Effects of interval training on cardio metabolic risk factors and nitric oxide in type 2 diabetes patients: a randomized controlled trial

Tahereh Arefirad¹ · Nader Shakeri¹ · Khosro Ebrahim² · Ensieh Nasli-Esfahani³

Received: 14 November 2019 / Accepted: 30 December 2019 / Published online: 1 October 2020
© Springer Nature Switzerland AG 2020

Abstract

Purpose The purpose of this study was to investigate the effects of interval training on cardio metabolic risk factors and nitric oxide in type 2 diabetes patients.

Method This single blinded randomized controlled trial was conducted at cardiology clinic of Rajaee hospital in Karaj. Thirty female patients with type 2 diabetes randomly assigned to interval training exercise ($n = 15$) and control ($n = 15$). In interval training exercise patients received interval training exercise with 18 sessions (three sessions per week). Each training session took 25 min and consists a single set of exercise with 10 time repetitions. Training was performed on a cycle ergometer set in constant watt mode at a pedal cadence of 80–100 revolutions/min. Each repetition of the training takes 60 s and there will be a 60 s recovery period between each repetition. Each training session include a 3-min warm-up and 2-min cool-down at 50 W for a total of 25 min. Blood samples and of all the subjects were taken at baseline, 3 weeks after intervention and at the end of the study (6 weeks).

Results In intervention group, comparing with controls participants, a significant decrease were observed in levels of total cholesterol, triglyceride and HbA1c after training program ($p < 0.05$). Moreover, exercise significantly increased the level of NOx ($p < 0.05$). Other cardiometabolic risk factors including SBP, DBP, FPG, LDL, HDL, insulin level, insulin resistance, HR, VO2 max, did not show significant differences between the two groups ($p > 0.05$).

Conclusion Results of current study showed that interval training as a type of planned physical activity can be effective in lowering cardiovascular risk factors, especially lowering cholesterol and triglycerides, and can also have a beneficial effect on improving NO.

Keywords Interval training · Diabetes mellitus type 2 · Cardio metabolic risk factors · CMRFs · Nitric oxide · Insulin resistance

Introduction

Increasing trends of the number of patients with Diabetes and its related health and economic burden become a common health problem all over the world [1].

Researches show that there are more than 415 million people worldwide with diabetes, of which about 35 million are in the Middle East and about 8.5 million people live in Iran [1, 2]. Because diabetes is associated with cardiovascular outcomes and complications of small and large arteries, it is therefore considered as a major health problem in all parts of the world, especially in developing countries and Iran [2, 3].

Cardiovascular damage is one of the most common causes of mortality in diabetic patients. Expansion and vascular reactivity in diabetes are affected by early stages of the disease. This is due to changes in endothelial cell function [4, 5].

Many factors, such as insulin resistance, can interfere with endothelial dysfunction in diabetes [6, 7], increased glycerol [8], and increased blood pressure [9].

Another mechanism for endothelial dysfunction is endothelial-vascular dilatation in diabetes, which is associated with a decrease in the function of Nitric oxide (NO) [6]. NO is

✉ Nader Shakeri
nsprofsport@gmail.com

¹ Department of Exercise Physiology, Science and Research Branch, Islamic Azad University, Tehran, Iran

² Department of Exercise Physiology, Faculty of Physical Education & Sport Sciences, Shahid Beheshti University, Tehran, Iran

³ Diabetes Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

known to be a major regulator of blood flow [10]. This factor is produced by nitric oxide synthase (NOs) 2. [11] Recent evidence suggests that NO is an important indicator of metabolism, body composition, and insulin sensitivity [10, 11].

In this regards, many probable associated factors such as genetic factors, pathogens, toxic subnets, external environmental factors, stressors have been studied. On the other hands many investigations focus on the effects of modifiable factors that mostly rooted in life style. The results of evaluations reveal that changes in patterns of physical activities and following the exercise programs could be effective in controlling the risk factors, including high blood pressure, high cholesterol, obesity, and insulin resistance reduced [12]. Exercise also stimulates NO release from endothelial cells [13].

Despite the obvious benefits of interval training, the main exercise-mediated mechanisms involved in the improvement of vascular function in coronary artery disease have not been clearly identified. Today, specialists' attention has grown to a high intensity and low volume exercise program. Past research has shown that this type of exercise increases the lipid oxidation during exercise in women, improves insulin function [17, 18], and increases the oxidative capacity of skeletal muscle [14–16], and even in mice With metabolic syndrome, the exercise was more effective than moderate exercise to reduce the risk of cardiovascular risk factors [17].

