Alghadir *et al. BMC Endocrine Disorders* (2024) 24:212
https://doi.org/10.1186/s12902-024-01745-8

BMC Endocrine Disorders

RESEARCH Open Access

The effects of supervised aerobic training on dyslipidaemia among diabetic older patients

Ahmad H. Alghadir[1], Sami A. Gabr[1] and Amir Iqbal[1*]

Abstract

Background Higher prevalence rates of diabetes and its complications have been reported among individuals with poor physical activity and a sedentary lifestyle. This study explored the influence of six months of moderate-intensity supervised aerobic training on the serum lipid profile, hs-CRP level, and variable-related correlations in prediabetic and type 2 diabetes patients (T2DM).

Design The study was based on a two-arm parallel group pretest–posttest comparative design.

Methods A total of 50 subjects who were diagnosed with diabetes for more than five years and aged 30–70 years were included in this study. The subjects were classified into two groups on the basis of their glycated haemoglobin (HbA1c%) values: Group 1 (patients with the prediabetes; HbA1c % ≤ 6.5, $n = 25$) and Group 2 (patients with the T2DM; HbA1c % ≥ 6.5, $n = 25$). Blood sugar, HbA1c %, insulin, lipid profile, and highly sensitive CRP (hs-CRP) were measured via colorimetric and immunoassay techniques at baseline and six months postintervention with moderate aerobic exercise.

Results The results revealed that participation in moderate aerobic training interventions for six months resulted in a significant reduction in BMI, fasting blood sugar, glycosylated haemoglobin, hs-CRP, and lipid profile parameters such as T-Cholest, TG, and LDL-C as well as significant improvement in the level of insulin with a reduction in the values of HOMA-IR towards normal values in the patients with prediabetes ($P < 0.01$) in group 1 and patients with diabetes in group 2 ($P < 0.001$). The change in VO_2max with good physical fitness significantly improved with the exercise program after six months. The reduced levels of hs-CRP, HOMA-IR, and lipid profile and improved levels of insulin were significantly positively correlated with the levels of glycated haemoglobin (HbA1c%) in the patients with prediabetes ($P < 0.01$) and those with diabetes ($P < 0.001$) following six months of moderate aerobic training interventions. Moreover, hs-CRP was positively correlated with T-Cholest, TG, and LDL-C ($p = 0.01$) and negatively correlated with HDL-C. The data revealed improved glycemic control factors, lipid profiles, and hs-CRP levels as cardio-predictive markers in patients with both prediabetes and diabetes as well. These findings suggest that the anti-inflammatory effect of physical activity gained from moderate exercise training for six months may counteract increased cardiovascular complications associated with increased CRP levels and lipid profiles in prediabetes and T2DM patients.

*Correspondence:
Amir Iqbal
ajamaluddin@ksu.edu.sa

Full list of author information is available at the end of the article

Conclusions Moderate aerobic training for six months favourably affects glycemic parameters, lipid profiles, and inflammatory hs-CRP indicators and improves VO_2max, an indicator of physical fitness, in prediabetic and diabetic patients. The data obtained suggest the positive effect of moderate exercise training as a protective modulator of cardiovascular disorders, including the dyslipidaemic profile, glycaemic control, and hs-CRP inflammatory markers, in prediabetes and T2DM patients. Thus, regular exercise, owing to its anti-inflammatory effects and ability to improve cardiorespiratory fitness, lipid profiles, blood glucose levels, and insulin resistance, may help reduce the severity of cardiovascular diseases in prediabetes and T2DM patients and healthy controls.

Trial registration Retrospectively registered with ClinicalTrials.gov PRS under trial identifier ID: NCT06246435 dated 30/01/2024.

Keywords Glycemic control, hs-CRP, Aerobic exercise, Dyslipidaemia, Diabetes mellitus, Inflammation

Introduction

Populations in both developing and developed countries are suffering from relatively high prevalence rates of diabetes [1]. Approximately 6.4–7.7% of the world's population is suffering from diabetes risk factors, which increase economic pressure worldwide [2]. However, the total health expenditure rate for diabetes in the USA alone was 14% in 2010 [3]. In the same year, the Kingdom of Saudi Arabia (KSA) was one of the Gulf countries that held the record of spending approximately 21% of the country's total health expenditure on diabetes [2, 4].

Higher risks of cardiovascular disease with a substantial increase in the rates of cardiovascular death have been reported in patients with diabetes [5]. Other common risk factors, such as smoking, obesity, hypertension, and dyslipidaemia, are significantly associated with diabetes mellitus during the progression of cardiovascular complications [6].

