



Effects of exercise on sleep symptoms in patients with severe obstructive sleep apnea

Roberto Pacheco da Silva^{1,a}, Denis Martinez^{1,2,3,b},
Kelly Silveira da Silva Bueno^{1,c}, Jhoana Mercedes Uribe-Ramos^{2,d}

1. Programa de Pós-Graduação em Cardiologia e Ciências Cardiovasculares, Universidade Federal do Rio Grande do Sul – UFRGS – Porto Alegre (RS) Brasil.
 2. Programa de Pós-Graduação em Ciências Médicas, Universidade Federal do Rio Grande do Sul – UFRGS – Porto Alegre (RS) Brasil.
 3. Divisão de Cardiologia, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul – UFRGS – Porto Alegre (RS) Brasil.
- a. <http://orcid.org/0000-0002-5580-0465>
b. <http://orcid.org/0000-0002-3578-0372>
c. <http://orcid.org/0000-0002-1357-5781>
d. <http://orcid.org/0000-0003-0907-3831>

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ABSTRACT

Objective: To investigate the extent to which exercise is associated with symptoms in patients with severe obstructive sleep apnea (OSA). **Methods:** We included subjects with an apnea-hypopnea index (AHI) > 30 events/h who completed validated sleep and exercise questionnaires. We compared symptom frequency/scores between exercisers and nonexercisers, adjusting for the usual confounders. **Results:** The sample included 907 nonexercisers and 488 exercisers (mean age, 49 ± 14 years; mean AHI, 53 ± 20 events/h; 81% men). Nonexercisers and exercisers differed significantly in terms of obesity (72% vs. 54%), the mean proportion of sleep in non-rapid eye movement stage 3 sleep (9 ± 8% vs. 11 ± 6%), and tiredness (78% vs. 68%). Nonexercisers had a higher symptom frequency/scores and poorer sleep quality. Adjustment for exercise weakened the associations between individual symptoms and the AHI, indicating that exercise has a mitigating effect. In binary logistic models, exercise was associated with approximately 30% lower adjusted questionnaire¹ score > 2, tiredness; poor-quality sleep, unrefreshing sleep, and negative mood on awakening. Although the odds of an Epworth Sleepiness Scale score > 10 were lower in exercisers, that association did not withstand adjustment for confounders. **Conclusions:** Exercise is associated with lower frequency/intensity of symptoms in patients with severe OSA. Because up to one third of patients with severe OSA might exercise regularly and therefore be mildly symptomatic, it is important not to rule out a diagnosis of OSA in such patients.

Keywords: Sleep apnea syndromes; Exercise; Sleepiness; Polysomnography.

INTRODUCTION

Excessive daytime sleepiness and daytime fatigue are symptoms of obstructive sleep apnea (OSA).⁽¹⁾ OSA contributes to decreased energy levels and motivation throughout the day.⁽²⁾ Insufficient motivation is commonly reported as a cause of reduced participation in exercise programs.^(3,4) Approximately one quarter of patients with moderate-to-severe OSA are mildly symptomatic.⁽⁵⁾ Maintaining a regular exercise program could mitigate the symptoms of OSA.^(6,7) One confounder in the OSA-exercise association is exercise intensity.⁽⁸⁾ In a previous study conducted by our group, exercise was associated with a 34% lower adjusted risk of severe OSA.⁽⁹⁾

A considerable proportion of individuals with OSA exercise. It has been reported that 34% of patients with moderate-to-severe OSA exercise regularly,⁽⁸⁾ as do 21% of those with severe OSA,⁽⁹⁾ indicating the relevance of studying the relationship between OSA and exercise.

We tested the hypothesis that regular exercise is associated with sleep quality and OSA symptoms in patients with severe OSA. We examined the database of a university-affiliated sleep laboratory to investigate the relationship between physical activity and sleep symptoms in patients with OSA.

METHODS

This was a retrospective subgroup analysis of a previously published cross-sectional observational study.⁽⁹⁾ We examined data related to consecutive patients, ≥ 18 years of age, who were referred to our sleep laboratory between March of 2013 and August of 2015 for the investigation of sleep disorders. At the time of the original study, all of the participants gave written informed consent for the anonymous use of their data.

Questions about sleep quality, together with validated questionnaires on sleep,⁽¹⁰⁾ sleepiness,⁽¹¹⁾ and psychological symptoms,⁽¹²⁾ were employed to assess the variables of interest prior to polysomnography. The quality of sleep was determined with Likert scales, and the level of physical activity was assessed with the International Physical Activity Questionnaire (IPAQ).⁽¹³⁾ Participant occupations were also categorized by the level of physical activity required.⁽¹⁴⁾ In addition, the probability of a diagnosis of OSA was assessed with a truncated version of the **S**nooring, **T**iredness, **O**bserved apnea, high blood **P**ressure, **B**ody mass index, **A**ge, **N**eck circumference, and **G**ender (STOP-Bang) questionnaire.⁽¹⁵⁾ To determine the degree of daytime sleepiness, the Epworth Sleepiness Scale (ESS) was

Correspondence to:

Roberto Pacheco da Silva. Divisão de Cardiologia, Hospital de Clínicas de Porto Alegre, Rua Ramiro Barcelos, 2350, CEP 90035-903, Porto Alegre, RS, Brasil.
Tel.: 55 51 3359-8289. Fax: 55 51 3022-2282. E-mail: roberto.pacheco01@gmail.com
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¹ A truncated form of the **S**nooring, **T**iredness, **O**bserved apnea, high blood **P**ressure, **B**ody mass index, **A**ge, **N**eck circumference, and **G**ender questionnaire.

applied.⁽¹⁵⁾ Incomplete and inconsistent questionnaires were excluded.

