ABSTRACT
Out of the many sleep disorders, obstructive sleep apnea-hypopnea syndrome is one of the most harmful. This syndrome is an important risk factor for the development of cardiovascular disease and patient mortality. Exercise is a way to reduce cardiovascular mortality, which also results in improved sleep quality and may act on the pathogenesis of obstructive sleep apnea-hypopnea syndrome. However, evidence about the actual role of exercise in this syndrome is still scarce. We reviewed the existing literature about the possible benefits of exercise in patients with obstructive sleep apnea-hypopnea syndrome. We performed a search in the PubMed database using MESH Terms related to physical exercise and sleep apnea. Out of the 149 references identified, we selected randomized controlled trials or case studies in English or Portuguese that included patients with OSAHS. After searching titles, abstracts and full texts, we located only three studies that investigated the effects of exercise on the diagnostic and severity indices of obstructive sleep apnea-hypopnea syndrome. In these three papers, groups that exercised showed a reduction in the severity of the syndrome. Despite the insufficient level of evidence in the literature, the agreeing positive results of the studies suggest a potential benefit of exercise on obstructive sleep apnea-hypopnea syndrome.

Keywords: exercise; sleep apnea syndromes; cardiovascular diseases; sleep apnea, obstructive.

RESUMO
Dentre os distúrbios do sono, a síndrome da apneia-hipopneia obstrutiva do sono é um dos mais deletérios à saúde. Essa síndrome é um importante fator de risco para o aparecimento de doenças cardiovasculares, aumentando a taxa de mortalidade dos pacientes. Sabe-se que o exercício físico é uma das formas de reduzir a mortalidade cardiovascular, o que também resulta em melhora do sono e pode atuar sobre fatores fisiopatológicos da síndrome da apneia-hipopneia obstrutiva do sono. Contudo, evidências sobre o real papel do exercício físico na síndrome ainda são escassas. O objetivo dessa revisão foi investigar os possíveis benefícios do exercício físico na síndrome da apneia-hipopneia obstrutiva do sono. Foi realizada uma busca na base de dados do PubMed, utilizando termos MESH e outros relacionados ao exercício físico e à apneia do sono. Das 149 referências encontradas, foram selecionados os ensaios clínicos randomizados ou os estudos de casos, em inglês ou português, com amostra de indivíduos adultos portadores de síndrome da apneia-hipopneia obstrutiva do sono. Após seleção dos títulos, resumos e textos completos, foram localizados somente três estudos que investigaram os efeitos do exercício físico sobre os marcadores de presença e gravidade dessa síndrome. Nos três artigos, os grupos submetidos ao exercício evidenciaram redução na gravidade da síndrome. Apesar do nível de evidência insuficiente dos artigos, a concordância de resultados positivos dos estudos sugere potencial de benefício do exercício sobre a SAHOS.

Palavras-chave: exercício; síndromes da apneia do sono; doenças cardiovasculares; apneia do sono tipo obstrutiva.

INTRODUCTION
Exercise is a culturally and scientifically accepted non-drug intervention that is beneficial to health. There is evidence that it facilitates general wellness\(^1\) and sleep, in particular\(^2\). During sleep, breathing disorders can occur — in particular, obstructive sleep apnea-hypopnea syndrome (OSAHS), which is assuming epidemic proportions. Over two decades, reports of the prevalence of OSAHS increased from 4% in men and 2% in women\(^3\) to 32% of the total population\(^4\). The prevalence of OSAHS is 95% in the elderly, and more than 50 million Brazilians suffer from this syndrome\(^5\).

Additionally, OSAHS is an important risk factor for cardiovascular diseases\(^6\), including systemic hypertension\(^6,7\), resistant hypertension\(^8,9\), stroke\(^10\), obesity\(^11\) and metabolic syndrome\(^12\). American cardiology associations published a comprehensive document highlighting the need to inves-
Exercise and sleep apnea
tigate sleep apnea in cardiopathies\textsuperscript{13,14}. Patient mortality is increased with OSAHS and its comorbidities\textsuperscript{15,16}, while treatment for OSAHS reverses the consequences\textsuperscript{17} and reduces mortality\textsuperscript{18,19}.

Exercise reduces cardiovascular mortality\textsuperscript{20-22} and may modify the deleterious effects of OSAHS on the circulatory system\textsuperscript{23-26}. However, evidence about the role of exercise in OSAHS is still scarce. Thus, this review reports the direct and indirect benefits of exercise in OSAHS.

**METHODOLOGY OF THE REVIEW ON EXERCISE AS TREATMENT OF OSAHS**

Studies of exercise and OSAHS included in this review were randomized clinical trials or case studies written in English or Portuguese and examined adult human patients with OSAHS.