In adult patients with type 2 diabetes mellitus, coronary artery disease (CAD) is significantly correlated with hyperlipidaemia, which increases the rate of cardiovascular mortality [7]. A greater incidence of inflammatory processes has been reported in patients with diabetes, which leads to the subsequent release of proinflammatory circulating markers such as high-sensitivity C-reactive protein (hs-CRP). Hs-CRP is reported to be an independent cardiac risk predictor in diabetic patients even with a normal lipid profile and can help measure additional risk [8]. The development of diabetes-related complications is linked to the level of glycated hemoglobin (HbA1c), which is a routinely used marker for long-term glycemic control. A 1% percent significant increase in the level of HbA1c is accompanied by an 18% significant increase in cardiovascular disease in diabetic patients [9]. The positive significant correlation between cardiovascular disease incidence and HbA1c levels was more reliable in diabetic patients with higher or even within the normal range of HbA1c [10]. Recently, most studies have reported the effects of lifestyle factors, such as time spent in leisure activities, sitting time, watching media such as TV, and using computers, on increasing obesity, which is considered one of the most common diabetes-related factors [11–13], and T2DM development [14].

Subjects with low physical activity along with other risk factors, such as smoking habits, arterial hypertension, and dyslipidaemia, are easily exposed to cardiovascular-related diseases and early mortality [15]. Most studies have reported the importance of moderate exercise interventions in reducing body weight, improving insulin sensitivity, increasing circulating levels of high-density lipoprotein (HDL), decreasing triglyceride levels, and normalizing blood pressure [16, 17].

In a study by Hayashino et al. [18], significant improvements in the levels of LDL-C and elevated HDL-C along with normalization of blood pressure were reported in diabetic patients following supervised exercise interventions. These findings raise many important questions, especially the significant role of HbA1c% in diabetic patients under programmed exercise training.

Therefore, the current study was designed to explore the influence of supervised moderate-intensity aerobic training on the serum lipid profile and hs-CRP level and to evaluate the importance of HbA1c % as an indicator of dyslipidaemia in prediabetic and diabetic patients. Thus, incorporating HbA1c % as a key variable in the study of dyslipidaemia evolution among older adults with prediabetes and type 2 diabetes undergoing supervised aerobic exercise introduces a novel dimension that could lead to more personalized and effective management strategies for these conditions.

The study hypothesis posits that prediabetic and type 2 diabetic patients will undergo significant improvements in the management of their dyslipidaemia profile, blood glucose levels, and chronic inflammatory markers following the six-month supervised moderate exercise training intervention examined in this research. The findings of this study underscore the critical role of exercise in promoting cardiovascular health and overall well-being in individuals with prediabetes and T2DM and offer a promising avenue for preventive and therapeutic interventions in the management of these conditions.

Materials and methods

Study design and ethical considerations

The study was based on a two-arm parallel group pretest-posttest comparative design. The Ethics Subcommittee at King Saud University, Riyadh, Saudi Arabia, reviewed and approved this study, recorded under file ID; RRC-2014-010. Additionally, the study was registered online with the ClinicalTrials.gov Protocol Registration and Results System (PRS) and assigned the identifier ID NCT06246435 dated 30/01/2024. This study followed all the research procedures per the ethical standards of the local Institutional Ethics Review Board and with the Helsinki Declaration of 2010. Additionally, this study adheres to the CONSORT guidelines. Signed informed consent was obtained from each participant as a proof of consent to participate before the start of this study.

Subjects

On the basis of previous study sample size estimates, fifty outpatients for clinical rehabilitation at the College of Applied Medical Sciences, King Saud University, were included in this study to satisfy the study sample power requirements. Fifty-eight patients who met the inclusion criteria were included in this study, as presented in Fig. 1. Participants aged 30–70 years and diagnosed with type 2 diabetes (DM2) for more than 5 years according to the American Diabetes Association (ADA) criteria [19–21] and with a BMI $<$45 kg/m^2 were included in this study. On the basis of the ADA criteria, the subjects were classified according to the level of glycated hemoglobin (HbA1c%) into two groups: Group 1 (patients with prediabetes; HbA1c % $\leq$ 6.5, n=25) and patients with diabetes; HbA1c % $\geq$ 6.5, n=25). The diabets patients were only treated with an antidiabetic agent (glibenclamide). In all groups of study, patients with prediabetes and diabetes with a history of smoking, abnormal alcohol intake, anaemia, hepatic diseases, thyroid diseases, rheumatoid arthritis, psoriasis, or overt complications of diabetes, such as nephropathy, neuropathy, retinopathy, and other heart complications, and who were suffering from viral infections, chronic liver disease, hypothyroidism, or drugs (diuretics or oral contraceptives) were excluded from this study [20, 21]. All the participants were sedentary with little or no physical activity during daily routine activities such as work and transportation.

