Aerobic versus resistance exercises on systemic inflammation and sleep parameters in obese subjects with chronic insomnia syndrome

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Abstract

Background: Chronic primary insomnia is a prevalent sleep disorder that is associated with adverse effects on health outcomes. Exercise is often considered a non-pharmacological approach that could have beneficial effects on sleep.

Objective: The aim of the study was to compare the impact of aerobic and resistance exercise training on quality of sleep and inflammatory markers among subjects with chronic primary insomnia.

Material and Methods: Sixty previously sedentary subjects with chronic primary insomnia subjects enrolled in this study, their age ranged from 31-52 years. All participants were randomly assigned to aerobic exercise intervention group (group A, n=35) or resistance exercise intervention group (group B, n=35). Polysomnographic recordings for sleep quality assessment, IL-6, IL-10 and TNF-α were measured before and at the end of the study after six months.

Results: There was a significant increase in the total sleep duration, sleep efficiency, sleep onset latency and IL-10 in group (A) and group (B) in addition to significant reduction in awake time after sleep onset, REM latency, IL-6 and TNF-α after 6 months of aerobic and resistance exercise training. However, there were significant differences between both groups at the end of the study.

Conclusion: Aerobic exercise training is more appropriately than resistance exercise training in modulation of inflammatory and sleep quality among subjects with chronic primary insomnia.

Keywords: Aerobic exercise; chronic primary insomnia; inflammatory cytokines; resistance exercise; sleep quality.
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Introduction

Insomnia is a prevalent sleep disorder plaguing an estimated 15% of the population. However, insomnia is associated with deleterious effects on health, such as increased incidence of all-cause mortality, coronary artery disease, type 2 diabetes mellitus and hypertension. Moreover, impaired sleep is also linked to changes in metabolism, increased caloric intake, and obesity.

Sleep disruption show subsequent increases in blood pressure and elevation of inflammatory cytokines, including those implicated in atherogenesis such as C-reactive protein (CRP), tumor necrosis factor-α and interleukin. Low grade inflammation is, in part, responsible for the increased rate of coronary heart disease found in this population. Likewise, inflammatory processes are a hallmark etiological factor in cancer development and progression and are expressed not only at tumor sites but also peripherally. There is now increasing evidence from clinical studies that peripheral levels of pro-inflammatory biomarkers, (e.g., CRP) are predictive of cancer risk and survival.

Several studies have tested using exercise as a nondrug treatment for insomnia, where results of these studies suggested that long-term (three months or longer) exercise could contribute to better sleep quality or eased insomnia symptoms among insomniac populations. Aerobic exercise shown to improve both sleep quantity and quality. Progressive resistance exercise is an alternative modality that has also been shown to improve...
sleep quality. Like aerobic exercise, resistance exercise has been shown to improve comorbidities commonly associated with poor sleep, such as depression and cardiovascular disease, and may be suitable in those for whom aerobic exercise is not feasible or desirable. To our knowledge, the differences between the effects of resistance and aerobic exercise on sleep outcomes and inflammatory markers among subjects with insomnia has not been published. Thus, the purpose of this investigation was to compare the impact of aerobic and resistance exercise training on quality of sleep and inflammatory markers among subjects with Chronic Primary Insomnia.

Patients and methods

Subjects
Sixty previously sedentary subjects having chronic primary insomnia for longer than six months, their age ranged from 35-56 years and participated in this study. Exclusion criteria included history of use of psychotropic drugs, shiftwork, exercise training for more than one day/week, smoking, alcohol abuse, major psychiatric disorders and caffeine intake more than 300 mg/day. All subjects were cleared for participation by their personal physician, reported willingness to be randomly assigned to treatment conditions, and agreed not to participate in exercise outside the study. No attempts were made to control dietary intake. Subjects were randomized to either an aerobic exercise intervention group (group A) or resistance exercise intervention group (group B). Both groups participated in the exercise intervention conducted 3 times per week for 6 months. Exercise sessions were supervised and monitored by trained exercise specialists. The CONSORT diagram display the essential details of randomization (figure 1). Informed consent was obtained from all participants. This study was approved by the Scientific Research Ethical Committee, Faculty of Applied Medical Sciences at King University.

Methods

Measurements
The following measurements were taken before the study and after 6 months at the end of the study.