Sleep symptoms

Yes/no questions

All patients were interviewed by the researchers. During the interviews, the patients answered four questions—"Do you consider yourself sleepier than other persons?"; "Do you have usually difficulty initiating sleep?"; "Do you have usually difficulty maintaining sleep?"; and "Do you usually wake up feeling unrefreshed?"—in a yes/no format.

Likert scales

Using a 0-10 point Likert scale, the patients responded to the questions "How do you rate your sleep quality?" and "How do you rate your mood?"—a score of 0 indicating the worst (sleep quality or mood) and a score of 10 indicating the best. Sleep quality, as rated by the patients, was dichotomized, a score ≤ 5 being categorized as poor sleep quality and a score > 5 being categorized as satisfactory sleep quality. Scores on another question—"How do you rate your level of tiredness on waking up?"—also ranged from 0 (not tired at all) to 10 (most tired possible).

STOP-Bang questionnaire

The STOP-Bang questionnaire⁽¹⁵⁾ takes into account the following signs and symptoms of OSA: snoring; tiredness; observed apnea; high blood pressure; body mass index > 35 kg/m²; age > 50 years; neck circumference > 40 cm; and male gender. The questionnaire consists of eight yes/no questions, and a "yes" is equal to a score of 1. The total score therefore ranges from 0 to 8, higher scores indicating a higher probability of a diagnosis of OSA. A score ≥ 3 is associated with high sensitivity for the detection of OSA, and a score of 5-8 is associated with a high probability of moderate-to-severe OSA. Because body mass index, age, and gender were control variables in the multivariate models, we analyzed the STOP portion alone and did not include the Bang score in the comparisons.

ESS

The ESS is a self-report questionnaire, developed in 1991, that assesses the likelihood of the individual falling asleep in eight different situations.⁽¹⁶⁾ The scale has a maximum score of 24 points, and a score > 10 is considered indicative of excessive daytime sleepiness.

Physical activity

Physical activity was assessed with an abridged version of the IPAQ for young and middle-aged adults, which has been translated to Portuguese and validated for use in Brazil.⁽¹³⁾ The IPAQ was proposed by an international consensus group with representatives of 25 countries, including Brazil, under the auspices of the World Health Organization.⁽¹⁷⁾ The IPAQ is a

self-report questionnaire comprising 8 questions that estimate the time spent weekly in different types of at least moderate physical activity and being physically inactive (sitting). On the basis of the answers on the IPAQ, patients were classified as nonexercisers or exercisers. Individuals reporting at least 10 min of moderate- or high-intensity physical activity per day were classified as exercisers. Exercise was classified, by type, as endurance training, resistance training, or combined training (such as practicing a sport). Exercise intensity was classified as moderate or vigorous. Moderate exercise was defined as that which made the participant breathe somewhat harder than normal. Vigorous exercise was defined as that which made the participant breathe much harder than normal. The frequency of exercise was recorded in days per week, duration of exercise in minutes per day, and time sitting in hours per day. Participants who did not meet the criterion of ≥ 10 min of moderate- or high-intensity physical activity at least once a week were classified as nonexercisers. Incomplete or inconsistent questionnaires were excluded.

Occupational activity

We employed the Physical Demands - Strength Rating from the Dictionary of Occupational Titles⁽¹⁸⁾ to describe the strength requirements of each occupation. The rating is based on worker involvement in activities such as standing, walking, sitting, lifting, carrying, pushing, and pulling. By analogy with the IPAQ, in which only moderate and vigorous levels of exercise are considered in order to classify a person as physically active, participants performing sedentary or light work were classified as inactive, whereas those performing medium, heavy, or very heavy work were classified as active.