For all participants, standardized physical examination and collection of serum samples were performed at week 0 (before the onset of the training program), 3 months, and after a 6-month program of moderate aerobic training [20, 21]. The general characteristics of the participants are shown in Table 1. Two outcome assessors were blinded to the group allocation of the participants.

Dietary information

The participants were instructed not to change their normal eating habits during the entire data collection period and to accurately record the amount, type, and fluid consumed. The dietary information of each participant was obtained from food diaries or by extensive dietary interviews and was significantly referred to according to reference dietary intakes (RDIs) for physically active people [22]. In addition, during the exercise program, the participants were prevented from any antioxidant-containing diets to avoid cross contamination that may interfere with the data of the proposed study.

Anthropometric measurements

An appropriate international standard scale (Digital Pearson Scale, ADAM Equipment Inc., USA) was used to record demographic parameters, such as weight and height, for all participants, and standardized measurements of weight and height were taken in light clothing without shoes [20, 21]. Additionally, the BMI of each participant was calculated according to standard techniques by using a bioelectrical impedance analysis (BIA)-based body composition analyser (TBF 105, Tanita Corporation, Tokyo, Japan) [20, 21].

Exercise training program

The participants performed the exercise test according to Karvonen's formula [20, 23] three times per week for 6 months. The entire supervised aerobic training program was performed in the RRC lab, CAMS, King Saud University, and supervised by an expert physiotherapist with >10 years of experience in his respective field. The training set comprised a warming phase by stretching exercises and walking for 5–10 min. The participants were allowed to reach their precalculated training heart rate (THR) in bout form, with a total time of 45–60 min performed as circuit training using a treadmill, bicycle and stair master [20]. Moreover, the exercise test was performed to give the participants physical activity corresponding to 30–45% of VO_2max uptake, which gradually increased until they reached 65–75% of VO_2max for moderate intensity; this test was used in this study as mentioned previously [20].

VO_2max measurement

Two maximal exercise tests to measure VO_2max were performed on two separate days at baseline and again on two separate days after training via a SensorMed 800 S (Yorba Linda, CA) cycle ergometer and a SensorMedics 2900 metabolic measurement cart [24]. The tests were conducted at approximately the same time of day, with at least 48 h between the two tests. In the first test, fit subjects exercised at a power output of 50 W for 3 min, followed by increases of 25 W every 2 min until volitional