Therefore, considering that few studies have investigated the effect of periodic exercises in diabetic patients, the present study was designed to examine the effect of the type of periodic exercise on the NO level and insulin resistance and some cardio metabolic factors in diabetic patients to answer this question. Does this exercise affect the NO level and insulin resistance, and some cardio metabolic factors?

Material and methods

To assess the effects of interval training on NO, insulin resistance (IR) and some cardio-metabolic risk factors we designed a randomized controlled trial (RCT).

Study design and population

This study was a single-center; double blind RCT which conducted at Rajae hospital research unit at Karaj, Iran. Thirty female patients with type 2 diabetes randomly assigned to interval training exercise ($n = 15$) and control ($n = 15$).

Inclusion and exclusion criteria

Inclusion criteria: patients diagnosed with type 2 diabetes mellitus and aged 40–55 years, Not taking insulin for treatment; Baseline glycosylated hemoglobin (HbA1c) values of 6 to 9%; No previous exercise training in the last 6 months.

Exclusion criteria

All participants at least 3 months before the onset of work confirmed as diabetic patients based on their high levels of Fasting Blood Glucose (FBG) ($7 \text{ mmol / L} \leq$) or impaired 2 h Glucose Tolerance Test (GTT) ($11.1 \text{ mmol / L} \leq$).

Those who were taking insulin or had a history of the last stage of liver and kidney disease, neuropathy, retinopathy, cardiovascular disease or blood pressure, that was not controlled by commonly drugs, were excluded. All included participants, had a history of fun unprofessional physical activity.

Intervention

Fifteen patients received interval training exercise with 18 sessions (three sessions per week), and fifteen patients in control group had usual physical activity. Each training session took 25 min and consists a single set of exercise with 10 time repetitions. Training was performed on a cycle ergometer set in constant watt mode at a pedal cadence of 80–100 revolutions/min. Each repetition of the training takes 60 s and there will be a 60 s recovery pried between each repetition. Each training session include a 3-min warm-up and 2-min cool-down at 50 W for a total of 25 min. All patients received regular routine diabetes care throughout the study.

All of participants attended in the primary acquaintance session that were held a few days before the start of the research. Through which, the aims of the research and the methods of conducting the tests and the exercise program discussed in details. Each of the volunteers completed two forms on general information and physical activity questionnaires.

A program of exercises and rest

In this research, a periodic exercise expresses the 10-min jogging practice on a bicycle with a 90% maximum heart rate and 1-min rest periods among them.

Medical examination and iterance

To assess the cardiovascular response and perception the amount of their efforts during exercise, under the supervision of a cardiologist's physician, after 5-min physical warm-up, on a treadmill, the modified Bruce Sport Test were conducted for all of participants. The Heart rate measured by Telemetry and the perception of Borg's effort (0–20 scaled criterion).

When it was found that participants did not have cardiovascular problems, they randomly assigned to either control or periodic groups. The control group performed Bruce's modified test before and after 4 weeks of their blood sampling. After 2 days of the walking test, the participants of the interval

training group refer to the laboratory for implementation of the protocol (Figs. 1 and 2).

Maximum exercise test

After measuring the height and weight, the maximum exercise test was performed using the bicycle at the supine position. A 12 lead electrocardiogram (12 lead ECG) was taken before, during and after the test. The test started at 30 watts and added 15 watts each minute to reach the voluntary fatigue level. Peak of power output and peak of heart rate were recorded. The introduction of interval training followed, under the supervision of physician, during two complementary sessions. In these meetings, the output power of individuals was determined at a maximum intensity of 90%.

Practice protocol

Interval training included 18 sessions per 6 weeks (3 sessions per week). Each session consisted of 10 repetitions of the training sessions for 60 s with 60 s of recovery among them (1 * 10). The training followed on abicycle with a rhythm of 80 to 100 rpm. The workload of individuals in each group was based on 90% of maximum heart rate in rotations. During the recovery, people are allowed to rest or slowly pedal with 50 watts of resistance. Each session consisted of 3 min of physical warming and 2 min of cool down at 50 watts and a total of 25 min.

Two or three days after implementation of protocol, for second time, participants in both groups performed Bruce's modified exercise test.