Polysomnography

Subjects underwent overnight polysomnography as previously described.⁽¹⁹⁾ In brief, data were recorded from approximately 23:00 to 07:00. Electroencephalogram (electrodes C4-A1, F4-A1, and O2-A1), electrocardiogram (electrode D1 or modified V4), left and right electrooculogram (electrode A1), and submental electromyogram were recorded. Airflow was measured through a nasal cannula connected to a pressure transducer (Ultima PT2 Dual; Braebon Medical Corp., Kanata, Canada). Respiratory effort was assessed by respiratory inductance plethysmography (Ultima Q-RIP; Braebon Medical Corp.), and oxygen saturation by pulse oximetry (XPOD; Nonin Medical, Inc., Plymouth, MN, USA). The recordings were made at room temperatures between 22°C and 26°C. Sleep scoring followed the 2012 American Academy of Sleep Medicine rules.⁽²⁰⁾

Apnea was defined as a drop in airflow to $\geq 90\%$ of baseline for ≥ 10 s; hypopnea was defined as a drop in airflow to $\geq 50\%$ of baseline for ≥ 10 s, accompanied by $\geq 3\%$ arterial oxygen desaturation or an arousal. The apnea-hypopnea index (AHI) was

calculated by dividing the total number of apnea and hypopnea events by the total hours of sleep. During the night, snoring was rated, by the technicians, from 0 to 10 on an arbitrary scale. This rating was reconciled with the full-night tracing of snoring by the reviewing physician. Patients diagnosed with respiratory disorders other than OSA were excluded. Polysomnography records including at least 4 h of sleep and indicative of severe OSA, defined as an AHI ≥ 30 events/h, were included. On the night of the study, trained technicians weighed the patients, as well as measuring their blood pressure, neck circumference, and waist circumference. Patients were classified as hypertensive if their blood pressure was $\geq 140/90$ mmHg or if they had previously been diagnosed with or treated for hypertension.

Statistical analysis

Data were analyzed using the Predictive Analytics Software package, version 18.0 (SPSS Inc., Chicago, IL, USA). Continuous variables with normal distribution are presented as means and standard deviations. Differences between groups were calculated using Student's *t*-tests for independent samples. In univariate analyses, binary logistic regression was used in order to determine whether OSA symptoms and scores were significantly associated with the variables of interest—level of physical activity (nonexerciser vs. exerciser) and occupational activity (inactive vs. active)—or with well-known confounders such as male gender, body mass index > 30 kg/m², and age > 48 years. In multivariate analyses, the AHI, age, minimum oxygen saturation, age, and sleep quality were analyzed as continuous or dichotomous variables, the latter being dichotomized at the median. As a dichotomous variable, tiredness was based on the participant responses on the STOP portion of the STOP-Bang questionnaire. Due to the numerous comparisons and the large sample size, only results with a $< 1\%$ probability of a type I error were considered significant.

RESULTS

From a database of 5,984 sleep studies, we obtained the complete files of 1,395 untreated patients with severe OSA (Figure 1). Table 1 displays the characteristics of the sample according to the exercise status. Exercisers differed from nonexercisers regarding anthropometric features. However, the prevalence of comorbidities was similar between the two groups.

The training characteristics of the exercisers are shown in Table S1 (online supplement on the JBP website). A small proportion of the exercisers (1.6%) reported poorer sleep quality on the nights after a day on which they exercised. The rates of a positive sleep outcome after exercising were similar between men and women, those > 50 years of age, and between patients with a BMI < 30 kg/m² and those with a BMI ≥ 30 kg/m².

The largest effect size among all polysomnographic and sleep symptom variables, as indicated by Cohen's *d*, was that of exercise for the AHI (Table 2). Significant differences between exercisers and nonexercisers were also evident for other markers of OSA severity, such as minimum oxygen saturation, time at an oxygen saturation below 90%, and snoring intensity. The duration of non-rapid eye movement stage 3 sleep was longer in the exerciser group, as was that of rapid eye movement sleep. The frequency of symptoms and symptom scores were lower among the exercisers than among the nonexercisers; the STOP score had the largest effect size for symptoms. Fifteen patients had a score of 0 on the STOP portion of the STOP-Bang questionnaire. Between obese and nonobese exercisers, in terms of the frequencies of all symptoms and all symptom scores, the only significant difference found was that the proportion of patients with hypertension was higher among the patients who were obese than among those who were not. Among the nonexercisers, seven symptoms or symptom scores were significantly different between the obese and nonobese patients, the former being consistently more tired and sleepy than were the latter. Hypertension was reported less frequently on the STOP portion of the STOP-Bang questionnaire than was observed in the physical examination/anamnesis (Table 1). That discrepancy was seen more often among exercisers.

The association of exercise with eleven symptoms and symptom scores that were significantly different between exercisers and nonexercisers, as shown in Table 2, was further tested in a binary logistic model. Among those eleven variables, six remained significant, although with small effect sizes (odds ratios) after adjustment for age > 48 years, male gender, obesity, active occupation, and AHI > 43 events/h (Table 3).

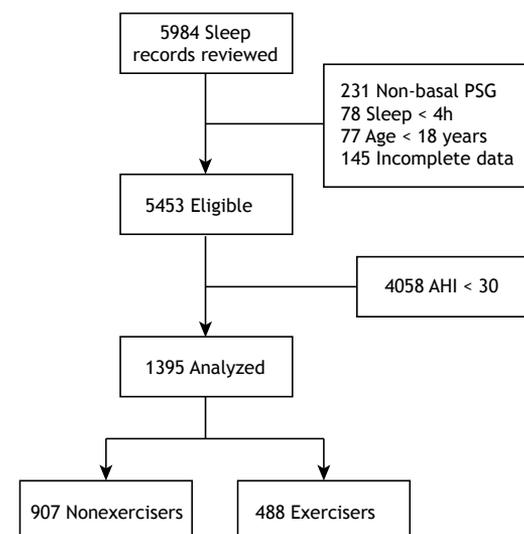


Figure 1. Flowchart of the record selection process. PSG: polysomnography; and AHI: apnea-hypopnea index (events/h).