A. Sleep measures: All participants underwent polysomnographic (PSG) recording before and after the exercise training. For the pre-intervention assessment, PSG recording was performed over 2 nights. The room used for the recordings had a large comfortable bed, acoustic isolation, and controlled temperature and light. Recordings were conducted by a trained sleep technician using a digital system (Philips-Respironics, USA).
B. Inflammatory cytokines: Blood samples were drained from the antecubital vein after a 12-hour fasting, the blood samples were centrifuged at + 4 °C (1000 g for 10 min). “Immulite 2000” immunassay analyzer (Siemens Healthcare Diagnostics, Deerfield, USA) analyzed Interleukin-6 (IL-6) and Interleukin-10 (IL-10) levels. However, tumor necrosis factor-alpha (TNF-α) was measured by ELISA kits (ELX 50) in addition to ELISA microplate reader (ELX 88; BioTek Instruments, USA).

Procedures
Following the previous evaluation, all patients will be divided randomly into the following groups:
A. Aerobic exercise training program: Patients in group (A) were submitted to a 40 min aerobic session on a treadmill (the initial, 5-minute warm-up phase performed on the treadmill at a low load, each training session lasted 30 minutes and ended with 5-minute recovery and relaxation phase) either walking or running, based on heart rate, until the target heart rate was reached, according to American College of Sport Medicine guidelines. The program began with 10 min of stretching and was conducted using the maximal heart rate index (HRmax) estimated by 220-age. First 3 months = 60–70% of HRmax, second 3 months = 70–80% of HRmax. B. Resistance exercise training: Patients of group (B) were submitted to a 40 min session of resistance training. The program began with 10 min of stretching and was conducted with exercises done on nine resistance machines. The resistance machines used were: chest press, bicep curl, triceps extension, lower back, abdominals, leg press, leg curl and leg extension. Subjects performed three sets of 8–12 repetitions, with 60 s of rest between each set. Resistance was increased by five pounds after the subject was able to complete three sets of eight repetitions on three consecutive days. Subjects were trained using between 60 and 80% of their one maximal repetition weight (1-RM).

Statistical analysis
The mean values of the investigated parameters obtained before and after three months in both groups were compared using paired "t" test. Independent "t" test was used for the comparison between the two groups (P<0.05).

Results
The two groups were considered homogeneous regarding the demographic variables (table 1). The mean age of group, (A) was 46.12 ± 3.65 years, and the mean age of group (B) was 44.87 ± 4.32 years. There was no significant differences in age, gender, body mass index (BMI), body fat, systolic blood pressure, diastolic blood pressure, hemoglobin and maximal heart rate (HRmax) between both groups.

| Characteristic      | Group (A)       | Group (B)       | Significance |
|---------------------|-----------------|-----------------|--------------|
| Age (years)         | 43.64 ± 3.97    | 41.51 ± 4.26    | P>0.05       |
| Gender (male/female)| 18/12           | 20/10           | P>0.05       |
| BMI (kg/m²)         | 34.19 ± 3.41    | 33.28 ± 3.92    | P>0.05       |
| Waist hip ratio     | 0.89 ± 0.27     | 0.88 ± 0.25     | P>0.05       |
| SBP (mmHg)          | 137.83 ± 8.14   | 135.92 ± 7.69   | P>0.05       |
| DBP (mmHg)          | 86.31 ± 5.16    | 84.72 ± 4.91    | P>0.05       |
| Hb (gm/dl)          | 11.74 ± 1.68    | 12.25 ± 1.42    | P>0.05       |
| HRmax (beat/min)    | 162.85 ± 13.12  | 164.76 ± 14.35  | P>0.05       |

BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; Hb: Hemoglobin; HRmax: Maximum heart rate.

There was a significant reduction in BMI, CD3, CD4 and CD8 awake time after sleep onset, REM latency, IL-6 and TNF-α in addition to significant increase in the total sleep duration, sleep efficiency, sleep onset latency and IL-10 after 6 months of in group(A) as a result of weight loss program (table 2); while the results of the control group (group B) were not significant (table 3). Also, there were significant differences between both groups at the end of the study(table 4).
Table (2): Mean value and significance of sleep parameters and inflammatory markers of group (A) before and at the end of the study.