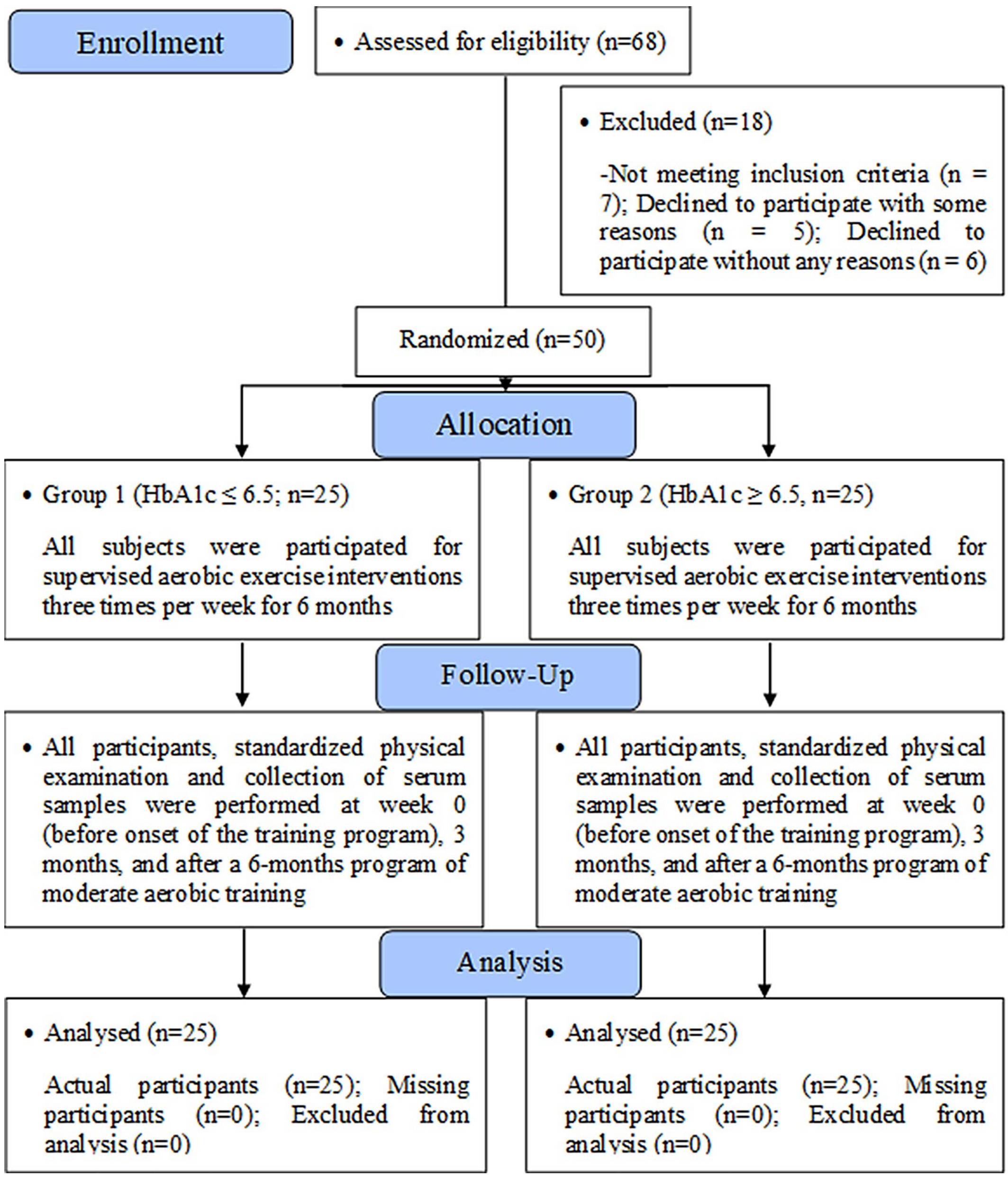

Fig. 1 A CONSORT (2010) flow diagram shows the study procedures, including participant enrollment, eligibility assessment, randomization, allocation to the intervention group, follow-up, and data analysis

exhaustion. However, for older, smaller, or less fit individuals, the test was started at 40 W, with increases of 10–20 W every 2 min thereafter.

In the second test, the subjects exercised for 10 min at an absolute power (50 W) and at a relative power output equivalent to 60% VO_2max. They then exercised for 3 min at a relative power output that was 80% of their VO_2max, after which the resistance was increased to the highest power output attained in the first maximal test. If the subjects were able to pedal after 2 min, the power output was increased every 2 min thereafter until they reached volitional fatigue. The average VO_2max from these two sets was taken as the VO_2max for that subject and used in analyses if both values were within 5% of each other. If they differed by >5%, the higher VO_2max value was used.

Blood sampling and analysis

All blood samples were taken from all the subjects before and after they participated in the training program at 0800 h following an overnight fast [20, 21]. Venous blood samples (5 mL) were collected in plain tubes from each participant. To obtain serum samples, the blood was allowed to clot for half an hour before being subjected to

Table 1 General characteristics of the subjects with diabetes. The glycated hemoglobin values are expressed as the means ± SDs

Parameters	Group 1 Pr-diabetes (HbA1c % ≤ 6.5)	Group 2 Diabetes (HbA1c % ≥ 6.5)
N	25	25
Male/Female	15/10	14/11
Age (years)	58.32 ± 1.84	56.48 ± 7.85
BMI (kg/m2)	23.3 ± 1.52	24.8 ± 1.5
Waist (cm)	76.1 ± 27.9	85.7 ± 18.5
Hips (cm)	85.9 ± 24.3	85.7 ± 22.3
Systolic BP (mmHg)	111.2 ± 9.5	108.9 ± 10.3
Diastolic BP (mmHg)	72.5 ± 13.7	72.5 ± 11.3
VO_2max (ml/kg*min)	32.44 ± 4.22	35.4 ± 3.9
Disease Duration (years)	5.65 ± 3.8	8.5 ± 4.2

centrifugation for 15 min at 2000 rpm [20, 21]. Then, the serum samples were given a coded study identification number and stored at 80 °C until analysis [20, 21].

Analysis of blood sugar, glycated haemoglobin (HbA1c%), and insulin levels

A glucose oxidase and peroxidase (GOD-POD) colorimetric method (Quanti Chrom Glucose Assay Kit, DIGL-100, BioAssay Systems, Hayward, CA, USA) was used to estimate the blood glucose level of each participant before and after the exercise program, as described previously [20, 21]. In addition, a commercial kit (Bio-Rad, Richmond, CA, USA) with a normal range from 3.5 to 5.5% (coefficient of variation 5%) was used to measure the levels of HbA1c% in the blood of the participants before and after the exercise test [20, 21]. Moreover, the serum insulin level was determined via ELISA (human insulin ELISA kit, KAQ1251, Invitrogen Corporation, Camarillo, CA, USA) [20, 21]. In addition, HOMA-IR was used to evaluate insulin resistance as follows: {HOMA-IR= (fasting serum insulin (μU/ml) × fasting plasma glucose (mmol l^{-1})/22.5)}.

The assays were performed according to the instructions provided by the manufacturers.