Main outcome measures

The following variables were measured before and after the intervention: Systolic and Diastolic Blood Pressure, anthropometric measurements (body weight, height,), nitric oxide, fasting blood sugar, insulin resistance, glycosylated haemoglobin (HbA1C), fasting total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglyceride (TG).

Procedures

All of the patients referred to the Rajaei Hospital research unit. If the patient was volunteered, the inclusion criteria for entering the study were evaluated by the co-researcher and then random allocation was made to the interval training exercise and control groups. A physical therapist was responsible for interval training exercise and a nurse carries out the assessment of the primary and secondary outcome, did not know about the type of intervention of the groups.

Blood samples were taken after 12 overnight fasting and centrifuged, within 40 min of collection; all sample analyses were performed at the Rajaei hospital laboratory, affiliated to Alborz University of Medical Sciences. In current study serum NOx level was assessed using commercially available kits based on the Griess reaction (GR) method, which allow the spectrophotometric detection of nitrate (NO₃⁻) and nitrite (NO₂⁻). [18]. The method of NOx determination was validated in the previous studies in Iran [19–21]. In this method briefly using zinc sulfate all serums were deproteinized and then centrifuged at 10,000×g for 10 min, then 100 µL of the supernatant and 100 µL vanadium chloride (8 mg/mL) was transferred to a microplate well to convert nitrate (NO₃⁻) to nitrite (NO₂⁻). In the GR method, Griess reagents including 50 µL sulfanilamide (2%) and 50 µL N-(1-Naphthyl) ethylenediamine dihydrochloride (0.1%) were added and samples were incubated for 30 min at 37 °C; absorbance was read at 540 nm using the enzyme-linked immunosorbent assay. In this method, inter-assay and inter assay coefficients of variation was 2.5% and 4.6% respectively.

Data analyzing and statistical method

Statistical analysis was performed using the SPSS 20.0 software (SPSS Inc.; Chicago, IL, USA). Normal distribution of continuous variables was assessed using Kolmogorov-Smirnov test and due to lack of normality, continuous variable were presented as median (inter-quartile range (IQR)). Continuous variable without normal distribution were compared between groups using Mann-Whitney U test. Categorical data were presented as number (percentage) and were compared using

Fig. 1 Research plan

Fig. 2 A training session

Maximum sports test after protocol execution:

Chi-square test between study groups. The threshold of statistical significance was set at $P < 0.05$ at least.

Ethical considerations

The ethics committee of Alborz University approved the study. This trial was registered in Iranian Registry of Clinical Trials (IRCT2017082835945N1). The process of study and aims and scope of project were discussed by participants and participation was voluntary. All of participants verbally agreed to participate in the study and completed the forms of ethical consent.

Results

Baseline demographic and anthropometric characteristics of two intervention and control groups are presented in Table 1. As it is evident from results; there were not any significant differences demographic and anthropometric characteristics except for waist circumference (Table 1).

The effects of interval training on the variables related to cardiovascular risk factors and inflammatory factors is presented in Table [2]. In intervention group, comparing with controls participants, significant decrease were detected in levels of total cholesterol, triglyceride and HA1c significantly which were measured after training program. Moreover, at the same comparing setting; exercise significantly increased the level of nitrite oxide. Other variables including SBP, DBP,

FPG, LDL, HDL, insulin level, insulin resistance, heart rate(HR), VO2 max, did not show significant differences between the two groups (Table 2).

Discussion

To assess the effects of interval training on cardio-metabolic factors, nitric oxide and insulin resistance an experimental pretest posttest study on 20 female type 2 Diabetes patients, aged 40 to 55 years old, confirmed a significant effects of training programs on levels of total cholesterol, triglyceride and HA1c. Moreover, exercise significantly increased the level of nitrite oxide.

Accordingly, interval training can be effective in decreasing the cholesterol and triglyceride levels as two important risk factors for cardiovascular diseases.

Through a clinical trial; twelve-week randomized parallel set for examining the effects of different exercise programs on fasting levels of lipids, glucose and insulin and changes in body weight, fat mass and dietary intake. Participants randomized to; Group 1 (Control, $n = 16$); Group 2 (Aerobic, $n = 15$); Group 3 (Resistance, $n = 16$); Group 4 (Combination, $n = 17$). The planned training program comprising of resistance or combination exercise, at moderate-intensity for 30 min, 5 days/week resulted in improvements in the cardiovascular risk profile in overweight and obese participants compared to no exercise. Based on the results, comparing with aerobic and resistance training, combination exercise had greater benefits for weight loss, fat loss and cardio-respiratory fitness [17]. Another research confirmed that, interval training in obese diabetic women can reduce total cholesterol and LDL levels and increase HDL of serum [22]. Through another related experience researcher concluded that interval training has a significant effect on lowering total cholesterol and, like the findings of the present study, did not have a significant effect on lowering LDL cholesterol [23].