|                                | Mean + SD         | t-value | Significance |
|--------------------------------|-------------------|---------|--------------|
| **BMI (kg/m²)**                | **Pre** | **Post** | **t-value** | **P-value** |
|                                | 34.19 ± 3.41      | 28.26 ± 3.12* | 7.95 | <0.05 |
| **Total sleep duration (min)** | 320.67 ± 25.92    | 354.23 ± 28.51* | 11.46 | <0.05 |
| **Sleep efficiency (%)**       | 67.85 ± 6.34      | 83.32 ± 7.19* | 10.13 | <0.05 |
| **Sleep onset latency (min)**  | 12.37 ± 2.68      | 16.11 ± 2.75* | 7.26 | <0.05 |
| **Awake time after sleep onset (min)** | 78.91 ± 7.54 | 63.25 ± 6.82* | 9.67 | <0.05 |
| **REM sleep latency (min)**    | 90.13 ± 8.63      | 71.27 ± 6.94* | 10.21 | <0.05 |
| **TNF-α (pg/mL)**              | 6.17 ± 1.82       | 3.75 ± 1.41* | 6.83 | <0.05 |
| **IL-6 (pg/mL)**               | 2.76 ± 0.84       | 1.69 ± 0.73* | 5.72 | <0.05 |
| **IL-10 (pg/ml)**              | 5.91 ± 1.35       | 8.22 ± 1.64* | 6.43 | <0.05 |

BMI: Body mass index; REM: rapid eye movements; TNF-α: tumor necrosis factor – alpha; IL-6: Interleukin-6; IL-10: Interleukin-10; (*) indicates a significant difference between the two groups, P < 0.05.

Table (3): Mean value and significance of sleep parameters and inflammatory markers of group (B) before and at the end of the study.

|                                | Mean + SD         | t-value | Significance |
|--------------------------------|-------------------|---------|--------------|
| **BMI (kg/m²)**                | **Pre** | **Post** | **t-value** | **P-value** |
|                                | 33.28 ± 3.72      | 33.75 ± 3.78 | 0.481 | >0.05 |
| **Total sleep duration (min)** | 323.74 ± 27.19    | 319.24 ± 26.97 | 1.82 | >0.05 |
| **Sleep efficiency (%)**       | 69.15 ± 5.84      | 68.21 ± 5.76 | 1.17 | >0.05 |
| **Sleep onset latency (min)**  | 12.71 ± 2.53      | 12.15 ± 2.68 | 0.614 | >0.05 |
| **Awake time after sleep onset (min)** | 76.54 ± 6.91 | 78.13 ± 7.11 | 1.15 | >0.05 |
| **REM sleep latency (min)**    | 88.75 ± 8.42      | 89.66 ± 8.54 | 0.871 | >0.05 |
| **TNF-α (pg/mL)**              | 5.98 ± 1.75       | 6.11 ± 1.81 | 0.493 | >0.05 |
| **IL-6 (pg/mL)**               | 2.65 ± 0.71       | 2.94 ± 0.78 | 0.476 | >0.05 |
| **IL-10 (pg/ml)**              | 6.13 ± 1.47       | 5.86 ± 1.43 | 0.392 | >0.05 |

BMI: Body mass index; REM: rapid eye movements; TNF-α: tumor necrosis factor – alpha; IL-6: Interleukin-6; IL-10: Interleukin-10.
Discussion

Insomnia is one of the most common sleep disorders and is a risk factor for future cardiac events, including acute myocardial infarction and coronary heart disease, even among individuals free of cardiovascular disease27. However, exercise promoted increased sleep efficiency and duration in populations suffering from chronic sleep complaints28,29. Concerning sleep quality parameter, the results of the present study revealed that there was a significant increase in the total sleep duration, sleep efficiency and sleep onset latency in group (A) and group (B) in addition to significant reduction in awake time after sleep onset and REM latency after 6 months of aerobic and resistance exercise training. However, there were significant differences between both groups at the end of the study, these results are in line with many previous studies as Reid and colleagues had Sev...twenty-one sedentary volunteers performed moderate training for 60 minutes/day, 3 days/week for 24 weeks at a work rate equivalent to their ventilatory aerobic threshold. They proved that sleep parameters, awake time and REM sleep latency were decreased after 6 months exercise training in relation baseline values31.