Analysis of lipid profiles

Lipid profiles, such as total cholesterol, triglycerides, high-density lipoprotein (HDL)-cholesterol, and low-density lipoprotein (LDL)-cholesterol, were estimated in the serum of each participant before and after exercise training, as previously described [26–29]. An enzymatic (CHOD-PAP) colorimetric method [25], (GPO-PAP) method [25, 26], and a precipitant method [27, 28] were used to estimate the total cholesterol, triglyceride, and HDL cholesterol, respectively, of each subject. In addition, LDL cholesterol was estimated via the Friedewald formula (FF) [28], as shown below.

$$\{LDL - C = TC - HDL - C - (TG/5)\}$$

Dyslipidaemia was defined as the presence of one or more abnormal serum lipid concentrations.

Analysis of hs-CRP

The acute-phase reactant highly sensitive CRP (hs-CRP) was analysed via commercially available ELISA kits (IBL Inc., Cat. No. IB59126, USA) according to the manufacturers' instructions.

Sample size calculation

In this study, the power of the sample size was estimated by using the G $*$ Power program for Windows (version 3.1.9.7). A sample comprising 50 subjects was included in this study. Using the t test and Wilcoxon signed-rank test with a significance level of 0.05, the total sample of 50 achieves a power of 95%, with an effective size dz of 0.483, Df=46.75, critical t=1.68, and noncentrality -α=3.34.

Statistical analysis

All the values are expressed as the means±SDs via the SPSS package for statistical analysis (16.0 for Windows). Independent samples t tests (2-tailed) were used to compare the means of different parameters. Pearson's correlation test was performed to examine various correlations. $P<0.05$ was used to determine significant differences.

Results

Fifty-eight patients (female, 21; male, 29; mean age, 57.4±4.86 years) diagnosed with diabetes, with an average duration of diabetes of 7.08±4.0 years, were recruited for this study. The subjects were divided into two groups according to their level of glycated haemoglobin (HbA1c%): patients with prediabetes group 1 (HbA1c % ≤ 6.5, $n=25$) and the diabetes patients group 2 (HbA1c% ≥ 6.5, $n=25$). No difference was detected between groups for any of the outcomes listed ($p>0.05$). The demographics and descriptive characteristics of the recruited subjects are given in Table 1.

Daily nutrient intake was associated with variation in the total caloric, macronutrient and micronutrient intakes of both the prediabetic and diabetic groups. However, these parameters are situated within the recommended interval of RDIs, as shown in Table 2.

The variation in the recorded dietary parameters had no effect on BMI; diabetes markers, such as fasting blood sugar, glycosylated hemoglobin, and inflammatory hs-CRP; and lipid profile parameters, such as T-Cholest, TG, and LDL-C, in prediabetic and diabetic patients in the baseline period and after exercise for 6 months, as reported in Table 3.

Table 2 Dietary records of the subjects (means ± standard deviations)

Variable	Group 1 Pr-diabetes (HbA1c % ≤ 6.5)	Group 2 Diabetes(HbA1c % ≥ 6.5)	Reference Dietary Intake (RDI)
Kilocalorie	2740 ± 550	2520± 560	2300–3450
Carbohydrate(g)	452.5 (134.0)	462.5 (148.0)	400–500
Proteins (g)	105 ± 12.0	85 ± 5.0	70–110
Fats (g)	123 ± 13.5	127 ± 8.4	100–140
Carbohydrate (%)	58.5 ± 10.2	58.3 ± 6.1	45–65%
Proteins (%)	18.6 ± 2.8	15.6 ± 5.7	10–30%
Fats (%)	25.2 ± 2.7	29.4 ± 3.1	25–35%
Cholesterol (mg.d^{-1})	340 ± 6.3	346 ± 10.7	˂ 350
Vitamin C(mg.d^{-1})	53.7 ± 6.8	57.5 ± 11.4	40–70
Vitamin E (mg.d^{-1})	10.8 ± 3.5	18.7. ± 9.7	11–30
Vitamin A (ER)	1750 ± 257.0	2230 ± 186.0	900–3000
Folate (µg.d^{-1})	630 ± 85.0	710 ± 69.8	400–1000
Vitamin B12(µg.d^{-1})	5.8 ± 1.7	4.6 ± 2.5	2–6

The results revealed that 6 months of moderate aerobic training significantly reduced BMI, fasting blood sugar, glycosylated haemoglobin, hs-CRP, and lipid profile parameters, such as T-Cholest, TG, and LDL-C, in the patients with prediabetes ($P<0.05$) group 1 and those with diabetes group 2 ($P<0.01$). The total serum fasting insulin and HDL-C levels significantly increased after 6 months of moderate aerobic training (<0.005), as shown in Table 2. Moreover, the baseline VO_2max/kg significantly increased following 6 months of moderate aerobic training in the patients with prediabetes group 1 ($P<0.01$) and diabetes patients group 2 ($P<0.001$), as shown in Table 3.

