

Exercise intervention as a protective modulator of dyslipidaemia in male cigarette smokers

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Abstract

Introduction. Tobacco smoking is a major avoidable cause of morbidity. Smoking is one of the important factors which can alter normal lipid profile and it is among the major risk factors in the genesis of coronary atherosclerosis. The aim of this study was to determine the impact of high-intensity interval training on blood lipids and serum cotinine in Egyptian male smokers.

Methods. Overall, 30 sedentary male smokers with dyslipidaemia, with mean age of 30.16 ± 3.22 years, were enrolled in a high-intensity interval training program calculated as 85–95% of their individualized maximum heart rate. The training program was applied for 30 minutes, 3 times per week for 8 weeks. Serum cotinine, low-density lipoprotein, high-density lipoprotein, triglycerides, and total cholesterol levels were measured before and after the intervention.

Results. After the training program, a significant improvement (decrease) was observed in cotinine, low-density lipoprotein, triglycerides, and total cholesterol (by 39.94%, 7.13%, 5.09%, and 4.72%, respectively). Also, there was a significant improvement (increase) in high-density lipoprotein (by 17.07%).

Conclusions. It is recommended for smokers to participate in high-intensity interval training to improve their lipid profile and decrease cotinine. These factors can play a role in reducing the risk for atherosclerosis.

Key words: smoking, interval training, lipid profile, cotinine

Introduction

The population in Egypt shows an increment in the degree of smoking. Around 95% of Egyptian tobacco users smoke every day. It was detailed that in 2004, nearly 170,000 tobacco-related deaths occurred in Egypt. Considering the wellbeing and financial burdens of smoking, as well as poor resources, it is essential for developing countries to fight smoking and its hazards. The commonly observed complications of smoking in Egypt were cardiovascular system complications, such as atherosclerosis and hypertension, chronic obstructive pulmonary disease, bladder cancer, pancreatic cancer, erectile dysfunction, spermatic mutation, and foetal exposure to nicotine [1].

It has been found that the smoking population in Egypt is steadily expanding, and both sexes now smoke, which makes this habit even more widely accepted. Cigarettes and smoking tobacco will proceed to grow over the following years [2]. Cigarettes are the foremost common source of nicotine; moreover, smoked tobacco contains extra harmful chemicals and constituents, which exert an unfavourable impact on the respiratory system [3].

At present, 19.4% of adults in Egypt smoke tobacco; 0.5% of women and 37.7% of men (95% of current smokers) are daily smokers. Fabricated cigarettes constitute the prevalent item smoked by men (31.7%) [1].

In their meta-analysis, Aune et al. [4] summarize data on the smoking status and risk of sudden cardiac death. There was a 3-fold higher risk of sudden cardiac death among current smokers, a 38% higher relative risk among former smokers,

and a 2-fold higher risk among ever smokers compared with never smokers. In a separate investigation of studies that compared current smokers with non-current (never + former) smokers, a 2-fold risk increase was revealed. It is consistent with the key study as the inclusion of former smokers along with never smokers would have skewed the comparison community and contributed to an underestimation of the true connection between smoking and sudden cardiac death. There was a 58% rise in the relative risk for 10 cigarettes a day.

Studies have demonstrated that smoking cigarettes causes cancers of the oral cavity, bladder, larynx, pharynx, oesophagus, cervix, lung, kidney, pancreas, and stomach. It can also lead to acute myeloid leukaemia. It results in heart disease and stroke, too [5]. Given the variability of diseases caused by tobacco use, the health care cost of treating these diseases is considerable. About 3.4 billion EGP (US\$ 616 million) were spent yearly in Egypt to treat the diseases caused by smoking [6].

In Egypt, the percentage of tobacco-related cancers is highest among of cancers. Among men, it raised from 8.9% to 14.8% of total deaths after the age of 34 in years 1974–1987. Among women, it is still generally low. In 2004, tobacco-related deaths increased from 8% to 11% of total deaths after the age of 34. As it shortens life expectancy, tobacco use causes a significant financial burden owing to the rising health care costs and low efficiency [7].

Smoking prevalence varies greatly depending on gender, time span, and geographic region. In high-income countries, albeit with substantial time disparities, the number of male smokers significantly increased in the last century, peaking

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between 1950 and 1980, and then subsequently declining. In many low- and middle-income countries, smoking prevalence is increasingly growing in men, but not in women [8].