Yang and colleagues completed a systematic review with meta-analysis of six randomized trials and provided data on 305 participants (241 female). Each of the studies examined an exercise training program that consisted of either moderate intensity aerobic exercise or high intensity resistance exercise. The duration of most of the training programs was between 10 and 16 weeks. All of the studies used the self-reported Pittsburgh Sleep Quality Index to assess sleep quality. Compared to the control group, the exercise group had significantly reduced sleep latency and medication use32. While, Chen and coworkers enrolled twenty-seven participants in 12 weeks of exercise training, they proved that overall sleep quality, subjective sleep quality, sleep latency, sleep duration, sleep efficiency, and daytime dysfunction significantly improved after 12 weeks of intervention33. In addition, Santos et al. had twenty-two male, sedentary volunteers performed moderate training for 60 min/day, 3 days/week for 24 week at a work rate equivalent to their ventilatory aerobic threshold, their findings suggest that aerobic exercise training increased aerobic capacity parameters, decreased REM latency and decreased time awake34. Moreover, Passos and colleagues concluded that a 4-month intervention of moderate aerobic exercise delivered to twenty-one sedentary participants with chronic primary insomnia had polysomnographic data significantly improvements following exercise training, where total sleep time, sleep efficiency and rapid eye movements significantly increased. In addition, sleep onset latency and wake time after sleep onset significantly decreased following exercise training35.

Tan and co-workers enrolled 45 obese Finnish men with chronic insomnia symptoms in a six-month aer-

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| Table (4): Mean value and significance of sleep parameters inflammatory markers in group (A) and group (B) at the end of the study. |
|---------------------------------------------------------------|
| **Mean ± SD** | **t-value** | **Significance** |
|----------------|-------------|-----------------|
| **BMI (kg/m²)** | 28.26 ± 3.12* | 33.75 ± 3.78 | 6.19 | P<0.05 |
| **Total sleep duration (min)** | 354.23 ± 28.51* | 319.24 ± 26.97 | 9.24 | P<0.05 |
| **Sleep efficiency (%)** | 83.32 ± 7.19* | 68.21 ± 5.76 | 8.23 | P<0.05 |
| **Sleep onset latency (min)** | 16.11 ± 2.75* | 12.15 ± 2.68 | 6.35 | P<0.05 |
| **Awake time after sleep onset (min)** | 63.25 ± 6.82* | 78.13 ± 7.11 | 7.56 | P<0.05 |
| **REM sleep latency (min)** | 71.27 ± 6.94* | 89.66 ± 8.54 | 8.48 | P<0.05 |
| **TNF-α (pg/mL)** | 3.75 ± 1.41* | 6.11 ± 1.81 | 5.27 | P<0.05 |
| **IL-6 (pg/mL)** | 1.69 ± 0.73* | 2.94 ± 0.78 | 4.75 | P<0.05 |
| **IL-10 (pg/mL)** | 8.22 ± 1.64* | 5.86 ± 1.43 | 5.18 | P<0.05 |

BMI: Body mass index; REM: rapid eye movements; TNF-α: tumor necrosis factor – alpha; IL-6: Interleukin-6; IL-10: Interleukin-10; (*) indicates a significant difference between the two groups, P < 0.05.
obic exercise program and resulted showed that sleep efficiency and quality improved significantly. Similarly, Ferris et al. in a study with a resistance exercise protocol quite similar to ours but conducted on only eight elderly subjects aged 78 years on average, applied six exercises for the upper and lower limbs with 10–12 repetitions at 50% 1 RM over a period of six months and reported that resistance exercise improved sleep parameters. In the other hand, two previous studies in older adults reported a small-to-moderate positive effect on sleep duration. The remaining study in younger adults with insomnia reported a large but non-significant negative effect on sleep duration following moderate-intensity resistance training.

Regarding, the mechanism underlying the effect of exercise on sleep, although the mechanisms by which training can improve sleep quality are not well understood. It has been proposed that exercise training improves sleep quality through increasing energy consumption, endorphin secretion, or body temperature in a manner that facilitates sleep for recuperation of the body. In addition, some other mechanisms, such as an increasing in energy consumption, endorphin secretion, body temperature, are also beneficial to improve sleep quality. Moreover, moderate training may decrease resting plasma concentrations of pro-inflammatory cytokines and increase anti-inflammatory cytokines, consequently improving the quality of sleep.