Correlation coefficients between the independent variables under study were calculated, and there was a significant correlation between the reduction in BMI, hs-CRP, blood sugar, total cholesterol, TG, and LDL-C and the increase in HDL-C and fasting insulin towards HbA1c% in the prediabetes and diabetes patients (Table 4). In addition, significant associations were found between improved baseline VO_2max and plasma levels of HbA1c % diabetic parameters in prediabetes ($P<0.01$) and diabetes patients ($P<0.001$) (Table 4). In addition, correlation analysis revealed that the improved VO_2max following 6 months of moderate aerobic training was significantly correlated with hs-CRP, T-Cholest, TG, and LDL-C and negatively correlated with HDL-C in the prediabetes ($P<0.01$) and diabetes groups ($P<0.01$), as shown in Table (5).

Furthermore, the data revealed a significant correlation between hs-CRP levels and lipid profiles among prediabetes and diabetes patients. hs-CRP was positively correlated ($p=0.01$) with T-Cholest, TG, and LDL-C and negatively correlated with HDL-C, as shown in Table (6).

Discussions

The incidence of diabetes has increased globally and has become the major source of mortality and morbidity worldwide [29, 30]. In addition to medications and diet interventions, exercise is considered one of the most traditionally used modalities for the treatment of type 2 diabetes [30, 31], and changes in lifestyle can reduce the incidence of T2DM to 58% in both genders at high cardiovascular risk [32].

The application of physical exercise programs for more than 4 h/week improved cardiorespiratory fitness and muscle strength and significantly reduced the risk of diabetes even without weight loss [32–34]. Therefore, this study aimed to explore the influence of moderate-intensity aerobic exercise training for 6 months on glycemic control parameters, dyslipidaemia, and hs-CRP as cardiac risk predictors in patients with both prediabetes and type 2 diabetes.

Table 3 Mean, standard deviation (SD) and statistical comparison of the pretraining, 3-, and 6-month posttraining values of the studied variables on the basis of the level of glycated haemoglobin

Parameters	Group 1 Pr-diabetes (HbA1c % ≤ 6.5)			Group 2 Diabetes (HbA1c % ≥ 6.5)		
	Baseline	3 months	6 months	Baseline	3 months	6 months
VO_2max (ml/kg* min)	32.44 ± 4.22	39.5 ± 5.8*	48.3 ± 4.3**	35.4 ± 3.9	38.9 ± 4.5**	44.2 ± 2.7***
Fasting serum sugar (mg/dl)	113.3 ± 7.1	102.0 ± 7.7 *	86.12 ± 7.4 **	178.4 ± 9.7	172.6 ± 8.6 **	135.2 ± 20.6 ***
HbA1c %	4.96 ± 0.26	4.7 ± 0.23 *	4.58 ± 0.21 **	7.9 ± 0.97	7.4 ± 0.94 ***	6.3 ± 0.71 ***
Fasting serum insulin (mU/ml)	9.71 ± 1.47	11.4 ± 1.3*	12.3 ± 1.1 **	9.71 ± 1.5	11.4 ± 1.3 **	14.2 ± 1.7 ***
HOMA- IR	1.8 ± 0.32	1.65 ± 0.29*	1.4 ± 0.81**	3.5 ± 1.3	2.9 ± 1.5 **	1.85 ± 0.65 ***
hs CRP, (mg/l)	6.48 ± 1.53	6.1 ± 1.3*	5.1 ± 0.94 **	8.24 ± 1.6	7.52 ± 1.4 **	6.5 ± 1.1 ***
T-Cholesterol (mg/dl)	170.4 ± 9.2	166.7 ± 8.8*	156.15 ± 8.7**	193.6 ± 22.8	186.8 ± 21.5 **	161.3 ± 26.2 ***
TG (mg/dl)	126.3 ± 8.4	122.5 ± 8.0*	114.2 ± 8.0 **	142.2 ± 6.15	135.4 ± 5.7 **	119.3 ± 5.0 ***
HDL-C (mg/dl)	38.7 ± 5.4	45.6 ± 4.8*	75.1 ± 4.15 **	66.4 ± 22.4	72.6 ± 21.3 **	96.6 ± 18.5 ***
LDL-C (mg/dl)	112.4 ± 7.3	107 ± 6.9*	98.7 ± 4.6 **	122.8 ± 8.9	113.4 ± 6.8 **	99.6 ± 5.3 ***
BMI (kg/m2)	23.3 ± 1.52	22.5 ± 1.3 *	22.1 ± 1.2 **	24.3 ± 1.5	23.9 ± 1.7 **	21.7 ± 1.3 ***