Table 1. Characteristics of the participants, by exercise status.^a

Characteristic	Regular exercise		p*
	No (n = 907)	Yes (n = 488)	
Male gender	730 (80.5)	396 (81.1)	0.41
Age (years)	48 ± 14	50 ± 14	0.03
Body mass index (kg/m ²)	34.6 ± 7.4	31.3 ± 5.3	< 0.001
Body mass index > 30 kg/m ²	649 (71.6)	262 (53.7)	< 0.001
Neck circumference (cm)	41.6 ± 4.8	40.5 ± 4.6	< 0.001
Waist circumference (cm)	108 ± 17	104 ± 16	< 0.001
Heart rate (bpm)	85 ± 13	82 ± 13	< 0.001
Systolic blood pressure (mm Hg)	140 ± 19	139 ± 19	0.29
Diastolic blood pressure (mm Hg)	84 ± 13	82 ± 13	0.03
Time sitting per day (hours)	5.9 ± 2.7	5.7 ± 2.4	0.23
Smoking (previous or current)	315 (34.7)	157 (32.2)	0.18
Comorbidities			
Hypertension	538 (59.3)	264 (54.1)	0.06
Diabetes	29 (3.2)	14 (2.9)	0.44
Heart failure	10 (1.1)	8 (1.6)	0.27
Asthma	21 (2.3)	7 (1.4)	0.18
Myocardial infarction	25 (2.8)	15 (3.1)	0.43
Chronic bronchitis	8 (0.9)	4 (0.8)	0.58
Emphysema	5 (0.6)	4 (0.8)	0.39
Renal failure	2 (0.2)	1 (0.2)	0.72
Cancer	7 (0.8)	6 (1.2)	0.28
Arterial disease	15 (1.7)	5 (1.0)	0.24
Stroke	10 (1.1)	7 (1.4)	0.38
Mental disorder	31 (3.4)	14 (2.9)	0.35
Other chronic disease	5 (0.6)	3 (0.6)	0.57

^aData are presented as mean ± standard deviation or as n (%). *Nonexercisers vs. exercisers (Student's t-test); significant at p ≤ 0.01.

Figure 2 shows the univariate analyses in which the six sleep quality variables that were significantly different between exercisers and nonexercisers were included as dependent variables in a binary logistic regression to test their association with exercise as the independent variable. Five of those dependent variables remained significantly associated with exercise after adjustment for age > 48 years, male gender, obesity, active occupation, and AHI > 43 events/h, exercisers showing an approximately 30% reduction in the odds of having a sleep symptom or unfavorable symptom score. There was an association between an ESS score > 10 and exercise. However, that association did not withstand adjustment (Figure 2). The ESS score correlated weakly with an AHI > 43 events/h (rho = 0.22; p < 0.001). Although age and AHI were also tested as continuous variables, the versions that were dichotomized at the median were used in the figure for visualization purposes, because the results were similar. Due to its high collinearity with AHI, the minimum oxygen saturation was not included in the models.

To determine whether AHI severity had a dose-response relationship with the frequency of symptoms and symptom scores, we divided the sample into five AHI categories (Table 4). Significantly lower proportions

of moderate and vigorous exercisers, for all exercise types, were observed only among the patients with an AHI > 70 events/h. Of the patients in the AHI > 70 events/h category, only 7.8% reported exercising vigorously. In addition, 22.3% of those patients had a normal ESS score. Significant differences among the AHI categories in terms of the frequency of symptoms and symptom scores were seen only for the patients in the AHI 60-70 events/h category, and those differences were small. One single question ("Do you consider yourself sleeper than other persons?") also showed a significant, albeit weak, association with the subcategories of AHI severity (gamma = 0.25; p for trend < 0.001). It is surprising that only 89.4% of the patients in the sample answered "yes" to the snoring question of the STOP portion of the STOP-Bang questionnaire, and that even a few of the patients in the AHI > 70 events/h category answered "no".

DISCUSSION

The present study provides data that underscore the difficulty of detecting OSA on the basis of its symptoms, even in the most severe cases. In addition, we have quantified the differences in symptom frequency and symptom scores between exercisers and nonexercisers.