The search strategy is described in Appendix A and was conducted on December 16, 2010. For the search, we used the Medical Subject Headings (MeSH) terms “sleep apnea syndromes”, “sleep apnea, central”, “sleep apnea, obstructive” and “exercise” with their respective entry terms and Boolean operators in PubMed. Using these terms resulted in 149 results. One of the investigators (RPS) reviewed the results of this search, first by title, then by the abstract and full text. Finally, we selected 45 potentially relevant articles for review and discussed these with the other authors. After reading the full texts, three articles were chosen, as described in Table 1.

**Data collection process**

Data extraction was conducted by the first author and reviewed by the second author. Any discrepancies were corrected by consensus of the authors. The following information was extracted from articles: (1) authors; (2) years of publication; (3) type of study; (4) sample size; (5) age of the sample; (6) weight; (7) body mass index (BMI); (8) intervention; (9) apnea-hypopnea index (AHI) pre- and post-treatment and (10) statistical significance of change with treatment. These data are shown in Table 1.

The references obtained for the other topics described below in this paper, were based non-systematic reviews.

**OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME**

There are two types of sleep apnea: central, which is caused by the central nervous system, and obstructive, which involves physical changes in the pharynx\textsuperscript{27}. In central apnea, which is caused by failure of the ventilatory drive, there is no movement of the thorax and abdomen. Regardless of the cause, episodes of airflow reduction to 10\% or less of basal value for 10 seconds or more are called apneas. Reductions of 50\% or more of ventilatory flow, associated with a decrease of at least 3\% in oxygen saturation or an arousal, are called hypopneas. This situation normalizes rapidly after an arousal interrupts the apnea, resulting in the recovery of ventilation and normalization of arterial blood oxygen\textsuperscript{28}.

The severity of OSAHS is determined by the apnea-hypopnea index (AHI). The total number of apneas and hypopneas of the individual is divided by the number of hours of sleep. Normal values are below 5/hour; OSAHS is diagnosed as mild if AHI is between 5 and 14, moderate if AHI is between 15 and 29 and severe if AHI ≥30. Patients with OSAHS (AHI >5) present additional symptoms, including

<table>
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<tr>
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<th>Design</th>
<th>Sample analyzed (n)</th>
<th>Age (years)</th>
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<td>6 months, 3 times/week; Aerobic exercise, 30-45 minutes, 50-80% VO2max; and resistance exercise</td>
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<td>Giebelhaus</td>
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<td>Case study</td>
<td>11</td>
<td>52±6</td>
<td>80*</td>
<td>27±5</td>
<td>6-months, 2 times/week; Aerobic exercise, 120 minutes; and power exercise (repetitive light weight-lifting)</td>
<td>33±22</td>
<td>24*</td>
<td>&lt; 0.05</td>
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<tr>
<td>Sengul</td>
<td>2009</td>
<td>Randomized controlled trial</td>
<td>10</td>
<td>54±7</td>
<td>86±8</td>
<td>30±5</td>
<td>3-months, 3 times/week; Aerobic exercise, 45-60 minutes, 60-70% VO2max; and breathing exercise, 15-30min Control group</td>
<td>15±5</td>
<td>11±5</td>
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</table>

Data presented as mean±standard deviation. AHI: apnea-hypopnea index; BMI: body mass index; VO2max: peak oxygen uptake.

* This study did not report standard deviation for this variable.
excessive daytime sleepiness and snoring. Although not all snorers have OSAHS, untreated snoring can have cardiovascular consequences. In obstructive sleep apnea, there are several mechanisms of airway occlusion. These include fat accumulation in the neck, anatomic abnormalities, disorders of the upper airway muscles and unbalances in respiratory control, all of which contribute to airway obstruction during sleep.

OSAHS AND CARDIOVASCULAR INJURY

The main cardiovascular consequences arising from OSAHS are generated by cyclic intermittent hypoxia and arousals. Intermittent hypoxia and arousals result in chronic hyperactivity of the sympathetic nervous system, increased heart rate, blood pressure, sensitivity of central and peripheral chemoreceptors and decreased baroreceptor activation. They can also result in oxidative stress, inflammation, endocrine disorders and endothelial dysfunction. These changes are mechanisms that underlie the onset of cardiovascular and metabolic diseases. Concomitantly, patients present a reduction in exercise capacity associated with reduced peak oxygen consumption, chronotropic incompetence and altered blood pressure response and heart rate.

The potential mechanism for the reduction of peak VO2 in patients with OSAHS is related to the patient’s base pathology. During exercise, peak VO2 increases in response to metabolic demand by muscle activation. For this, the cardiovascular system is responsible for optimizing the delivery of blood and oxygen to working muscles and increasing cardiac output (CO). Any factor that limits CO (filling pressure, ventricular compliance, heart rate, contractility, blood pressure and/or afterload) can interfere with the exercise capacity of the individual.