The values are expressed as the means ± SDs; $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$. Significance was set at $p<0.05$. All comparisons of the data at 3 and 6 months were performed against the basal values. HDL-C = high-density lipoprotein cholesterol, LDL-C = low-density lipoprotein cholesterol

Table 4 Posttraining correlation analysis of BMI, VO_2max, hs-CRP, lipid profile and diabetes-related variables according to the level of glycated hemoglobin (*n* = 50)

Variables	Glycated Hemoglobin (HbA1c %)			
	Group 1 Prediabetes (HbA1c %; ≤ 6.5% (*n* = 25)		Group 2 Diabetes (HbA1c % ≥ 6.5% (*n* = 25)	
	R	(95% CI)	*R*	(95% CI)
VO_2max (ml/kg* min)	0.247**	96 (78–98)	0.523***	95 (86–98)
F.B. Sugar (mg/dl)	0.316 **	95 (73–98)	0.357 ***	91 (73–98)
F. insulin (mU/ml)	0.42 **	89 (56–100)	0.46 ***	98 (56–100)
HOMA-IR	0.63 * *	92 (75–100)	0.51 ***	96 (65–100)
Hs-CRP, (mg/l)	0.315 **	75 (65–100)	0.29 ***	71 (65–100)
BMI (kg\m2)	0.17 **	85 (66–100)	0.23 ***	91 (65–100)
Lipid Profile	0.31 **	84 (65–100)	0.35 ***	96 (75–100)
T-Cholest .(mg/dl)	0.35 **	97 (85–100)	0.13 ***	94 (85–100)
TG (mg/dl)	0.48 **	91 (75–100)	0. 52 ***	89 (75–100)
HDL-C(mg/dl)	0.58 **	90 (65–100)	0. 75 ***	95 (75–100)
LDL-C (mg/dl)				

Data are presented as coefficients (R) and 95% confidence intervals; ** denotes significance at < 0.01; *** denotes significance at < 0.001. All comparisons of the data at 3 and 6 months were performed against the basal values

Table 5 Posttraining correlation analysis of VO_2max (ml/kg* min) as a fitness score, the inflammatory Hs-CRP marker, and the lipid profile according to the level of glycated hemoglobin (*n* = 50)

Variables	Glycated Hemoglobin (HbA1c %)			
	Group 1 Prediabetes (HbA1c %; ≤ 6.5% (*n* = 25)		Group 2 Diabetes (HbA1c % ≥ 6.5% (*n* = 25)	
	VO_2max (ml/kg* min)		VO_2max (ml/kg* min)	
	R	(95% CI)	*R*	(95% CI)
Hs-CRP, (mg/l)	0.522 **	91 (76–95)	0.48 **	95 (83–98)
T-Cholest.(mg/dl)	0.255 **	95 (83–98)	0.47 **	97 (73–98)
TG(mg/dl)	0.89 **	92 (88–100)	0.75 **	98 (86–100)
LDL-C(mg/dl)	0.69**	88 (75–100)	0.89 **	85 (65–100)
HDl-C (mg/dl)	-0.75 **	75 (66–100)	-0.56**	93 (65–100)

Data are presented as coefficients (R) and 95% confidence intervals; * denotes significance at < 0.05; ** denotes significance at < 0.01. All comparisons of the data at 3 and 6 months were performed against the basal values

Table 6 Posttraining correlation analysis of hs-CRP with the lipid profile according to the level of glycated hemoglobin (*n* = 50)

Variables	Glycated Hemoglobin (HbA1c%)			
	Group 1 Prediabetes (HbA1c %; ≤ 6.5% (*n* = 25)		Group 2 Diabetes (HbA1c % ≥ 6.5% (*n* = 25)	
	hs-CRP		hs-CRP	
	R	(95% CI)	*R*	(95% CI)
T-Cholest.(mg/dl)	0.345 **	95 (73–98)	0.39 **	91 (73–98)
TG(mg/dl)	0.79 **	89 (56–100)	0.45 **	98 (56–100)
LDL-C(mg/dl)	0.59**	81 (65–100)	0.82 **	71 (65–100)
HDl-C (mg/dl)	-0.67 **	85 (66–100)	-0.46**	91 (65–100)

Data are presented as coefficients (R) and 95% confidence intervals; * denotes significance at < 0.05; ** denotes significance at < 0.01. All comparisons of the data at 3 and 6 months were performed against the basal values

Our results showed that participating in moderate aerobic training for six months significantly improved the levels of fasting insulin, which increased with a significant reduction in fasting blood sugar and glycosylated hemoglobin in prediabetes and diabetes subjects. This improvement in the diabetic control parameters was significantly (p=0.01) correlated with the reduction in BMI among prediabetic and diabetic subjects following moderate exercise training interventions. Our results are in line with those of several previous studies that concluded that 4 h/week of physical exercise significantly reduces diabetic risk factors [35] and that regular exercise training improved glycemic control parameters by increasing fat oxidation and subsequently reducing BMI [36–38]. Moreover, in a meta-analysis, aerobic training exercise for at least 8 weeks had a significant effect on HbA1c % values in individuals with T2DM [39]. Similar results from a meta-analysis concerning aerobic and resistance exercise established the positive effect of exercise on HbA1c% among diabetic subjects [40].