Several other studies that have examined the effect of intermittent exercise on cardiovascular risk factors have found that these exercises can be effective in lowering cholesterol levels. On the other hand, most of these studies have found

Table 1 Baseline characteristics of subjects according to study groups

Variable	Control group	Intervention group	<i>P</i> value
Age (year)	46.07 ± 4.77	44.87 ± 5.89	0.54
Weight (kg)	74.66 ± 13.91	72.67 ± 14.57	0.57
Height (cm)	160.54 ± 7.97	156.23 ± 6.34	0.12
Diabetes duration	5.07 ± 4.27	5.43 ± 4.43	0.83
BMI (kg/m ²)	29.28 ± 5.65	29.19 ± 4.69	0.97
Waist to hip ratio	0.91 ± 0.06	0.94 ± 0.06	0.09

BMI body mass index; Values are reported as mean ± SD

Table 2 Effect of interval training on the variables related to cardiovascular risk factors and inflammatory factors

Variable	Baseline measurement		Second measurement		Last measurement		Two-way Repeated measure ANOVA		
	Control group	Intervention group	Control group	Intervention group	Control group	Intervention group	Group	Time	Interaction
DBP (mmHg)	76.67 ± 6.17	76.67 ± 4.88	77 ± 4.93	76.33 ± 3.99	77.33 ± 5.94	76 ± 5.07	0.68	0.96	0.57
SBP (mmHg)	131.67 ± 15.20	137.33 ± 15.34	133.34 ± 11.86	135.96 ± 12.68	133.06 ± 14.53	133.24 ± 15.60	0.59	0.77	0.38
HDL	38.09 ± 5.90	35.81 ± 7.26	40.59 ± 12.25	40.32 ± 9.07	46.61 ± 21.98	42.11 ± 6.65	0.43	0.01	0.82
LDL	111.93 ± 30.36	102.6 ± 27.85	114.74 ± 33.51	90.83 ± 24.76	112.75 ± 42.88	93.87 ± 36.05	0.1	0.70	0.44
TC	186.93 ± 40.84	184.8 ± 28.11	185.33 ± 41.74	173.13 ± 20.53	187.00 ± 42.40	166.66 ± 24.16	0.33	<0.001	<0.001
TG	168.46 ± 32.95	170.47 ± 49.42	169.00 ± 31.76	164.86 ± 43.51	169.06 ± 29.48	159.46 ± 44.66	0.22	<0.001	<0.001
FBS	177.2 ± 83.43	147.53 ± 41.44	169.27 ± 72.52	139.46 ± 34.50	174.01 ± 69.63	153.84 ± 46.52	0.32	0.27	0.51
Insulin	7.88 ± 6.05	7.44 ± 6.31	8.26 ± 5.14	7.16 ± 5.88	7.44 ± 5.94	6.08 ± 4.905	0.39	0.52	0.46
HOMA-IR	14.65 ± 12.28	11.22 ± 9.18	14.88 ± 11.24	10.29 ± 8.43	13.76 ± 12.65	9.91 ± 8.92	0.25	0.71	0.48
HbA1c	7.1 ± 1.85	6.67 ± 1.31	7.39 ± 1.95	6.64 ± 1.24	7.32 ± 2.13	6.55 ± 1.18	0.36	0.14	0.02
Maximum Heart rate	169.87 ± 23.08	162.73 ± 26.06	166.17 ± 23.49	166.43 ± 17.61	173.13 ± 28.06	180.78 ± 32.98	0.93	0.22	0.27
VO2 max	35.81 ± 5.06	38.76 ± 6.85	36.74 ± 5.44	37.83 ± 4.13	36.43 ± 7.66	35.66 ± 2.93	0.57	0.47	0.20
NOx (μM)	14.96 ± 2.76	15.16 ± 4.17	15.20 ± 2.57	15.99 ± 3.90	15.74 ± 3.87	19.22 ± 5.55	0.06	<0.001	0.01

DBP Diastolic blood pressure, SBP Systolic blood pressure, NO Nitric oxide (NO)

that intermittent exercise improves the insulin resistance, but in the current study, this effect did not detected [24–26].