Our results demonstrate that both aerobic and resistance exercise training causes a decrease in TNF-α, IL-6 and CRP levels, in addition to increase in IL-10 level which suggests that exercise training can reduce inflammation with more significant changes following aerobic exercise training. Several studies have shown that moderate physical exercise promotes the modulation of inflammation. Several large cohort studies have found a relationship between self-reported physical activity levels and systemic markers of inflammation: higher levels of physical activity are coupled to lower levels of circulating inflammatory markers in elderly individuals. Regarding the aerobic exercise training, our results agreed with Nicklas et al. that regular aerobic exercise training was efficient in lowering IL-6 levels even without weight loss. Also, Santos and colleagues had twenty-two male, sedentary, healthy, elderly volunteers performed moderate aerobic exercise training for 60 min/day, 3 days/week for 24 week and concluded that 6 months of aerobic exercise training can improve sleep in the elderly via anti-inflammatory effect of aerobic training which modifies cytokine profiles (reduced IL-6 and TNF-α and increased IL-10). In addition, Salamat and colleagues reported significant difference in IL-6 between endurance and resistance groups that following 8 weeks of training in overweight men and concluded that endurance and concurrent exercise training in part has a positive effect on pre-inflammatory cytokines.

In the other hand, Kohut et al. reported that 10-months of aerobic, but not resistance exercise, significantly reduces serum inflammatory mediators in older adults. In addition, Bote et al. demonstrated that 8-months (2 sessions/week, 60-min/session) of aquatic-based exercise training tempered neutrophil activation (chemotaxis) and decreased systemic levels of IL-8 and noradrenalin compared to controls. However, our results regarding resistance exercise training agreed with White et al. found alterations in the biomarkers of inflammation after 8 weeks of resistance training in individuals with multiple sclerosis. Where, Prestes et al. performed a resistance training for 16 weeks in elderly sedentary and found reductions in the levels of IL-6 after training. Moreover, our results confirmed that aerobic exercise training is more appropriate to modify the inflammatory markers among elderly and these agreed with Ploeger et al. reported that moderate aerobic exercise training has been recommended as an anti-inflammatory therapy.

The three possible mechanisms of exercise anti-inflammatory effects include reduction in visceral fat mass, reduction in the circulating numbers of pro-inflammatory monocytes and an increase in the circulating numbers of regulatory T cells. Moreover, Hong and colleagues show that cardiorespiratory fitness is associated with reduced low grade inflammation that may in part be mediated by enhancing the ability of immune cells to suppress inflammatory responses via adrenergic receptors.

The current study has important strengths and limitations. The major strength is the supervised nature of the study. However, all exercise sessions were supervised. Moreover, the study was randomized; hence, we can extrapolate adherence to the general population. In the other hand, the major limitations is only obese middle aged subjects were enrolled in the study, so the value of this study only related to obese subjects in this age group, also small sample size in both groups may limit the possibility of generalization of the findings in
the present study. Finally, within the limit of this study, aerobic exercise training is recommended for modulation of inflammatory and sleep quality among subjects with Chronic Primary Insomnia. Further researches are needed to explore the impact of weight reduction on quality of life and other biochemical parameters among subjects with Chronic Primary Insomnia.

Conclusion
Aerobic exercise training is more appropriately than resistance exercise training in modulation of inflammatory and sleep quality among subjects with Chronic Primary Insomnia.

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Conflict of interest
None declared.