OSAHS affects left ventricular function. The increased ventricular afterload results from the increase in negative intrathoracic pressure during airway obstruction. As a result of the larger intrathoracic pressure swings, there are fluctuations in the ejection fraction, heart rate, and CO. The rapid increase in CO and the increase in coronary vascular tone during the apnea cycle can cause episodes of myocardial ischemia. Other factors that can affect left ventricular function include a reduction in vagal activity, increased platelet aggregation, and insulin resistance.

The intermittent hypoxia associated with OSAHS reduces the production of nitric oxide (NO) and impairs endothelial function. Nitric oxide-dependent mechanisms may reduce the exercise capacity of patients with the disease.

OSAHS AND OBESITY

The main risk factor for development of OSAHS is obesity, and about 70% of patients with breathing-related sleep disorders are obese. This risk factor also contributes to the onset of cardiovascular and metabolic disease in this population. The risk of developing moderate to severe sleep disorders is increased by six times with a 10% increment in body mass. Each 1% increase in body mass is associated with a 3% increase in AHI.

Patients with higher BMI show a higher prevalence of most types of severe OSAHS. The increase in body fat and intra-abdominal pressure reduces functional residual capacity. Combined with the increased consumption of oxygen in tissues, it results in faster depletion of oxygen stocks during apnea. Due to more intense oxygen desaturation in obese individuals as compared with non-obese individuals, strategies for weight loss, including exercise, have been suggested as an alternative to reduce the severity of OSAHS.

Weight loss via increased physical activity and changes in diet and lifestyle has been studied as a treatment for sleep disorders. Therefore, increasing physical activity could reduce the body mass of these patients, improve their sleep disturbance and be considered an important goal for treatment.

BENEFITS OF EXERCISE ON SLEEP

Although sleep and exercise act in diametrically opposed ways from the physiological point of view, the benefits of these two states are related. Advances in knowledge have revealed new associations between the mechanisms that act on exercise and sleep. Therefore, promoting or improving sleep through exercise is believed to be healthy, safe and simple and might even be an alternative in the treatment of insomnia. Both aerobic and resistance exercises improve sleep quality. Gary and Lee reported that a 12-week walking program increased the total sleep time for patients by 20%, improving their quality of life.

The elderly population seems to benefit the most from physical activity. Besides improved quality of sleep, older adults also show improvements in their chronic pain and functional capacity. Compared to the elderly, young adults and children need longer and more intense exercise to obtain similar benefits.

The facilitation of sleep induction after exercise supports the role of sleep in the conservation of energy, in muscle recovery and body temperature regulation. Exercise causes energy depletion, muscle micro-damage, body temperature elevation and changes in melatonin levels, all of which are restored during sleep.

The reduction of body temperature is part of the process of inducing sleep. Melatonin, produced by the pineal gland in darkness, shortens sleep latency and reduces body temperature. The hypothesis that exercise downregulates temperature explains the increase in deep sleep after exercise.
Physical activities may upregulate the body's ability to lose heat, facilitating the sleep–related temperature drop. The optimum benefit of exercise is obtained when it is practiced 4–8 hours before bedtime. However, exercise at any time of day enhances sleep. In addition to aerobic and resistance exercises, Tai Chi Chuan also improves the sleep of practitioners.

**POTENTIAL CARDIOVASCULAR BENEFITS OF PHYSICAL ACTIVITY IN OSAHS**

Cardiovascular function is also affected by OSAHS. During cardiopulmonary exercise testing (CPET), 35% of OSAHS patients have a hypertensive response and 45% show abnormal VO\textsubscript{2} peaks (84% below expected values). During CPET, chronotropic incompetence and a delay in HR recovery may predict cardiovascular events and mortality in OSAHS patients. Resistance training affects HR in the long run, through adjustments in the autonomic nervous system. These adjustments are represented by a reduction in sympathetic activation and increased parasympathetic activity, resulting in a decrease in resting HR.

Nitric oxide is the most potent vasodilator produced in the body. During exercise, the shear stress (the tangential force that blood flow exerts on the vessel wall) stimulates the endothelium, increasing NO production and the vasodilatory response. This causes increased blood flow, triggering acute, subacute and chronic adaptive responses to exercise throughout the entire cardiovascular and muscular systems. Exercise may have a hypotensive effect of variable magnitude according to the type, intensity and duration of exercise. Activities with an intensity between 40 and 70% of peak VO\textsubscript{2}, longer than 30 minutes in duration and repeated 5 to 7 times per week lowers blood pressure.