Studies assessed the effect of interval exercise on inflammatory factors have often reported effective reducing of inflammatory factors [22, 23]. But in present study, al like as many other findings of researches, no such significant effect has been achieved [24, 27].

The results of related study reveal promising light on the complex series of cellular adaptations to chronic exercise. Through this experience researchers confirmed that, a 10-week treadmill training program in rats lead to significant increase in total NOS activity in the soleus which could be due to increased NOS interaction with Hsp90 and phosphorylation. These changes may be affective in altering blood flow of muscle and redox status of skeletal muscle [12]. Other similar researches show consistent findings of beneficial results of regular training program on insulin-stimulated IRS-1-associated PI3-kinase activation; enhanced facilitating of insulin-mediated glucose uptake and promoting the status of skeletal muscle [15, 16].

The assessment of the effects of 6 weeks moderate and high-intensity endurance training and resistance training on the vasorelaxation responsiveness of the aorta, iliac, and femoral vessels in type 1 diabetic rats shown that vasorelaxation effects mainly associated with high-intensity endurance training [13].

Another research disused that dietary supplementation of L-arg. Along with the regular physical exercise improved agonist-mediated, endothelium-dependent vasodilation. This

research groups emphasized that; multiple interventions seem to be more effective on endothelium-dependent vasodilation [14].

There were some limitations to this study, such as the lack of measurement of vasodilatory response from blood flow during exercise. It looks like exercises Exercise causes changes in local response for a specific period of time, with longer training periods leading to structural changes in the arteries, which obviously should have a longer training period. Thus, two general limitations of this study are the lack of measurement during the training program, the intervention and the duration of the training period to better reflect the short- and long-term changes caused by aerobic exercise.

Conclusion

In conclusion, this study showed that interval training as a type of planned physical activity can be effective in lowering cardiovascular risk factors, especially lowering cholesterol and triglycerides, and can also have a beneficial effect on improving blood sugar in diabetic patients and reduction of long term adverse health outcomes. Given the absence of a significant relationship between periodic exercise and inflammatory factors as well as contradictory findings in similar studies, further studies are needed. These data reveal the importance of the specificity of the training programs to reach the expected benefits of vascular responses.

Acknowledgments The authors would like to express their thanks for partnership of all participant and also Pershan club staffs. We also appreciate Rajae Hospital research unit for their administrative assistance.

Authors' contributions TA, NS and KE developed the main concept of study. TA and EN and draft of manuscript. All co-authors had contribution and participated in the revision and approval of the manuscript.

Compliance with ethical standards

Competing interests The authors declare that they have no competing interests.

