an association with more severe ED was not confirmed by the multivariate analysis. This difference is probably due to a confounding effect of diabetes, suggested by the fact that 9 out of 10 diabetic patients also suffered from hypertension (data not shown in tables).

An association between MS and ED was not found. Nevertheless, it is possible that the classification used underestimated the actual proportion of affected patients since it was based on patient report and did not include triglycerides or cholesterol plasmatic measurements.⁶² As a marker of systemic endothelial dysfunction, dyslipidemia may be more prevalent in ED patients.⁶³ Fibrats and Statins, lipid-lowering drugs, can also induce ED as a side effect,⁶⁴ which was not observed in our sample.

Similarly, this study did not prove an association between BMI and ED, with patients in BMI interval 25–29 reporting more symptoms than those included in higher BMI categories. This is probably related to the fact that the BMI interval 25–29 included older patients (43% patients between 56 and 65 years and 50% of patients older than 65 years), compared to the other categories (data not shown in tables). In our sample, aging is an important confounding factor when analyzing BMI data.

Concerning smoking habits, only ex-smokers showed a statistically significant association with ED, probably due to the fact that this group reported having had heavier smoking habits (34 pack-years), compared to current smokers (25 pack-years). In a recent cross-sectional study⁶⁵ smoking habits of more than 23 years or 20 cigarettes per day were significantly associated with ED.

Regarding chronic medication, an association was found between ACEI/ARB and ED. In fact, anti-hypertensive therapy is associated with adverse sexual effects, most commonly involving diuretics and beta-blockers.⁶⁶ ACEI/ARB were the most frequently used drugs and its association with ED may be due to hypertension itself.

Table 4 Multivariate logistic regression^a on the association between some clinical variables and ED.

Variable	<i>p</i>	OR	95% CI ^b
Age ^c	0.005	1.226	1.062–1.415
BMI ^c	0.932	0.989	0.759–1.287
Smoking habits (past and current)	0.853	1.136	0.293–4.407
Alcohol consumption	0.683	0.994	0.964–1.024
Diabetes	0.037	31.205	1.222–796.557
Hypertension	0.077	10.453	0.776–140.760
OSAS severity	0.661	1.580	0.204–12.233

OSAS (obstructive sleep apnea syndrome).

^a Dependent variable was categorized as “absent and mild ED” and “mild to moderate to severe ED”.

^b 95% confidence interval.

^c Analyzed as categorical variables.

This study has some strong points in its favor. We used a validated instrument to diagnose ED in clinical settings, which was designed by urologists, and so added a multidisciplinary approach to OSAS. Patients with co-morbidities were not excluded, which made it possible to measure the impact on erectile function. The effect of chronic medication was also evaluated.

However, this study also has limitations. Although it was a representative population for estimating prevalence, we analyzed multiple clinical variables, some of them shared by our small number of subjects, which may have prevented us from establishing more statistically significant associations. The size of our sample did not lend itself to such extended analysis. The study was small because there was a high refusal rate for patient participation (54%), possibly related to the embarrassment about describing such an intimate subject.

For future research larger scale studies are needed to be able to evaluate multiple clinical variables. Among the extended co-morbidities inherent to OSAS it is extremely important not to neglect complications such as ED. If we can use a bio-psychosocial approach with our patients, it will certainly have greater impact.

Conclusions

ED is very common among patients with OSAS and may be under recognized because patients do not spontaneously report the problem. Several factors are associated with ED among patients with OSAS and those include age, diabetes, past smoking habits, hypertension and ACEI/ARB therapy.

Conflicts of interest

The authors have no conflicts of interest to declare.

Acknowledgments

I would like to thank Professor Marta Drummond, first for joining this project, and then for her tireless technical, bibliographical and motivational support.

I would also express my gratitude to Dr. Francisco Botelho for helping with the statistical analysis.

I would like to thank Sleep Laboratory professionals (clinicians, technicians and secretaries) for their cooperation in the collection of all relevant clinical information.

Finally, I would like to thank my parents, Joana Lascasas and Roberto Moreira for all their technical and emotional support.