Meta-analysis of more than a dozen studies on the effect of resistance exercises, such as weight training, revealed that increases in peak VO\textsubscript{2} and the metabolic equivalent of task (MET) caused a 2% (-3±3 mmHg) and 4% (-3±2 mmHg) reduction in systolic and diastolic pressure at rest, respectively, in hypertensive subjects. For each MET increase in peak VO\textsubscript{2} of the individual, there is a reduction between 8 and 17% in cardiovascular mortality.

**EXERCISE AS TREATMENT OF OSAHS**

The three studies that investigated the effect of exercise on AHI were summarized in Table 1. Norman et al. studied 8 men and 1 woman with a mean age of 49 years who underwent exercise 3 times a week for 6 months. Their exercise sessions consisted of 30–45 minutes of walking on a treadmill and riding a stationary bicycle with an intensity equivalent to 50–80% of the subject's peak VO\textsubscript{2}. Bodybuilding exercises were used to complement each training session.

The authors observed a 46% reduction in AHI, with a 5% reduction in BMI from 31 to 30 kg/m\textsuperscript{2} and of cervical circumference from 43 to 41 cm. Five patients treated with a continuous positive airway pressure (CPAP) device showed a reduction in AHI from 21 to 11/h, much like the group without the equipment, whose AHI was reduced from 22 to 12/h. In both cases, there was a change in the OSAHS classification, from moderate to light, irrespective of the use of CPAP.

Due to the 5% reduction in BMI, it is difficult to attribute the reduction in AHI exclusively to the direct effect of exercise. However, one can infer that the reduction in AHI was greater than expected by simple weight loss, using as a basis the data of Young et al., which showed a 3% reduction in AHI for each 1% reduction in weight. In that case, the expected drop in AHI for that magnitude of weight loss would be approximately 15%, which is quite different from the 46% reported.

Giebelhaus et al. showed that exercising just 2 days a week also improves AHI. The physical training program, lasting 6 months, consisted of 120 minutes of aerobic exercise and 120 minutes of weight training on separate days. Ten men and one woman with a mean age of 52 years were evaluated. All study subjects were treated with a CPAP machine for a period of 3–12 months (6±1.4 months). The authors observed a 27% reduction in AHI from 33 to 24/h, i.e., from severe to moderate OSAHS. In that sample, the change in body weight of the patients from 79.7 to 80.4 kg was not significant, leaving no doubt about the isolated effect of exercise.

Sengul et al. performed a randomized controlled study that evaluated aerobic performance and AHI after 3 months of physical exercise in patients with mild OSAHS who were not using CPAP. Twenty subjects were studied, 10 participating in the intervention group and 10 in the control group. Only the mean age was significantly different among groups: 54 years in the intervention group and 48 years in the control group. Both groups predominantly included individuals not practicing regular physical activity. The training applied to the intervention group consisted of aerobic exercises, performed three times per week on a treadmill and ergometric bike for 45–60 minutes with an intensity of 60–70% of peak VO\textsubscript{2}. Breathing exercises were also performed for 15 to 30 minutes. The controls remained without intervention.

In the same study, after 3 months, the authors observed that the controls maintained constant anthropometric and AHI variables. The intervention group showed a decrease in AHI from 15 to 11 events per hour of sleep, or a reduction of 27%, with no reduction in anthropometric variables such as BMI and neck circumference. In this study, the effects of exercise and weight loss on AHI were also confounded. There was a 2% drop in BMI from 29.8 to 29.2 kg/m\textsuperscript{2}, which would explain a 6% reduction in AHI but not the 27% observed.
FINAL CONSIDERATIONS
Despite being a less controllable form of therapy, changes in lifestyle are part of the medical prescription. Exercise has been shown in the three reviewed trials to be an effective intervention for reduction of OSAHS severity. Furthermore, exercise can play an important role in treating the main OSAHS factors, through reduction of both the cardiovascular risk factors and the body mass of patients. Preventing weight gain through exercise can prevent the emergence or worsening of OSAHS. Physical training reduces cardiovascular events and OSAHS severity, regardless of the use of other therapies such as CPAP or decreasing BMI. The limited number of studies requires additional investigation of the effectiveness of the role of exercise in OSAHS before this treatment modality can be universally recommended. Nevertheless, the agreement among the reviewed articles suggests a potential benefit of exercise on OSAHS.

FINANCIAL SUPPORT
Students received grants from the Brazilian government through Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and National Council of Technological and Scientific Development (CNPq). The main support was offered by the Research Incentive Fund (FIPE) of the Hospital de Clínicas de Porto Alegre.

REFERENCES


### APPENDIX A

Strategy of literature search performed on December 16, 2010.

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