The administration of nicotine causes significant changes in the plasma lipid profile, with increased lipid peroxidation in plasma and significantly higher levels of plasma total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) in smokers compared with non-smokers [9]. Apparently, passive cigarette smoke exposure can lead to a significant accumulation of nicotine, followed by the presence of its metabolites in various body fluids [10].

Nicotine in tobacco smoke induces adverse health effects: raises heart rate and blood pressure, impairs breathing functions, limits circulation, and affects blood vessels [11]. Cotinine is an active nicotine metabolite that stays in the blood for a half-life of 18–20 hours, making analyses simpler [12].

The pack-year is a measuring unit of how much a person smoked over a long period. This is calculated by multiplying the number of cigarette packs smoked per day by the number of years that the person smoked [13]. Quantification of smoked pack-years is important in clinical care, where the degree of exposure to tobacco is associated with the risk of disease, such as lung cancer; 1 pack-year is equivalent to smoking 20 cigarettes (1 pack) per day for 1 year, or 40 cigarettes per day for half a year [14].

Lifestyle and population activity play a crucial role in Egypt's determination of fitness, illness, disability, and premature mortality. The prevalence of cardiovascular diseases and associated risk factors among the adult population is increasing, including 24% smoking prevalence and increased use of shisha tobacco. Egypt is one of the world's most overweight countries; approximately 2/3 of the Egyptian population (62.2%) are overweight and 1/3 (31.3%) are obese. About 40% of the Egyptian population suffer from raised blood pressure and 37% present raised cholesterol level. Almost 1/4 (24.4%) are current smokers. Moreover, the majority of the population reported low consumption of fruit and vegetables [15].

Short-term human studies have shown that oral nicotine administration increases LDL-C and plasma TC and decreases high-density lipoprotein cholesterol (HDL-C) in regular dietary condition. Cigarette smoking was responsible for a 5–9 mg/dl drop in HDL-C levels [16].

A possible mechanism for how cigarette smoking changes serum lipid levels has been suggested. The absorption of nicotine leads to the excretion of cortisol, catecholamines, and growth hormones, which activates adenyl cyclase in fat tissue. This results in lipolysis of the stored triglycerides and the release of free fatty acids. This, in turn, leads to increased liver synthesis of triglycerides and very low-density lipoprotein [17].

As cigarettes kill 50% of long-term users prematurely, serious consideration should be given to any additional measures that may minimize death or illness [18]. Huge amounts of harmful substances consumed by smokers with the tobacco aerosol increase the level of free radicals and decrease antioxidant activity, resulting in an oxidative-antioxidant imbalance and oxidative stress induction. They therefore stimulate inflammation and hinder the immune response. Additionally, oxidant aggregation also affects lipid peroxidation, protein, and nucleic acids. In addition, respiratory dysfunction, cough, increased mucus production, dyspnoea, or wheezing may be observed. Smoking tobacco can eventually lead to nicotine addiction [19].

Aberrant blood vessel and systemic circulation dysfunction are primary causes of vascular disorders: coronary, cere-

brovascular, renal stenosis and peripheral artery disease. Epidemiological and basic scientific evidence supports genetic reasons, which are intensified by such risk factors as obesity, hypercholesterolaemia, hypertension, diabetes, and smoking [20].

Physical activity is the right choice for smokers who are very adherent to the habit and cannot take the decision to stop smoking. Exercise can mitigate some of the negative consequences of quitting smoking [21].

High-intensity interval training (HIIT) involves physical exercise that is characterized by short, sporadic bursts of vigorous activity, interposed by rest periods or exercise at low intensity. HIIT can serve as an effective alternative to traditional endurance training, bringing about similar or even superior changes in a range of physiological, as well as performance- and health-related markers in both diseased and healthy populations [22].

Interval exercise appears to be an important factor in improving cardiovascular function, aerobic capacity, and quality of life in smokers, which may have significant implications for serum lipid concentrations and antioxidant capacity [23]. HIIT was traditionally applied in older, ill, and at-risk populations with longer work intervals (2–4 minutes), while more recent HIIT concepts provide work intervals of 30–60 seconds [24].