Table 2. Objective and subjective sleep characteristics, by exercise status.^a

Characteristic	Nonexercisers (n = 907)	Exercisers (n = 488)	Effect size*	p [†]
Polysomnography variables (ordered by effect size)				
Apnea-hypopnea index (events/h)	56 ± 21	48 ± 17	0.42	< 0.001
Snoring score (AU) ^b	6.7 ± 1.9	6.1 ± 1.8	0.32	< 0.001
TB90% (min)	50 ± 52	36 ± 43	0.29	< 0.001
N3 sleep (%)	9 ± 8	11 ± 8	0.25	< 0.001
Lowest oxygen saturation (%)	75 ± 10	77 ± 9	0.21	< 0.001
REM sleep (%)	11 ± 6	12 ± 6	0.17	0.006
Total sleep time (min)	396 ± 53	395 ± 53	0.02	0.64
Sleep efficiency (%)	86 ± 10	86 ± 11	0.00	0.57
N1 sleep (%)	6 ± 3	6 ± 3	0.00	0.03
Symptoms and scores				
Total STOP score	3.0 ± 0.9	2.7 ± 1.0	0.32	< 0.001
Total STOP score > 2	664 (73.2)	304 (62.3)	0.28	< 0.001
Snores loudly	814 (89.7)	426 (87.3)	0.13	0.09
Often tired	703 (77.5)	332 (68.0)	0.27	< 0.001
Observed apnea	687 (75.7)	349 (71.5)	0.12	0.07
High blood pressure	475 (52.4)	216 (44.3)	0.18	0.004
Sleep quality score (AU) ^b	5.5 ± 2.4	6.0 ± 2.2	0.26	< 0.001
Unrefreshing sleep	580 (63.9)	263 (53.9)	0.23	< 0.001
Sleepier than other people	515 (56.8)	229 (46.9)	0.22	< 0.001
Difficulty initiating sleep	315 (34.7)	168 (34.4)	0.01	0.97
Difficulty maintaining sleep	384 (42.3)	185 (37.9)	0.10	0.07
Mood score (AU) ^b	5.6 ± 2.6	6.1 ± 2.5	0.20	< 0.001
Low energy on waking score (AU) ^c	2.7 ± 1.7	2.4 ± 1.2	0.20	< 0.001
Total Epworth Sleepiness Scale score ^d	13 ± 6	12 ± 5	0.18	0.002
Epworth Sleepiness Scale score > 10	600 (66.2)	288 (59.0)	0.17	0.005
Stanford Sleepiness Scale score (AU) ^c	2.5 ± 1.3	2.3 ± 1.3	0.15	0.07
Feeling blue score (AU) ^e	0.56 ± 1	0.59 ± 1.1	0.03	0.62
Waking up tired score (AU) ^b	2.5 ± 2.7	2.5 ± 2.7	0.00	0.93

AU: arbitrary units; TB90%: time with oxygen saturation below 90%; N3: non-rapid eye movement stage 3; REM: rapid eye movement; N1: non-rapid eye movement stage 1; and STOP: **S**nooring, **T**iredness, **O**bserved apnea, high blood **P**ressure. ^aData are presented as mean ± standard deviation or as n (%); ^bScale of 0-10; ^cScale of 0-7; ^dScale of 0-24; ^eScale of 0-4. *Cohen's d. [†]Nonexercisers vs. exercisers (Student's t-test); significant at p ≤ 0.01.

Exercise-induced changes in symptoms might reduce the sensitivity of screening instruments, although the magnitude of that effect could not be determined in our study. Our results suggest that exercise reduces sleep symptom frequency and symptom scores by approximately 30% in patients with OSA, an association that withstood adjustment for confounders such as gender, age, and body mass index.

We found no relationship between occupational physical activity level and any of the sleep symptoms studied, indicating that regular exercise is not comparable to hard work in terms of the possible repercussions for OSA symptoms. It is plausible that a higher occupational physical activity level could be responsible for more intense symptoms of fatigue, countering the positive effects of occasional exercise. In our sample, however, that supposition can be dismissed, given that our multivariate analyses confirmed the lack of association between the occupational physical activity level and the symptoms tested.

Even after OSA symptoms are recognized by a patient, years can pass before that patient is diagnosed and treated.^(21,22) Patients often underreport their symptoms, and sleep quality is rarely specifically assessed during a clinical consultation. In that context, exercise may contribute to delaying the diagnosis.

Sleepiness is a presumed but nonspecific symptom of OSA. The well-known poor correlation between sleepiness and OSA severity limits the usefulness of the ESS in OSA screening.⁽²³⁾ In our sample of patients with severe OSA, the ESS score correlated only weakly with an AHI > 43 events/h. The question "Do you consider yourself sleepier than other persons?" showed a significant, albeit weak, association with the subcategories of AHI severity. However, a difference in ESS score between those subcategories was observed only for the AHI 60-70 events/h category. Even in the AHI > 70 events/h category, 22.0% of patients still had a normal ESS score.