References
1. Chung KF, Yeung WF, Ho FY, et al. Cross-cultural and comparative epidemiology of insomnia: the Diagnostic and statistical manual (DSM), International classification of diseases (ICD) and International classification of sleep disorders (ICSD). Sleep Med 2015; 16(4):477–82.
2. Khan M, Aouad R. The Effects of Insomnia and Sleep Loss on Cardiovascular Disease. Sleep Med Clin 12(2017) 167–177
3. Tobaldini E, Costantino G, Solbiati M, et al. Sleep, sleep deprivation, autonomic nervous system and cardiovascular diseases. Neurosci Biobehav Rev 2017; 74(Pt B):321–9.
4. Bathgate CJ, Edinger JD, Wyatt JK, Krystal AD. Objective but not subjective short sleep duration associated with increased risk for hypertension in individuals with insomnia. Sleep. 2016; 39(5):1037-1045.
5. Broussard JI, Van Cauter E. Disturbances of sleep and circadian rhythms: novel risk factors for obesity. Curr Opin Endocrinol Diabetes Obes 2016; 23(5):353–9.
6. Nedelcheva AV, Kilkus JM, Imperial J, et al. Sleep curtailment is accompanied by increased intake of calories from snacks. Am J Clin Nutr 2009; 89(1): 126–33.
7. Mullington JM, Simpson NS, Meier-Ewert HK, Haack M. Sleep loss and inflammation. Best Pract Res Clin Endocrinol Metab. 2010; 24(5): 775-784.
8. Meier-Ewert HK, Ridker PM, Rifai N, et al. Effect of sleep loss on C-reactive protein, an inflammatory marker of cardiovascular risk. J Am Coll Cardiol. 2004; 43(4):678-683.
9. Patel SR, Zhu X, Storfer-Isser A, et al. Sleep duration and biomarkers of inflammation. Sleep. 2009; 32(2):200-204.
10. Chrysohoou, C., Kollia, N., Tousoulis, D., 2018. The link between depression and atherosclerosis through the pathways of inflammation and endothelium dysfunction. Maturitas 109, 1–5.
11. Halari, A., 2017. Inflammation-associated co-morbidity between depression and cardiovascular disease. Curr. Top. Behav. Neurosci. 31, 45–70
12. Li, J., Jiao, X., Yuan, Z., Qi, H., Guo, R., 2017b. C-reactive protein and risk of ovarian cancer. Medicine (Baltimore) 96, e7822.
13. Chan, D.S.M., Bandera, E.V., Greenwood, D.C., Norat, T., 2015. Circulating C-Reactive Protein and breast cancer risk—Systematic literature review and meta-analysis of prospective cohort studies. Cancer Epidemiol. Biomarkers Prev. 24, 1439–1449.
14. Zheng, R.-R., Huang, M., Jin, C., Wang, H.-C., Yu, J.-T., Zeng, L.-C., Zheng, F.-Y., Lin, F., 2016. Cervical cancer systemic inflammation score: a novel predictor of prognosis. Oncotarget 7, 15230–15242.
15. Passos GS, Poyares D, Santana MG, et al. Effects of moderate aerobic exercise training on chronic primary insomnia. Sleep Med 2011; 12:1018–27.
16. Reid KJ, Baron KG, Lu B, Naylor E, Wolfe L, Zee PC. Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. Sleep Med 2010; 11:934-40.
17. Hartescu I, Morgan K, Stevinson CD. Increased physical activity improves sleep and mood outcomes in inactive people with insomnia: a randomized controlled trial. J Sleep Res 2015; 24:526–34.
18. Passos GS, Poyares D, Santana MG, Garbuio SA, Tufik S, Mello MT. Effect of acute physical exercise on patients with chronic primary insomnia. J Clin Sleep Med 2010; 6:270-5.
19. Sharif F, Seddigh M, Jahanbin I, Keshavarzi S. The effect of aerobic exercise on quantity and quality of sleep among elderly people referring to health centers of Lar City, Southern of Iran; a randomized controlled clinical trial. Curr Aging Sci 2015; 8:248-55.
20. Singh N, Clements K, Fiatarone M. A randomized controlled trial of the effect of exercise on sleep. Sleep 1997; 20:95e101.
randomized controlled trials. *Sleep Medicine Reviews* 39 (2018) 52-68.

22. Singh NA, Clements KM, Fiatarone MA. A randomized controlled trial of progressive resistance training in depressed elders. *J Gerontol A Biol Sci Med Sci* 1997; 52A:M27-35.

23. Williams MA, Haskell WL, Ades PA, Amsterdam EA, Bittner V, Franklin BA, et al. Resistance exercise in individuals with and without cardiovascular disease: 2007 update a scientific statement from the american heart association council on clinical cardiology and council on nutrition, physical activity, and metabolism. *Circulation* 2007; 116:572-84.

24. Rechtschaffen A, Kales AA. Manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. *Los Angeles: Brain Information Service/Brain Research Institute/UCLA*; 1968.

25. Robergs RA, Landwehr R. The surprising history of the “HRmax=220-age” equation. *J Exerc Physiol Online* 2002; 5(2):1-10.

26. Ramalho AC, de Lourdes Lima M, Nunes F, Cambuí Z, Barbosa C, Andrade A, Viana A, Martins M, Abrantes V, Aragão C, Temistocles M. The effect of resistance versus aerobic training on metabolic control in patients with type-1 diabetes mellitus. *Diabetes Res Clin Pract* 2006; 72(3):271–6.