References

- Ogurtsova K, da Rocha FJ, Huang Y, Linnenkamp U, Guariguata L, Cho N, et al. IDF diabetes atlas: global estimates for the prevalence of diabetes for 2015 and 2040. *Diabetes Res Clin Pract*. 2017;128:40.
- Sardu C, De Lucia C, Wallner M, Santulli G. Diabetes mellitus and its cardiovascular complications: new insights into an old disease. *J Diabetes Res*. 2019;2019.
- Herman WH. The global burden of diabetes: an overview. *Diabetes mellitus in developing countries and underserved communities*: Springer; 2017. p. 1–5.
- Basha B, Samuel SM, Triggler CR, Ding H. Endothelial dysfunction in diabetes mellitus: possible involvement of endoplasmic reticulum stress? *Exp Diabetes Res*. 2012;2012.
- Romano M, Pomilio M, Vigneri S, Falco A, Chiesa P, Chiarelli F, et al. Endothelial perturbation in children and adolescents with type 1 diabetes: association with markers of the inflammatory reaction. *Diabetes Care*. 2001;24(9):1674.
- Merdzo I, Rutkai I, Sure VN, McNulty CA, Katakam PV, Busija DW. Impaired mitochondrial respiration in large cerebral arteries of rats with type 2 diabetes. *J Vasc Res*. 2017;54(1):1.
- Hwang M, Lee S. Insulin resistance: vascular function and exercise. *Integr Med Res*. 2016;5(3):198.
- Hadi HA, Carr CS, Al SJ. Endothelial dysfunction: cardiovascular risk factors, therapy, and outcome. *Vasc Health Risk Manag*. 2005;1(3):183.
- de Boer I, Bangalore S, Benetos A, Davis A, Michos E, Muntner P, et al. Diabetes and hypertension: a position statement by the American Diabetes Association. *Diabetes Care*. 2017;40(9):1273.
- Atochin DN, Huang PL. Endothelial nitric oxide synthase transgenic models of endothelial dysfunction. *Pflugers Archiv: European Journal of Physiology*. 2010;460(6):965.
- Cook S, Hugli O, Egli M, Ménard B, Thalmann S, Sartori C, et al. Partial gene deletion of endothelial nitric oxide synthase predisposes to exaggerated high-fat diet-induced insulin resistance and arterial hypertension. *Diabetes*. 2004;53(8):2067.
- Harris MB, Mitchell BM, Sood SG, Webb RC, Venema RC. Increased nitric oxide synthase activity and Hsp90 association in skeletal muscle following chronic exercise. *Eur J Appl Physiol*. 2008;104(5).
- Murias JM, Dey A, Campos OA, Estaki M, Hall KE, Melling CW, et al. High-intensity endurance training results in faster vessel-specific rate of vasorelaxation in type 1 diabetic rats. *PLoS ONE*. 2013;8(3).
- Hambrecht R, Hilbrich L, Erbs S, Gielen S, Fiehn E, Schoene N, et al. Correction of endothelial dysfunction in chronic heart failure: additional effects of exercise training and oral L-arginine supplementation. *J Am Coll Cardiol*. 2000;35(3):706.
- Kirwan JP, Del Aguila LF, Hernandez JM, Williamson DL, O'Gorman DJ, Lewis R, et al. Regular exercise enhances insulin activation of IRS-1-associated PI3-kinase in human skeletal muscle. *J Appl Physiol*. 2000;88(2):797–803.
- Bailey S, Winyard P, Vanhatalo A, Blackwell J, DiMenna F, Wilkerson D, et al. Acute L-arginine supplementation reduces the O₂ cost of moderate-intensity exercise and enhances high-intensity exercise tolerance. *Journal of Applied Physiology (Bethesda, Md: 1985)*. 2010;109(5):1394.
- Ho SS, Dhaliwal SS, Hills AP, Pal S. The effect of 12 weeks of aerobic, resistance or combination exercise training on cardiovascular risk factors in the overweight and obese in a randomized trial. *BMC Public Health*. 2012;12:704.
- Pitocco D, Zaccardi F, Di Stasio E, Romitelli F, Santini SA, Zuppi C, et al. Oxidative stress, nitric oxide, and diabetes. *Rev Diabet Stud*. 2010;7(1):15–25.
- Ghardashi Afousi A, Gaeini A, Gholami BB. The effect of aerobic interval training on endothelial vasculature function in type 2 diabetes patient. *Rehabil Nurs*. 2016;2:27–39.
- Ghasemi A, Zahediasl S, Azizi F. Reference values for serum nitric oxide metabolites in an adult population. *Clin Biochem*. 2010;43(1–2):89–94.
- Ghasemi A, Hedayati M, Biabani H. Protein precipitation methods evaluated for determination of serum nitric oxide end products by the Griess assay. *JMSR*. 2007;2(15):29–32.
- Akbarnejad A et al. comparison of interval and continuous exercise on cardiometabolic risk factors in overweight/obese women. *Journal of Sport Biosciences* 2011, 9: 77–93.
- Kazemi A, Rahmati M, Farabi M, Taherabadi SJ. Effect of eight weeks high intensity interval training on body weight and serum levels of TNF- α , insulin and lipid profile in obese children. *Razi Journal of Medical Science*. 2016;22:1–7.
- Smith-Ryan AE, Trexler ET, Wingfield H, Blue MN. Effects of high-intensity interval training on cardiometabolic risk factors in overweight/obese women. *J Sports Sci*. 2016;34(21):2038.
- Kessler H, Sisson S, Short K. The potential for high-intensity interval training to reduce cardiometabolic disease risk. *Sports Medicine (Auckland, NZ)*. 2012;42(6):489.
- García-Hermoso A, Cerrillo-Urbina A, Herrera-Valenzuela T, Cristi-Montero C, Saavedra J, Martínez-Vizcaino V. Is high-intensity interval training more effective on improving cardiometabolic risk and aerobic capacity than other forms of exercise in overweight and obese youth? A meta-analysis. 2016.
- Ghafari M, Banitalebi E, Heidari A. Impact of high-intensity interval training and at concurrent strength-endurance training on the levels of some Adipokines associated with insulin resistance in women with diabetes mellitus. 2017.

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.