Subjects and methods

Subjects

A single-arm pre-post clinical study was performed. The sample size was set by using G*Power software, version 3.1.9.2. The appropriate minimum sample size for this study was 25 patients. So, the investigation was carried out among 30 sedentary male smokers with dyslipidaemia, with a mean age of 30.16 ± 3.22 years. Their mean body mass index (BMI) equalled 28.00 ± 1.49 kg/m². They were recruited from a smoking cessation clinic of the New Cairo Hospital, Cairo, Egypt. It was observed that the age of subjects attending the clinic was 30–40 years. A lipid profile panel was performed for all subjects to collect the study sample in accordance with the predetermined inclusion criteria, which were as follows: male sex, sedentary lifestyle, dyslipidaemia (TC: 240–300 mg/dl, LDL-C: 160–200 mg/dl, HDL-C: 15–35 mg/dl), receiving no lipid lowering medications at the time of the study, cigarette smoking only. The exclusion criteria involved a chronic chest disease, hypertension, cancer, renal or cardiovascular disease, receiving medication for dyslipidaemia, smoking any items other than cigarettes, alcohol addiction, and musculoskeletal disorders that interfered with performing the exercise program. Any patient who missed the program for more than 2 weeks or wished to withdraw was also excluded. All participants were provided with a careful explanation of the study procedures. The exercise program was established in accordance with the American College of Sports Medicine guidelines and was conducted between August 2017 and December 2018, over an 8-week period, at the New Cairo Hospital and the Faculty of Physical Therapy, Cairo University, Egypt.

Procedures

Anthropometric measurements

Height (cm) was measured by using a wall stadiometer with the participant dressed in light clothes and without shoes. In the same conditions, weight (kg) was assessed with cali-

brated weight and height scales (floor type model ZT-120, China). BMI was identified for each participant as body mass (kg) divided by body height squared (m²) [25] to fulfil the inclusion criteria of the study.

Study protocol

The study protocol was explained in detail to each patient before the initial assessment. A complete history and physical examination were taken for all smokers, with particular attention paid to identifying long-term complications of smoking. At the first training session, all patients were individually instructed about HIIT and how to stop it if they could not continue. Also, the subjects were familiarized with a treadmill, running twice before the start of the study. Resting heart rate (HR_{rest}, bpm) was registered in the morning and after sitting for 10 minutes with a pulsometer (Tunturt TPM-400, Japan) before the exercise program commencement. HR_{rest} was the minimum heart rate estimated within the last minute of the rest period [26]. Also, individual maximum heart rate (HR_{max}) was determined as 220 – age [27]. Blood samples were collected after an overnight fasting for 12 hours (drinking water only) for lipid profile evaluation before the study and at least 48 hours after the last exercise session in the study. Another blood sample was collected to measure cotinine level. Laboratory kits and Stat Fax (2100 US) were used to establish serum cotinine and the lipid profile. The chemical analysis was performed in the Biochemistry Department Laboratory, Kasr El Ainy School of Medicine, Cairo University, Egypt. After the collection of baseline data, all patients engaged in an 8-week exercise program of HIIT on an electronic treadmill (JS 1688, China) The apparatus is equipped with a display screen showing time in minutes and speed in kilometres per hour. Also, a stopwatch was used to adjust the time for each exercise phase (warm-up, active phase, and cool-down). All patients were instructed not to change their lifestyle or dietary habits during the study.

Exercise training protocol

- Before starting the HIIT program, all patients were able to exercise for at least 20–30 minutes at 70–85% of their previously measured HR_{max}, without exhaustion.
- Warm-up and cool-down for at least 5 minutes were performed before and after each HIIT session.
- If any patient experienced chest pain or breathing difficulties during the HIIT workout, cool-down was immediately implemented.
- The exercise intensity was prescribed as training heart rate depending on each patient’s HR_{max} and HR_{rest}. Aerobic exercise intensity was determined with the Karvonen formula [28]:

$$\text{target HR} = [(\text{HR}_{\text{max}} - \text{HR}_{\text{rest}}) \% \text{intensity}] + \text{HR}_{\text{rest}}$$

where HR_{max} = 220 – age

- The exercise session began with a warm-up phase, performed by walking on the treadmill (5 minutes) at 30% of HR_{max} as a preparation for the more strenuous activity, associated with the second phase of the exercise program. Then, the active phase of exercise occurred, in which the patient applied HIIT for about 20 minutes. Four 5-minute sets were held in each session (1 minute running at 85–95% of HR_{max} and 4-minute recovery at 60–70% of HR_{max}), followed by cool-down (5 minutes) with a gradual decrease of treadmill intensity up to 30% of HR_{max}, as a recovery from

the strenuous activities to the resting phase. Pulse rate was continuously measured during the exercise session. The patients were instructed to report any significant symptoms that they felt during the session. The exercise program was applied for 30 minutes, 3 sessions per week (on non-consecutive days) for 8 weeks.