27. Laugsand LE, Vatten LJ, Platou C, et al. Insomnia and the risk of acute myocardial infarction. *Circulation* 2011; 124:2073–81.

28. Dolezal BA, Neufeld EV, Boland DM, Martin JL, Cooper CB. Interrelationship between Sleep and Exercise: A Systematic Review. *Adv Prev Med.* 2017; 2017:1364387.

29. Erlacher C, Erlacher D, Schredl M. The effects of exercise on self-rated sleep among adults with chronic sleep complaints. *Journal of Sport and Health Science* 4 (2015) 289-298.

30. Reid KJ, Baron KG, Lu B, Naylor F, Wolfe L, Zee PC. Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. *Sleep Med.* 2010 Oct; 11(9):934-40.

31. Lira FS, Pimentel GD, Santos RV, Oyama LM, Damaso AR, Oller do Nascimento CM, Viana VA, Boscolo RA, Grassmann V, Santana MG, Esteves AM, Tufik S, de Mello MT. Exercise training improves sleep pattern and metabolic profile in elderly people in a time-dependent manner. *Lipids Health Dis.* 2011 Jul 6; 10:1-6.

32. Yang PY, Ho KH, Chen HC, Chien MY. Exercise training improves sleep quality in middle-aged and older adults with sleep problems: a systematic review. *J Physiother.* 2012; 58(3):157-63.

33. Chen M., Liu H, Huang H, Chiou A. The effect of a simple traditional exercise programme (Baduanjin exercise) on sleep quality of older adults: A randomized controlled trial. *International Journal of Nursing Studies* 49 (2012) 265–273.

34. Santos RV, Viana VA, Boscolo RA, Marques VG, Santana MG, Lira FS, Tufik S, de Mello MT. Moderate exercise training modulates cytokine profile and sleep in elderly people. *Cytokine*. 2012 Dec; 60(3):731-5.

35. Passos GS, Poyares D, Santana MG, Teixeira AA, Lira FS, Youngstedt SD, dos Santos RV, Tufik S, de Mello MT. Exercise Improves Immune Function, Antidepressive Response, and Sleep Quality in Patients with Chronic Primary Insomnia. *Biomed Res Int.* 2014; 2014:498961.

36. Tan X, Alen M, Wiklund P, Partinen M, Cheng S. Effects of aerobic exercise on home-based sleep among overweight and obese men with chronic insomnia symptoms: a randomized controlled trial. *Sleep Medicine* 25 (2016) 113–121.

37. Ferris LT, Williamsn JS, Shen C. Resistance training improves sleep quality in older adults – a pilot study. *J Sports Sci Med* 2005; 4:354–60.

38. Singh N, Clements K, Fiatarone M. A randomized controlled trial of the effect of exercise on sleep. *Sleep* 1997; 20:95-101.

39. Chen K-M, Huang H-T, Cheng Y-Y, Li C-H, Chang Y-H. Sleep quality and depression of nursing home older adults in wheelchairs after exercises. *Nurs Outlook* 2015; 63:357-65.

40. Herring MP, Kline CE, O’Connor PJ. Effects of exercise on sleep among young women with generalized anxiety disorder. *Ment Health Phys Act* 2015;9: 59-66.

41. Horne JA, Moore VJ (1985) Sleep EEG effects of exercise with and without additional body cooling. *Electroencephalography and Clinical Neurophysiology* 60: 33–38.

42. Driver HS, Taylor SR (2000) Exercise and sleep. *Sleep Medicine Reviews* 4: 387–402.

43. Li F, Fisher KJ, Harmer P, Irbe D, Tarsee RG, Weimer CJ (2004) Tai chi and self-rated quality of sleep and daytime sleepiness in older adults: a randomized controlled trial. *Journal of American Geriatrics Society* 52: 892–900.

44. Yang, P.Y., Ho, K.H., Chen, H.C., Chien, M.Y., 2012. Exercise training improves sleep quality in middle-aged and older adults with sleep problems: a systematic review. *J. Physiother.* 58 (3) 157–163.

45. Kapsimalis F, Basta M, Varouchakis G, Gourgoulianis K, Vgonzas A, Kryger M. Cytokines and pathological sleep. *Sleep Med* 2008; 9:603–14.