Appendix A. Erectile function survey (IIEF-5 – International Index of Erectile Function, five-item version)

- (1) How would you rate your level of confidence in achieving and maintaining an erection?
 1. Too low/none
 2. Low
 3. Normal
 4. High
 5. Too high

- (2) When you achieve erection by sexual stimulation, how often is that erection sufficiently firm for penetration?
 1. Almost never/never
 2. A few times (less than half of the times)
 3. Sometimes (about half of the times)
 4. Often (more than half of the times)
 5. Almost every time/always
- (3) During sexual intercourse, how many times have you managed to maintain an erection after penetration?
 1. Almost never/never
 2. A few times (less than half of the times)
 3. Sometimes (about half of the times)
 4. Often (more than half of the times)
 5. Almost every time/always
- (4) During sexual intercourse, is it difficult to maintain an erection until the end of sexual activity?
 1. Extremely difficult
 2. Very difficult
 3. Difficult
 4. Slightly difficult
 5. Not difficult
- (5) When you try to have attempt sexual intercourse, how often are you successful?
 1. Almost never/never
 2. A few times (less than half of the times)
 3. Sometimes (about half of the times)
 4. Often (more than half of the times)
 5. Almost every time/always

References

1. NIH Consensus Development Panel on Impotence: Impotence. *JAMA*. 1993;270:83–90.
2. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The International Index of Erectile Function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology*. 1997;49:822–30.
3. Teles AG, Carreira M. Prevalence, severity, and risk factors for erectile dysfunction in a representative sample of 3548 Portuguese men aged 40 to 69 years attending primary healthcare centers: results of the Portuguese erectile dysfunction study. *J Sex Med*. 2008;5:1317–24.
4. Malhotra A, White DP. Obstructive sleep apnoea. *Lancet*. 2002;360:237–45.
5. Young T, Palta M, Dempsey Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. *N Engl J Med*. 1993;328:1230–5.
6. Pagel JF. The burden of obstructive sleep apnea and associated excessive sleepiness. *J Fam Pract*. 2008;57 Suppl. 8:S3–8.
7. Kapur V, Strohl KP, Redline S, Iber C, O'Connor G, Nieto J. Underdiagnosis of sleep apnea syndrome in U.S. communities. *Sleep Breath*. 2002;6:49–54.
8. Young T, Evans L, Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep*. 1997;20:705–6.
9. Douglas N. Sleep apnea syndrome. In: Fauci, Braunwald, Kasper, Hauser, Longo, Jameson, Loscalzo, editors. *Harrison's principles of internal medicine*, vol. II, 17th ed. McGraw Hill; 2008. p. 1665–8 [chapter 259].
10. Calhoun DA. Obstructive sleep apnea and hypertension. *Curr Hypertens Rep*. 2010;12:189–95.
11. Chowdhury M, Adams S, Whellan DJ. Sleep-disordered breathing and heart failure: focus on obstructive sleep apnea and treatment with continuous positive airway pressure. *J Card Fail*. 2010;16:164–74.