- All 30 patients exhibited a high adherence to the training program. No serious adverse effects were reported.

Statistical analysis

The data obtained in the study group were statistically analysed to compare the pre- and post-intervention measures within the group. The statistical analysis was conducted by using the SPSS statistical package, version 25 for Windows (SPSS Inc., Chicago, USA). The data were normally distributed, as determined by the Shapiro-Wilk test (parametric data). Additionally, testing for the homogeneity of variance revealed that there was no significant difference ($p > 0.05$). Descriptive statistics included the mean and standard deviation for all variables. Paired *t*-test served to compare pre- and post-treatment values of LDL-C, HDL-C, TC, triglycerides, and cotinine variables within the study group. All statistical results were significant at the level of probability of $p < 0.05$.

Informed consent

Informed consent has been obtained from all individuals included in this study.

Results

This study was carried out to determine the impact of an exercise intervention as a protective modulator of dyslipidaemia in male cigarette smokers.

Demographic and clinical characteristics of patients

The mean age, BMI, years of smoking, number of cigarettes smoked per day, pack-years, and pre-study HR_{max} are presented in Table 1.

Table 1. Mean values of demographic and clinical data

Variables	Mean ± SD
Age (years)	30.16 ± 3.22
Body mass index (kg/m ²)	28.00 ± 1.49
Years of smoking	11.74 ± 3.02
Number of cigarettes per day	18.00 ± 9.46
Pack-years	11.14 ± 7.56
Maximum heart rate (bpm)	191.97 ± 5.73

Serum cotinine and lipid profile

The statistical analysis revealed that after 8 weeks of HIIT, there was a significant improvement (decrease) in cotinine, TC, LDL-C, and triglycerides by 39.94%, 4.72%, 7.13%, and 5.09%, respectively. Also, a significant improvement (increase) in HDL-C by 17.07% was observed (Table 2).

Table 2. Pre- and post-treatment serum cotinine and lipid profile

Variables	LDL-C (mg/dl)	HDL-C (mg/dl)	TC (mg/dl)	Triglycerides (mg/dl)	Cotinine (mg/dl)
Pre-treatment	184.68 ± 21.62	29.65 ± 6.76	271.55 ± 28.29	221.84 ± 33.94	13.52 ± 2.14
Post-treatment	171.52 ± 19.73	34.71 ± 6.50	258.74 ± 28.80	210.55 ± 32.26	8.02 ± 1.86
Improvement (%)	↓ 7.13	↑ 17.07	↓ 4.72	↓ 5.09	↓ 39.94
<i>p</i>	0.0001	0.0001	0.0001	0.0001	0.0001
Significance	S	S	S	S	S

LDL-C – low-density lipoprotein cholesterol, HDL-C – high-density lipoprotein cholesterol, TC – total cholesterol, ↑ – increase, ↓ – decrease, S – significant

Discussion

Smoking is the second major modifiable risk factor for cardiovascular diseases [29]. It directly harms and affects cardiac vasculature and leads to the development of other risk factors, such as thrombus formation, dyslipidaemia, and glucose intolerance [30].

Smoking is well recorded as being the most significant aetiological factor in lung cancer growth. Overall, 80–94% of lung cancer patients on average are smokers or former smokers with 30–50 tobacco pack-years. Smoking may also increase pulmonary and circulatory morbidity following a variety of surgery interventions that are due to chronic bronchitis and tobacco-induced atherosclerosis of coronary arteries. Postoperative complications, according to several authors, occur 1.4–4.3 times more frequently among smokers as compared with non-smokers [31].

Tobacco smoking is one of the principal threats to public health. Tobacco is a highly addictive drug. Smoking still remains among the most common global causes of disease and death [32]. The habit is common in Egypt, with 19.4% (9.7 million) of adults consuming tobacco products, 37.7% of men and 0.5% of women. A total of 95% of those are everyday smokers. The most widespread product smoked by males is cigarettes (31.7%), followed by shisha (6.2%); however, 0.2% of manufactured cigarettes and 0.3% of shisha products are smoked by females. In the recent 30 years, the number of smokers in Egypt has been rising by 8–9% annually, i.e., more than twice as fast as the rate of population growth [33].