The diagnosis and treatment of OSA are typically delayed.⁽²¹⁾ In exercisers, that delay can be longer

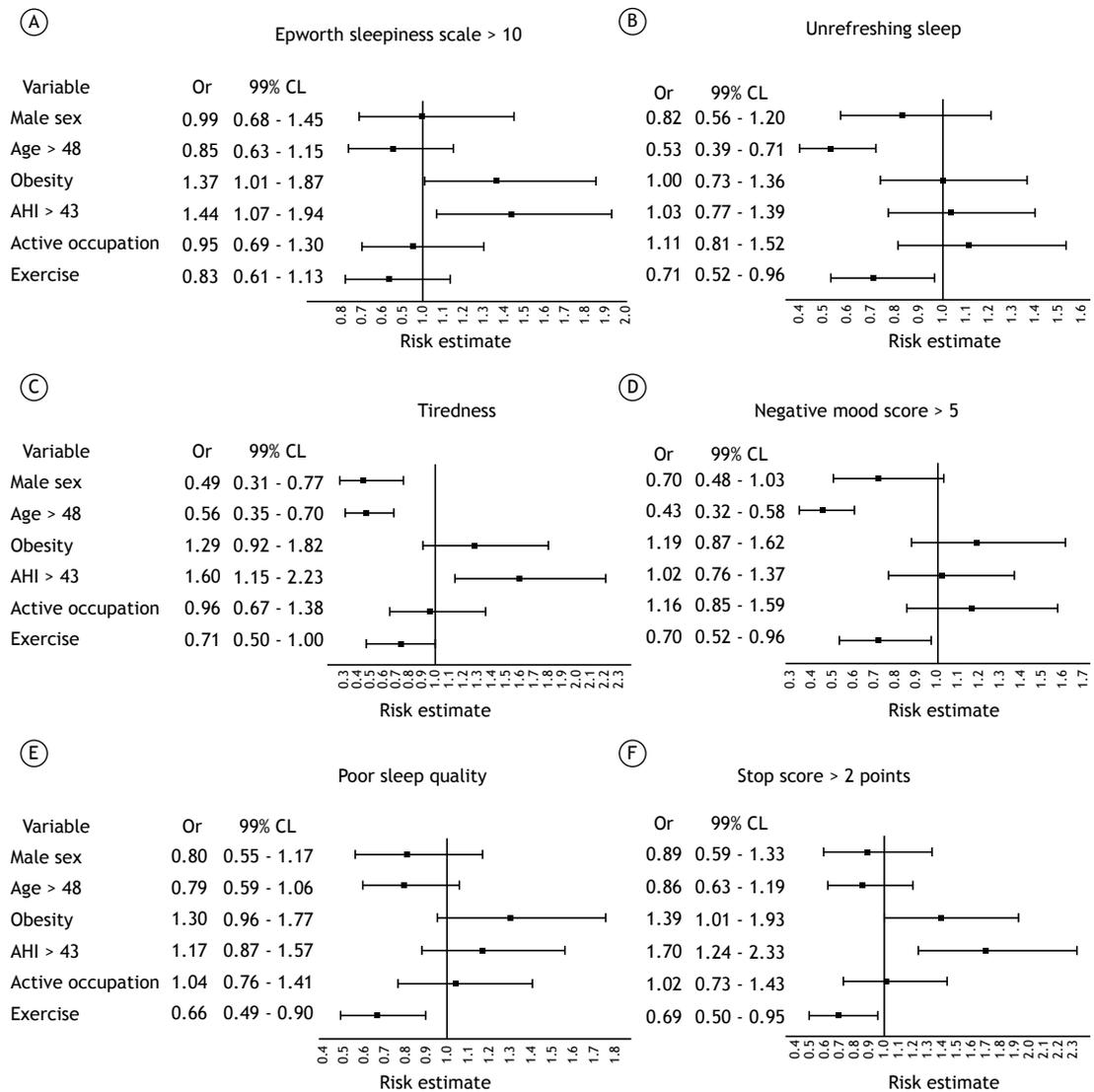


Figure 2. Forest plots of the binary logistic models estimating the odds ratio of six dependent variables. The following symptoms or dichotomized scores are included: a) Epworth Sleepiness Scale score > 10; b) tiredness; c) poor sleep quality (score ≤ 5 on the sleep quality scale); d) unrefreshing sleep; e) negative mood score > 5; and f) Snoring, Tiredness, Observed apnea, high blood Pressure (STOP) questionnaire score > 2 points. The variables of interest, regular exercise (nonexercisers vs. exercisers), and occupational activity (inactive vs. active) were adjusted for an apnea-hypopnea index > 43 events/h and for the confounders age > 48 years, male gender, and obesity (body mass index > 30 kg/m²). Of the symptoms and scores listed above, the only one that did not present a significant association with regular exercise was an Epworth Sleepiness Scale score > 10.

if combined with a reassuring report of intense exercise. This is of particular clinical interest, given that patients with severe OSA could be at a higher risk of cardiovascular events if they engage in vigorous exercise. Of the individuals in the AHI > 70 events/h category, only a small proportion reported exercising vigorously. However, the criterion for vigorous exercise is subjective. Breathing “much harder than normal” might be achieved by such patients at lower levels of effort than by an individual without OSA.

To our knowledge, there have been no previous studies on the symptoms of patients with severe OSA and their commitment to exercise programs.