46. Donges CE, Duffield R, Drinkwater EJ. Effects of
resistance or aerobic exercise training on interleukin-6, C - reactive protein, and body composition. Med Sci Sports Exerc 2010; 42:304-313.

47. Balducci S, Zanuso S, Nicolucci A. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. Nutr Metab Cardiovasc Dis 2010; 20:608-617 PubMed.

48. Libardi CA, Souza GV, Cavaglieri CR. Effect of resistance, endurance, and concurrent training on TNF-a, IL-6, and CRP. Med Sci Sports Exerc 2012; 44:50-56.

49. Geffken DF, Cushman M, Burke GL, Polak JF, Sakkinen PA, Tracy RP. Association between physical activity and markers of inflammation in a healthy elderly population. Am J Epidemiol 2001; 153:242–250.

50. Colbert LH, Visser M, Simonsick EM, Tracy RP, Newman AB, Taaffe DR, Brach J, Rubin S, Harris TB. Physical activity, exercise, and inflammatory markers in older adults: findings from the Health, Aging and Body Composition Study. J Am Geriatr Soc 2004; 52:1098–1104.

51. Yu Z, Ye X, Wang J, Qi Q, Franco OH, Rennie KL, Pan A, Li H, Liu Y, Hu FB, Lin X. Associations of physical activity with inflammatory factors, adipocytokines, and metabolic syndrome in middle-aged and older Chinese people. Circulation 2009; 119:2969–2977.

52. Nicklas BJ, Hsu FC, Brinkley TJ, Church T, Goodpaster BH, Kritchevsky SB, Pahor M. Exercise training and plasma C-reactive protein and interleukin-6 in elderly people. J Am Geriatr Soc 2008; 56:2045–2052.

53. Santos R, Viana V, Boscolo R, Marques V, Santana M, Lira F, Tufik S, de Mello M. Moderate exercise training modulates cytokine profile and sleep in elderly people. Cytokine 2012; 60:731–735.

54. Salamat K, Azarbayjani M, Yusof A, Dehghan F. The response of pre-inflammatory cytokines factors to different exercises (endurance, resistance, concurrent) in overweight men. Alexandria Journal of Medicine (2016) 52, 367–370.

55. Kohut ML, McCann DA, Russell DW, Konopka DN, Cunnick JE, Franke WD, Vanderah E. Aerobic exercise, but not flexibility/resistance exercise, reduces serum IL-18, CRP, and IL-6 independent of beta-blockers, BMI, and psychosocial factors in older adults. Brain Behav Immun. 2006; 20 (3):201–209.

56. Bote ME, Garcia JJ, Hinchado MD, Ortega E. An exploratory study of the effect of regular aquatic exercise on the function of neutrophils from women with fibromyalgia: role of IL-8 and noradrenaline. Brain Behav. Brain Behav Immun 2014;39:107-12

57. White LJ, Castellano V, McCoY SC. Cytokine responses to resistance training in people with multiple sclerosis. J. Sports Sci 2006; 24:911-914.

58. Prestes J, Shiguemoto G, Botero JP. Effects of resistance training on resistin, leptin, cytokines, and muscle force in elderly post-menopausal women. J Sports Sci 2009; 27(14):1607-1615.

59. Ploeger HE, Takken T, de Greef MH, Timmons BW. The effects of acute and chronic exercise on inflammatory markers in children and adults with a chronic inflammatory disease: a systematic review. Exerc Immunol Rev 2009; 15:6–41 PubMed.

60. Mathur M, Pedersen B. Exercise as a mean to control low-grade inflammation. Mediators Inflamm 2008; 2008:109502.

61. Timmerman K, Flynn M, Coen P, Markofski M, Pence B. Exercise training-induced lowering of inflammatory (CD14+CD16+) monocytes: a role in the anti-inflammatory influence of exercise? Leukoc Biol 2008; 84: 1271–1278.

62. Wang J, Song H, Tang X, Yang Y, Vieira VJ, Niu Y, Ma Y. Effect of exercise training intensity on murine T regulatory cells and vaccination response. Scand J Med Sci Sports 2012; 22(5):643-52.

63. Hong S, Dimitrov S, Pruitt C, Shaikh F, Beg N. Benefit of physical fitness against inflammation in obesity: role of beta adrenergic receptors. Brain Behav Immun. 2014; 39:113-20.