Nicotine administration caused significant changes in the plasma lipid profile, facilitated lipid peroxidation in plasma, and significantly increased the levels of plasma TC, LDL-C, and malondialdehyde in smokers compared with non-smokers [9]. This study was conducted to find out the effect of exercise intervention in male smokers as a protective modulator of dyslipidaemia.

In this study, 30 dyslipidaemic male smokers underwent an 8-week exercise routine. The participants engaged in HIIT (mode: running on a treadmill; duration: 30 minutes; frequency: 3 days per week, non-consecutive days; intensity: high, 85–95% of estimated HRmax; recovery at 60–70% of HRmax).

The study revealed a significant positive modulation of the lipid profile and serum nicotine (cotinine) as a result of the treatment. Cotinine, TC, LDL-C, and triglycerides were significantly decreased by 39.94%, 4.72%, 7.13%, 5.09%, respectively, and a significant improvement (increase) in HDL-C by 17.07% was observed.

Lifestyle modification with optimized HIIT appears to be a better approach to the prevention and management of adolescent obesity and metabolic, cardiovascular, and hormonal disorders than moderate-intensity interval training,

as improvements in the lipid profile have been observed, particularly in plasma triglycerides in the HIIT group [34]. HIIT combined with a quit program also led to a higher quit rate than a moderate intervention of physical exercise [35].

Wisløff et al. [36] analysed 14 studies investigating HIIT effect on cholesterol levels. HIIT improved HDL-C after at least 8 weeks of training, implying that a moderate decrease in body fat (or body weight) needs to be accompanied by HIIT to improve TC, LDL-C, and blood triglycerides. Elmer [37] reported that plasma triglyceride concentrations were significantly decreased (–31 ± 28 mg/dl) after HIIT as compared with endurance training.

An HIIT regimen of 8 weeks implemented by Musa et al. [38] turned out successful in bringing about beneficial improvements in HDL-C and TC/HDL-C but not TC in young adult men with typical TC levels. These results support the guidelines for HIIT as an alternative form of exercise for people with appropriate physical fitness to boost blood lipid profiles.

Moderate-intensity exercise of 5 minutes has been found to be associated with a short-term reduction in nicotine administration and the willingness to smoke. Hence, very brief exercise breaks can be useful as a smoking cessation aid [28].

After 2 weeks of HIIT training, a statistically significant decrease of 10.4% (*p* = 0.01) was observed in cholesterol levels, which were lower (by 8.76%, *p* = 0.02) than pre-training values after detraining [39].

A high-intensity tracking interval protocol (4-minute walking intervals at 85–95% of HRmax) resulted in significant changes in TC and HDL-C among obese postmenopausal women. The findings suggest that 12 weeks of HIIT can lead to satisfactory changes in TC and HDL-C [40].

The effect of exercise on blood lipids, TC, and cholesterol fractions has been taken into consideration in many studies. Triglycerides were found to decrease in most trials, while TC quite often decreased and sometimes did not change, increasing HDL-C and decreasing LDL-C, respectively [41].

Linke [42] indicated that individuals who performed intermittent exercise more frequently experienced higher smoking craving reduction.

Exercise sessions are associated with lower cravings, and similar patterns exist for symptoms of tobacco withdrawal. Thus, exercise may have the capability to help in the initial stages of smoking cessation attempts [43].

In response to the images in brain areas associated with reward processing and visual attention, smokers showed increased activity after no exercise. While the same activation areas were not observed after exercise, some kind of 'default mode' within the brain was reflected. Smokers also reported lower cigarette cravings after exercise than when they were inactive. Research indicates that performing exercise could improve the mood (possibly by increasing dopamine levels),

thus reducing the salience or significance of a cigarette craving. Another hypothesis is that exercise induces changes in blood flow to areas of the brain that are less active in anticipating the reward and enjoyment produced by smoking [44].

There is some evidence that nicotine withdrawal symptoms may be mitigated by exercise and other physiotherapy interventions that stimulate the release of endorphins. Exercise and increased physical activity as an aid to cessation can help reduce cravings, adverse mood changes, and symptoms of withdrawal. Exercise raised self-efficacy and confidence for success in smokers who tried to quit. Used in combination with nicotine replacement therapy, exercise has been shown to promote abstinence, improve functional ability, and delay weight gain in women smokers. Increased physical activity can also help reduce insomnia and serve as a substitute or diversion activity for those trying to break their addiction [45].