12. Lee CH, Khoo SM, Tai BC, Chong EY, Lau C, Than Y, et al. Obstructive sleep apnea in patients admitted for acute myocardial infarction. Prevalence, predictors, and effect on microvascular perfusion. *Chest*. 2009;135:1488–95.
13. Dyken ME, Im KB. Obstructive sleep apnea and stroke. *Chest*. 2009;136:1668–77.
14. Idris I, Hall AP, O'Reilly J, Barnett A, Allen M, Andrews R, et al. Obstructive sleep apnoea in patients with type 2 diabetes: aetiology and implications for clinical care. *Diabetes Obes Metab*. 2009;11:733–41.
15. Beebe DW, Gozal D. Obstructive sleep apnea and the prefrontal cortex: towards a comprehensive model linking nocturnal upper airway obstruction to daytime cognitive and behavioral deficits. *J Sleep Res*. 2002;11:1–16.
16. Harris M, Glozier N, Ratnavadivel R, Grunstein RR. Obstructive sleep apnea and depression. *Sleep Med Rev*. 2009;13:437–44.
17. Hirshkowitz M, Schmidt MH. Sleep-related erections: clinical perspectives and neural mechanisms. *Sleep*. 2005;9:311–29.
18. Moreland RB. Is there a role of hypoxemia in penile fibrosis: a viewpoint presented to the society for the study of impotence. *Int J Impot Res*. 1998;10:113.
19. Seftel AD, Strohl KP, Loye TL, Bayard D, Kress J, Netzer NC. Erectile dysfunction and symptoms of sleep disorders. *Sleep*. 2002;25:643–7.
20. Zias N, Bezwada V, Gilman S, Chroneou A. Obstructive sleep apnea and erectile dysfunction: still a neglected risk factor? *Sleep Breath*. 2009;13:3–10.
21. Jankowsky JT, Seftel AD, Strohl KP. Erectile dysfunction and sleep related disorders. *J Urol*. 2008;179:837–41.
22. Teloken PE, Smith EB, Lodowsky C, Freedom T, Mulhall JP. Defining association between sleep apnea syndrome and erectile dysfunction. *Urology*. 2006;67:1033.
23. Luboshitzky R, Herer P, Levie M, Shen-Orr Z, Lavie P. Relationship between rapid eye movement sleep and testosterone secretion in normal men. *J Androl*. 1999;20:731.
24. Luboshitzky R, Zabari Z, Levi M, Shen-Orr Z, Herer P, Lavie P. Disruption of the nocturnal testosterone rhythm by sleep fragmentation in normal men. *J Clin Endocrinol Metab*. 2001;86:1134.
25. Luboshitzky R, Aviv A, Hefetz A, Shen-Orr Z, Herer P, Lavie L. Decreased pituitary-gonadal secretion in men with obstructive sleep apnea. *J Clin Endocrinol Metab*. 2002;87:3394.
26. Luboshitzky R, Lavie L, Shen-Orr Z, Lavie P. Pituitary gonadal function in men with obstructive sleep apnea. The effect of continuous positive airways pressure treatment. *Neuro Endocrinol Lett*. 2003;24:463–7.
27. Somers VK, Dyken ME, Clary MP, Abboud FM. Sympathetic neural mechanisms in obstructive sleep apnea. *J Clin Invest*. 1995;96:1897.
28. Soukhova-O'Hare GK, Shah ZA, Lei Z, Nozdrachev AD, Rao CV, Gozal D. Erectile dysfunction in a murine model of sleep apnea. *Am J Respir Crit Care Med*. 2008;178:644–50 [epub 2008 Jun 5].
29. Mayer P, Dematteis M, Pepin JL, Wuyam B, Veale D, Vila A, et al. Peripheral neuropathy in sleep apnea. A tissue marker of the severity of nocturnal desaturation. *Am J Respir Crit Care Med*. 1999;159:213–9.
30. Fanfulla F, Malaguti S, Montagna T, Salvini S, Bruschi C, Crotti P, et al. Erectile dysfunction in men in obstructive sleep apnea: an early sign of nerve involvement. *Sleep*. 2000;23:775–81.
31. Christou K, Markoulis N, Moulas AN, Pastaka C, Gourgoulis KI. Reactive oxygen metabolites (ROMs) as an index of oxidative stress in obstructive sleep apnea patients. *Sleep Breath*. 2003;7:105–10.
32. Phillips BG, Narkiewicz K, Pesek CA, Haynes WG, Dyken ME, Somers VK. Effects of obstructive sleep apnea on endothelin-1 and blood pressure. *J Hypertens*. 1999;17:61–6.
33. Aversa A, Bruzziches R, Francomano D, Natali M, Gareri P, Spera G. Endothelial dysfunction and erectile dysfunction in the aging man. *Int J Urol*. 2010;17:38–47 [epub 2009 Nov 25].
34. Christou K, Kostikas K, Pastaka C, Tanou K, Antoniadou I, Gourgoulis KI. Nasal continuous positive airway pressure treatment reduces systemic oxidative stress in patients with severe obstructive sleep apnea syndrome. *Sleep Med*. 2009;10:87–94 [epub 2008 Feb 20].
35. Karacan I, Karatas M. Erectile dysfunction in sleep apnea and response to CPAP. *J Sex Marital Ther*. 1995;21:239–47.
36. Rhoden EL, Telöken C, Sogari PR, Vargas Souto CA. The use of the simplified International Index of Erectile Function (IIEF-5) as a diagnostic tool to study the prevalence of erectile dysfunction. *Int J Impot Res*. 2002;14:245–50.
37. Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res*. 1999;11:319–26.
38. Ribeiro Pais JL, Santos A. Metric properties of a Portuguese version of the abridged 5-item version of the international index of erectile function (IIEF-5). *Psicologia Saúde e Doenças*. 2007;8:271–4.
39. Epstein LJ, Kristo D, Strollo Jr PJ, Friedman N, Malhotra A, Patil SP, et al. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med*. 2009;5:263–76.
40. American Thoracic Society. Medical Section of the American Lung Association. Indications and standards for cardiopulmonary sleep studies. *Am Rev Respir Dis*. 1989;139:559–68.
41. Standards of Practice Committee of the American Sleep Disorders Association. Practice parameters for the use of portable recording in the assessment of obstructive sleep apnoea. *Sleep*. 1994;17:372–7.
42. Indications for Polysomnography Task Force, American Sleep Disorders Association Standards of Practice Committee. Practice parameters for the indications for polysomnography and related procedures. *Sleep*. 1997;20:406–22.
43. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman Jr J, et al. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. *Sleep*. 2005;28:499–521.
44. Douglas NJ, Thomas S, Jan MA. Clinical value of polysomnography. *Lancet*. 1992;339:347–50.
45. Kuna ST. Portable-monitor testing: an alternative strategy for managing patients with obstructive sleep apnea. *Respir Care*. 2010;55:1196–215.
46. Littner MR. Portable monitoring in the diagnosis of the obstructive sleep apnea syndrome. *Semin Respir Crit Care Med*. 2005;26:56–67.
47. Guilleminault C. Suspicion of sleep-disordered breathing: which test to perform? *Sleep Med*. 2000;1:73–5.
48. Schmidt HS, Wise 2nd HA. Significance of impaired penile tumescence and associated polysomnographic abnormalities in the impotent patient. *J Urol*. 1981;126:348–52.
49. Guilleminault C, Eldridge FL, Tilkian A, Simmons FB, Dement WC. Sleep apnea syndrome due to upper airway obstruction: a review of 25 cases. *Arch Intern Med*. 1977;137:296–300.
50. Hirshkowitz M, Karacan I, Arcasoy MO, Acik G, Narter EM, Williams RL. Prevalence of sleep apnea in men with erectile dysfunction. *Urology*. 1990;36:232–4.
51. Seftel AD, Strohl KP, Loye TL, Bayard D, Kress J, Netzer NC. Erectile dysfunction and symptoms of sleep disorders. *Sleep*. 2002;25:643–7.
52. Schiavi RC, Mandeli J, Schreiner-Engel P, Chambers A. Aging, sleep disorders, and male sexual function. *Biol Psychiatry*. 1991;30:15–24.