Likewise, a commissioned systematic review⁽²⁴⁾ concluded that “there is uncertainty about the accuracy or clinical utility of all potential screening tools” in asymptomatic persons. Exercise might be a contributor to this uncertainty. Studies indicating that exercise reduces symptoms such as pain, tiredness, sleepiness, negative mood, and sleep quality⁽²⁵⁻²⁸⁾ indirectly corroborate our findings.

Although some sleep hygiene studies have recommended avoiding nighttime exercise, our data suggest otherwise. Only a small proportion of the exercisers reported poorer sleep quality after exercising the night before. That is in agreement with

Table 3. Univariate and multivariate analyses of the association of exercise with symptoms and scores, in order by effect size, as indicated by the adjusted odds ratio.

Dependent variable	Symptoms	Odds ratio (99% CI)	
		Model 1 (Univariate)	Model 2 (Adjusted*)
No exercise	Sleep quality score (AU, 0-10)	0.91 [†] (0.86-0.97)	0.93 [†] (0.87-0.99)
	Morning mood score (AU, 0-10)	0.98 (0.90-1.04)	0.97 (0.90-1.04)
	Epworth Sleepiness Scale score (0-24)	1.03 [†] (1.01-1.06)	1.02 (0.99-1.05)
	Low energy on waking score (0-7)	1.16 [†] (1.04-1.30)	1.16 [†] (1.03-1.30)
	Epworth Sleepiness Scale score > 10	1.36 [†] (1.01-1.83)	1.21 (0.89-1.65)
	Score on the STOP questionnaire (0-4)	1.34 [†] (1.15-1.57)	1.21 [†] (1.03-1.42)
	Sleepier than other people	1.48 [†] (1.11-1.99)	1.31 (0.96-1.77)
	High blood pressure	1.39 [†] (1.04-1.85)	1.35 (0.98-1.87)
	Unrefreshing sleep	1.51 [†] (1.12-2.03)	1.44 [†] (1.06-1.96)
	Score on the STOP questionnaire > 2	1.69 [†] (1.24-2.31)	1.45 [†] (1.05-2.01)
	Often tired	1.65 [†] (1.19-2.28)	1.51 [†] (1.08-2.12)

AU: arbitrary units; and STOP: **S**norring, **T**iredness, **O**bserved apnea, high blood **P**ressure. *Adjusted for age > 48 years, male gender, obesity, active occupation, and apnea-hypopnea index > 43 events/h. [†]Significant effect.

Table 4. Exercise description and symptom score by strata of severe apnea-hypopnea index.^{a,b}

Variable	AHI 30-40 (n = 505)	AHI 40-50 (n = 244)	AHI 50-60 (n = 194)	AHI 60-70 (n = 174)	AHI > 70 (n = 269)	p for trend*
Exercise frequency (days/week)	3.2 ± 1.4 [†]	2.9 ± 1.2 [†]	2.9 ± 1.6 [†]	3.0 ± 1.4 [†]	3.5 ± 1.5 [†]	0.06
Exercise Intensity						
Moderate	146 (34) [†]	60 (28) [†]	52 (30) [†]	38 (23) [†]	29 (12) [‡]	< 0.001
Vigorous	79 (22) [†]	34 (18) [†]	18 (13) ^{†,‡}	10 (7) [‡]	21 (9) [‡]	< 0.001
Exercise type						
Endurance	51 (15) [†]	21 (12) ^{†,‡}	10 (8) ^{†,‡}	9 (7) ^{†,‡}	11 (5) [‡]	< 0.001
Resistance	62 (18) [†]	28 (16) [†]	19 (13) ^{†,‡}	17 (12) ^{†,‡}	16 (7) [‡]	< 0.001
Combined	108 (28) [†]	44 (23) ^{†,‡}	40 (24) ^{†,‡}	22 (15) ^{†,‡,§}	22 (9) [§]	< 0.001
Total STOP score	2.7 ± 1.0 [†]	2.9 ± 0.9 [†]	2.8 ± 0.9 [†]	3.2 ± 0.8 [‡]	3.1 ± 0.8 [‡]	< 0.001
Snoring loudly	433 (85) [†]	215 (89) ^{†,‡}	172 (89) ^{†,‡}	165 (94) [‡]	255 (95) [‡]	< 0.001
Often tired	346 (68) [†]	172 (71) [†]	142 (74) ^{†,‡}	150 (86) [§]	225 (84) ^{†,§}	< 0.001
Observed apnea	329 (65) [†]	188 (78) [‡]	148 (77) [‡]	146 (83) [‡]	255 (84) [‡]	< 0.001
High blood pressure	240 (47) [†]	125 (51) [†]	86 (44) [†]	100 (57) [†]	140 (52) [†]	0.09
Sleep quality (AU) ^c	5.9 ± 2.2 [†]	6.0 ± 2.1 [†]	5.8 ± 2.2 [†]	5.5 ± 2.6 ^{†,‡}	4.9 ± 2.5 [‡]	< 0.001
Unrefreshing sleep	304 (60) [†]	143 (59) [†]	114 (59) [†]	110 (63) [†]	172 (64) [†]	0.22
Sleepier than other people	233 (46) [†]	113 (47) [†]	104 (54) ^{†,‡}	107 (61) ^{†,§}	187 (70) [§]	< 0.001
Negative mood on waking score (AU) ^c	5.9 ± 2.5 ^{†,‡}	5.9 ± 2.4 ^{†,‡}	6 ± 2.5 [‡]	5.5 ± 2.6 ^{†,‡}	5.2 ± 2.7 [†]	0.001
Low energy on waking score (AU) ^d	2.6 ± 1.4 [†]	2.5 ± 1.3 [†]	2.5 ± 1.2 [†]	2.7 ± 1.3 [†]	2.8 ± 1.3 [†]	0.26
Epworth Sleepiness Scale score	11.4 ± 5.1 [†]	12.1 ± 5.3 ^{†,‡}	11.5 ± 5.1 [†]	13.2 ± 5.3 [‡]	15.0 ± 5.4 [§]	< 0.001
Epworth Sleepiness Scale score > 10	269 (58) [†]	154 (63) [†]	108 (58) [†]	121 (69) ^{†,‡}	209 (78) [‡]	< 0.001