Teenagers who increased the number of days with at least 20 minutes of exercise were statistically more likely to decrease their daily use of cigarettes, with those in an unfit condition exhibiting the highest probability of reducing smoking [46].

Functional magnetic resonance imaging was used to analyse how the brain processed cigarette images during exercise, showing regional brain activity changes after exercise in response to smoking-related images [28].

The mechanism of the beneficial effect of exercise on withdrawal and cravings is not sufficiently clear. However, exercise has been shown to exhibit some similarities to smoking in its effects on central nervous system stimulation and neurobiological processes in the brain [47].

Limitations

The limitations of the study refer to the sample size and the sample profile.

Conclusions

The results of this study support the importance of exercise in the form of an HIIT program as a nonpharmacological treatment of dyslipidaemia. Exercise can modulate the lipid profile and nicotine concentration in smokers, which, in turn, may reduce the risk of vascular disorders and other adverse health effects of smoking.

Disclosure statement

No author has any financial interest or received any financial benefit from this research.

Conflict of interest

The authors state no conflict of interest.

References

- Fouda S, Kelany M, Moustafa N, Abushouk AI, Hassane A, Sleem A, et al. Tobacco smoking in Egypt: a scoping literature review of its epidemiology and control measures. *East Mediterr Health J*. 2018;24(2):198–215; doi: 10.26719/2018.24.2.198.
- Hajjar RR, Atli T, Al-Mandhari Z, Oudhri M, Balducci L, Silbermann M. Prevalence of aging population in the Middle East and its implications on cancer incidence and care. *Ann Oncol*. 2013;24(Suppl. 7):vii11–vii24; doi: 10.1093/annonc/mdt268.
- Amann M. Pulmonary system limitations to endurance exercise performance in humans. *Exp Physiol*. 2012; 97(3):311–318; doi: 10.1113/expphysiol.2011.058800.
- Aune D, Schlesinger S, Norat T, Riboli E. Tobacco smoking and the risk of sudden cardiac death: a systematic review and meta-analysis of prospective studies. *Eur J Epidemiol*. 2018;33(6):509–521; doi: 10.1007/s10654-017-0351-y.
- Wigand JS. Additives, cigarette design and tobacco product regulation. A report to: World Health Organization Tobacco Free Initiative Tobacco Product Regulation Group. Kobe; 2006.
- Fouad H, El Awa F, El Naga RA, Emam AH, Labib S, Pali-pudi KM, et al. Prevalence of tobacco use among adults in Egypt, 2009. *Glob Health Promot*. 2016;23(Suppl. 2): 38–47; doi: 10.1177/1757975913499801.
- El Ansari W, El Ashker S, Moseley L. Associations between physical activity and health parameters in adolescent pupils in Egypt. *Int J Environ Res Public Health*. 2010;7(4):1649–1669; doi: 10.3390/ijerph7041649.
- Negri E. Gender differences in smoking-related diseases. *J Health Inequal*. 2019;5(1):43; doi: 10.5114/jhi.2019. 87830.
- Meenakshisundaram R, Rajendiran C, Thirumalaikol-undusubramanian P. Lipid and lipoprotein profiles among middle aged male smokers: a study from southern India. *Tob Induc Dis*. 2010;8(1):11; doi: 10.1186/1617-9625- 8-11.
- Baselt RC. Disposition of toxic drugs and chemicals in man, 10th ed. Seal Beach: Biomedical Publications; 2017.
- Jang T-W, Kim H-R, Choi SE, Yim H-W, Lee H-E, My-ong J-P, et al. Smoking rate trends in Korean occupational groups: analysis of KNHANES 1998–2009 data. *J Occup Health*. 2012;54(6):452–458; doi: 10.1539/joh. 12-0148-oa.
- Bhalala O. Detection of cotinine in blood plasma by HPLC MS/MS. *MIT Undergrad Res J*. 2003;8:45–50.
- Fathy M, Hamed M, Youssif O, Fawzy N, Ashour W. Association between environmental tobacco smoke exposure and lung cancer susceptibility: modification by antioxidant enzyme genetic polymorphisms. *Mol Diagn Ther*. 2014;18(1):55–62; doi: 10.1007/s40291-013-0051-6.
- Agaku IT, King BA, Husten CG, Bunnell R, Ambrose BK, Hu SS, et al. Tobacco product use among adults – United States, 2012–2013. *MMWR. Morb Mortal Wkly Rep*. 2014; 63(25):542–547.
- WHO and ARE-Ministry of Health & Population. Egypt national STEPwise survey of non-communicable diseases risk factors. 2012.
- Nayak M, Dodiya D, Nayak J. Assessment of lipid profile in smokers versus non-smokers. *Int J Res Med*. 2016; 5(2):26–29.
- Jain RB, Ducatman A. Associations between smoking and lipid/lipoprotein concentrations among US adults aged ≥ 20 years. *J Circ Biomark*. 2018;7:1849454418 779310; doi: 10.1177/1849454418779310.
- Huang LZ, Grady SR, Quik M. Nicotine reduces L-DO-PA-induced dyskinesias by acting at $\beta 2^*$ nicotinic receptors. *J Pharmacol Exp Ther*. 2011;338(3):932–941; doi: 10.1124/jpet.111.182949.
- Kopa PN, Pawliczak R. Health consequences of smoking – focusing on alternative smoking methods. *Polish J Allergol*. 2019;6(3):100–109; doi: 10.5114/pja.2019.88291.
- Hong X-Y, Lin L, Gu W-W. Risk factors and therapies in vascular diseases: an umbrella review of updated systematic reviews and meta-analyses. *J Cell Physiol*. 2019; 234(6):8221–8232; doi: 10.1002/jcp.27633.
- Marcus BH, Lewis BA, Hogan J, King TK, Albrecht AE, Bock B, et al. The efficacy of moderate-intensity exercise