53. Margel D, Cohen M, Livne PM, Pillar G. Severe, but not mild, obstructive sleep apnea syndrome is associated with erectile dysfunction. *Urology*. 2004;63:545–9.
54. Perimenis P, Konstantinopoulos A, Karkoulas K, Markou S, Perimeni P, Spyropoulos K. Sildenafil combined with continuous positive airway pressure for treatment of erectile dysfunction in men with obstructive sleep apnea. *Int Urol Nephrol*. 2007;39:547–52.
55. Li X, Dong Z, Wan Y, Wang Z. Sildenafil versus continuous positive airway pressure for erectile dysfunction in men with obstructive sleep apnea: a meta-analysis. *Aging Male*. 2010;13:82–6.
56. Taskin U, Yigit O, Acioglu E, Aricigil M, Toktas G, Guzelhan Y. Erectile dysfunction in severe sleep apnea patients and response to CPAP. *Int J Impot Res*. 2010;22:134–9.
57. Gonçalves MA, Guilleminault C, Ramos E, Palha A, Paiva T. Erectile dysfunction, obstructive sleep apnea syndrome and nasal CPAP treatment. *Sleep Med*. 2005;6:333–9.
58. Cruz IA, Drummond M, Winck JC. Obstructive sleep apnea symptoms beyond sleepiness and snoring: effects of nasal APAP therapy. *Sleep Breath*. 2011 [epub ahead of print].
59. Andersen ML, Santos-Silva R, Bittencourt LR, Tufik S. Prevalence of erectile dysfunction complaints associated with sleep disturbances in Sao Paulo, Brazil: a population-based survey. *Sleep Med*. 2010;11:1019–24.
60. Stannek T, Hürny C, Schoch OD, Bucher T, Münzer T. Factors affecting self-reported sexuality in men with obstructive sleep apnea syndrome. *J Sex Med*. 2009;6:3415–24.
61. Gur S, Kadowitz PJ, Hellstrom WJ. A critical appraisal of erectile function in animal models of diabetes mellitus. *Int J Androl*. 2009;32:93–114.
62. Alberti KG, Zimmet P, Shaw J. Metabolic syndrome—a new world-wide definition. A consensus statement from the International Diabetes Federation. *Diabet Med*. 2006;23:469–80.
63. Shin D, Pregoner Jr G, Gardin JM. Erectile dysfunction: a disease marker for cardiovascular disease. *Cardiol Rev*. 2011;19:5–11.
64. Rizvi K, Hampson JP, Harvey JN. Do lipid-lowering drugs cause erectile dysfunction? A systematic review. *Fam Pract*. 2002;19:95–8.
65. Wu C, Zhang H, Gao Y, Tan A, Yang X, Lu Z, et al. The association of smoking and erectile dysfunction: results from the Fangchenggang Area Male Health and Examination Survey (FAMHES). *J Androl*. 2012;33(1):59–65.
66. Manolis A, Doulas M. Sexual dysfunction: the 'prima ballerina' of hypertension-related quality-of-life complications. *J Hypertens*. 2008;26:2074–84.