AHI: apnea-hypopnea index (events/h); STOP: **S**norring, **T**iredness, **O**bserved apnea, high blood **P**ressure; and AU: arbitrary units. ^aData are presented as mean ± standard deviation or as n (%); ^bDue to rounding and incomplete questionnaires, percentages do not always add to 100%; ^cScale of 0-10; ^dScale of 0-7. *ANOVA or chi-square test; significant at p ≤ 0.01; ^{†,‡,§}Different symbols represent significantly different subsets of Bonferroni post-hoc test at 0.01 alpha level.

meta-analysis evidence about the effect of nighttime exercise on sleep.⁽²⁹⁾ Considering meta-analysis data from interventional studies,⁽²⁹⁾ it is plausible that exercise improves sleep quality in general and is associated with lower OSA severity even in a stratum restricted to severe OSA. Our results are not sufficiently robust to be conclusive, and additional studies are needed in order to confirm our findings.

In the present study, there were significant differences between exercisers and nonexercisers in terms of non-rapid eye movement stage 3 and

rapid eye movement sleep, although neither of those variables were included in the multivariate analyses. Including those variables in the models did not change the symptom-exercise associations.

Our study has some limitations. Due to the cross-sectional design of the study, we cannot infer any causal aspects of the OSA-exercise relationship. The external validity of the results is limited due to the exclusive sampling of patients with severe OSA from a population undergoing polysomnography at a sleep laboratory. Although that limits the

generalizability of the data to the overall population of patients with OSA, we decided to study only severe cases in order to obtain a group in which symptoms were more intense than in mild-to-moderate OSA. Although mild OSA is common,^(30,31) affecting up to one third of the general population,⁽³²⁾ patients have fewer symptoms or are asymptomatic in the incipient stages of the disease.⁽³³⁾ One additional reason for including only severe OSA cases in the present study is that the cardiovascular consequences of OSA,⁽³⁴⁾ which could impair exercise capacity, are more often seen in cases of moderate-to-severe OSA.⁽³⁾ The sample being derived from patients that were referred to a sleep laboratory in general represents a selection bias, also reducing the external validity of the results. Another limitation is that physical activity and sleep symptoms were assessed by means of questionnaires, given that such instruments introduce a measurement bias. In general, studies assessing the measurement properties of physical activity questionnaires indicate that their quality is insufficient to allow a reliable estimate of exercise level when compared with accelerometers.^(35,36) Despite these restrictions, the IPAQ has an acceptable level of reliability. It is convenient as well as being widely used in clinical scenarios and in cross-sectional studies in which the bias introduced will be the same in every group. However, the IPAQ may not be suitable for interventional studies

due to low reproducibility.⁽³⁷⁾ In sleep medicine, the STOP-Bang questionnaire is a common tool in OSA screening, despite its low-to-moderate accuracy. We analyzed the STOP portion alone and did not include the Bang score in the comparisons, because body mass index, age, and gender were control variables in the multivariate models.

The strength of the present study is that the data evaluated were derived from overnight in-laboratory polysomnography tests. The statistical power of our results (> 99%) and the choice of a 1% critical limit for the probability of a type I error support the internal validity of the study. The use of effect size to indicate the clinical relevance of a finding adds to the suitability of the statistical analyses.

This report indicates that patients with severe OSA often exercise and that regular exercise is associated with less frequent and less intense symptoms, independently of confounders. Compared with nonexercisers, exercisers appear to be less likely to complain of poor sleep quality and might therefore be more often dismissed by clinicians as not meeting the criteria for a diagnosis of OSA. Because up to one third of patients with severe OSA might engage in exercise on a regular basis, it is important to consider exercisers as potential cases of OSA even if they are only mildly symptomatic.

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