- as an aid for smoking cessation in women: a randomized controlled trial. *Nicotine Tob Res.* 2005;7(6):871–880; doi: 10.1080/14622200500266056.
22. Bartlett JD, Close GL, MacLaren DPM, Gregson W, Drust B, Morton JP. High-intensity interval running is perceived to be more enjoyable than moderate-intensity continuous exercise: implications for exercise adherence. *J Sports Sci.* 2011;29(6):547–553; doi: 10.1080/02640414.2010.545427.
 23. Koubaa A, Triki M, Trabelsi H, Baati H, Sahnoun Z, Hakim A. The effect of a 12-week moderate intensity interval training program on the antioxidant defense capability and lipid profile in men smoking cigarettes or hookah: a cohort study. *ScientificWorldJournal.* 2015;2015:639369; doi: 10.1155/2015/639369.
 24. Whitehurst M. High-intensity interval training: an alternative for older adults. *Am J Lifestyle Med.* 2012;6(5):382–386; doi: 10.1177/1559827612450262.
 25. Sedeaud A, Marc A, Marck A, Dor F, Schipman J, Dorsey M, et al. BMI, a performance parameter for speed improvement. *PLoS One.* 2014;9(2):e90183; doi: 10.1371/journal.pone.0090183.
 26. Racil G, Coquart JB, Elmontassar W, Haddad M, Goebel R, Chaouachi A, et al. Greater effects of high-intensity interval training on cardio-metabolic variables, blood leptin concentration and ratings of perceived exertion in obese adolescent females. *Biol Sport.* 2016;33(2):145–152; doi: 10.5604/20831862.1198633.
 27. Robergs RA, Landwehr R. The surprising history of the “HRmax = 220 – age” equation. *J Exerc Physiol Online.* 2002;5(2):1–10.
 28. Haasova M, Warren FC, Ussher M, Van Rensburg KJ, Faulkner G, Cropley M, et al. The acute effects of physical activity on cigarette cravings: exploration of potential moderators, mediators and physical activity attributes using individual participant data (IPD) meta-analyses. *Psychopharmacology.* 2014;231(7):1267–1275; doi: 10.1007/s00213-014-3450-4.
 29. Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. *Lancet.* 2004;364(9438):937–952; doi: 10.1016/s0140-6736(04)17018-9.
 30. Brunner H, Cockcroft JR, Deanfield J, Donald A, Ferrannini E, Halcox J, et al. Endothelial function and dysfunction. Part II: Association with cardiovascular risk factors and diseases. A statement by the Working Group on Endothelins and Endothelial Factors of the European Society of Hypertension. *J Hypertens.* 2005;23(2):233–246; doi: 10.1097/00004872-200502000-00001.
 31. Kozub M, Gachewicz B, Kasprzyk M, Roszak M, Gasiorowski L, Dyszkiewicz W. Impact of smoking history on postoperative complications after lung cancer surgery – a study based on 286 cases. *Kardiochir Torakochirurgia Pol.* 2019;16(1):13–18; doi: 10.5114/kitp.2019.83940.
 32. Ahammed B, Maniruzzaman MD, Kundu S, Al Mahmud J, Ferdousi F. Prevalence and risk factors associated with tobacco smoking among adults in India: a nationally representative household survey. *Fam Med Prim Care Rev.* 2019;21(4):307–317; doi: 10.5114/fmPCR.2019.86505.
 33. Gabr HM, Allam HK, Abdallah AR. Smoking among administrative university employees: prevalence and degree of nicotine dependence. *Egypt J Occup Med.* 2019;43(2):259–268; doi: 10.21608/EJOM.2019.31423.
 34. Alvarez C, Ramirez-Campillo R, Martinez-Salazar C, Castillo A, Gallardo F, Gomes Ciolac E. High-intensity interval training as a tool for counteracting dyslipidemia in women. *Int J Sports Med.* 2018;39(5):397–406; doi: 10.1055/s-0044-100387.
 35. Pavey TG, Gartner CE, Coombes JS, Brown WJ. Assessing the effectiveness of high intensity interval training (HIIT) for smoking cessation in women: HIIT to quit study protocol. *BMC Public Health.* 2015;15(1):1309; doi: 10.1186/s12889-015-2631-3.
 36. Wisløff U, Støylen A, Loennechen JP, Bruvold M, Rognum Ø, Haram PM, et al. Superior cardiovascular effect of aerobic interval training versus moderate continuous training in heart failure patients: a randomized study. *Circulation.* 2007;115(24):3086–3094; doi: 10.1161/CIRCULATIONAHA.106.675041.
 37. Elmer DJ. Effect of 8 weeks of high-intensity interval training versus traditional endurance training on the blood lipid profile in humans. Doctoral dissertation. Auburn: Auburn University; 2013.
 38. Musa DI, Adeniran SA, Dikko AU, Sayers SP. The effect of a high-intensity interval training program on high-density lipoprotein cholesterol in young men. *J Strength Cond Res.* 2009;23(2):587–592; doi: 10.1519/JSC.0b013e318198fd28.
 39. Ndlovu P. The effect of high intensity interval training and detraining on the health-related outcomes of young women. Master’s thesis. Stellenbosch: Stellenbosch University; 2013.
 40. ElDeeb AM, Elsis HF, Lasheen YR. Response of lipids, estradiol level, and liver size to diet and high-intensity interval training in postmenopausal women with fatty liver. *Bull Fac Phys Ther.* 2018;23(2):69–76; doi: 10.4103/bfpt.bfpt_6_18.
 41. Pedersen BK, Saltin B. Exercise as medicine – evidence from prescribing exercise as therapy in 26 different chronic diseases. *Scand J Med Sci Sports.* 2015;25(Suppl. 3):1–72; doi: 10.1111/sms.12581.
 42. Linke SE. Intermittent exercise in response to nicotine cravings in the context of an Internet-based smoking cessation program. Doctoral dissertation. San Diego: University of California; 2011.
 43. Prapavessis H, De Jesus S, Harper T, Cramp A, Fitzgeorge L, Mottola MF, et al. The effects of acute exercise on tobacco cravings and withdrawal symptoms in temporary abstinent pregnant smokers. *Addict Behav.* 2014;39(3):703–708; doi: 10.1016/j.addbeh.2013.10.034.
 44. Scerbo F, Faulkner G, Taylor A, Thomas S. Effects of exercise on cravings to smoke: the role of exercise intensity and cortisol. *J Sports Sci.* 2010;28(1):11–19; doi: 10.1080/02640410903390089.
 45. Pignataro RM, Ohtake PJ, Swisher A, Dino G. The role of physical therapists in smoking cessation: opportunities for improving treatment outcomes. *Phys Ther.* 2012;92(5):757–766; doi: 10.2522/ptj.20110304.
 46. Horn K, Branstetter S, Zhang J, Jarrett T, O’Hara Tompkins N, Anesetti-Rothermel A, et al. Understanding physical activity outcomes as a function of teen smoking cessation. *J Adolesc Health.* 2013;53(1):125–131; doi: 10.1016/j.jadohealth.2013.01.019.
 47. Roberts V, Maddison R, Simpson C, Bullen C, Prapavessis H. The acute effects of exercise on cigarette cravings, withdrawal symptoms, affect, and smoking behaviour: systematic review update and meta-analysis. *Psychopharmacology.* 2012;222(1):1–15; doi: 10.1007/s00213-012-2731-z.