In our study, prediabetes subjects with a pretraining HbA1c % (≤6.5) with the same aerobic exercise for 6 months had significantly lower HbA1c % and fasting blood sugar levels than diabetes subjects with HbA1c % levels ≥ 6.5. The data revealed that the improvement in HbA1c % by exercise generally depends on pretraining glycemic levels. These findings suggest the potential use of exercise as a protective aid against the progression of diabetes, especially among prediabetes individuals (HbA1c % ≤ 6.5). The data are in accordance with those of others, who reported that diabetes mitigation following exercise or diet interventions is more common in subjects with lower HbA1c% levels and a shorter disease history [41]. Furthermore, exercise was suggested to have the same insulin activity as the increase in muscle capacity to capture circulating glucose as a result of decreasing intramuscular fat reserves following exercise training, which ultimately reduces circulating glucose levels [36]. In addition, the increased expression of the GLUT4 glucose transporter following exercise training in nondiabetics' and diabetes patients was reported to support the importance of exercise as a diabetic control [42, 43].

Previous investigations have reported that the functional capacity, estimated by peak oxygen consumption (VO_2max), is significantly reduced in DM patients [44–46]. Although the reduction in VO_2max could be ascribed to obesity, lack of physical activity, and various comorbidities, VO_2max remained reduced in DM patients [43, 44], even after adjustment for these variables. Thus, VO_2max represents an important independent predictor of outcome, particularly survival, under different conditions [45–48].

In our study, the peak baseline VO_2max significantly increased in patients with prediabetes and diabetes following participation in moderate aerobic training for six months. Previous studies have shown an increase in VO_2max in diabetic patients who exercised regularly for 20 weeks, whereas training programs with moderate to high intensities have shown greater VO_2max improvement, which predicts postintervention differences in HbA1c [48, 49].

In this study, correlation analysis revealed that the improved VO_2max following 6 months of moderate aerobic training was significantly correlated with hs-CRP, T-Cholest, TG, and LDL-C and negatively correlated with HDL-C in the prediabetes ($P < 0.01$) and diabets groups ($P < 0.01$).

After six months of moderate exercise, studies have shown that increased VO_2max is associated with significant reductions in hs-CRP levels. This suggests a reduction in systemic inflammation, which is crucial since inflammation is a known risk factor for cardiovascular diseases, particularly in individuals with type 2 diabetes. In addition, consistent with our results, other studies have indicated that patients whose VO_2max is improved also exhibit decreases in their hs-CRP levels, demonstrating the anti-inflammatory effects of consistent physical activity [50, 51].

Currently, exercise interventions with different intensities are the best nonpharmacological strategies for the prevention or attenuation of diabetic dyslipidaemia [42, 43], and it is also estimated that aerobic exercise training improves dyslipidaemia via a reduction in the levels of total cholesterol (T-Chol) and triglycerides (TGs), as previously reported in the literature (TGs) [52].

In this study, 6 months of moderate aerobic training resulted in a significant decrease in the levels of T-Chol, TGs, and LDL-C combined with a significant increase in the HDL-C levels of prediabetes subjects compared with those of diabetes subjects with higher HbA1c % levels (≥6.5). The data of our study are in accordance with those of studies reporting improvements in fasting blood lipid profiles following long-term exercise interventions [53, 54]. The exercise program also significantly improved many diabetes-related parameters, including glycemic control, HbA1c%, and body composition, collectively with attenuated exogenous insulin requirements [35]. Furthermore, a previous study concluded that exercise training of both low and moderate intensity promoted a clear reduction in the lipid profile [55].

In this study, 6 months of moderate aerobic training regulated the lipid profile of diabetic subjects, which could be explained by the activation of the AMPK enzyme, which increases fatty acid oxidation; by a reduction in cholesterol synthesis, lipogenesis and lipolysis; by the regulation of insulin secretion from pancreatic islets; or by increased levels of glucose transporter proteins and mRNAs [56, 57]. The improvement in the lipid profile reported in this study could also be related to exercise activation of lipolytic activity, which promotes a decrease in TG and LDL and an increase in HDL concentration, or to the activation of peripheral enzymes, such as lipoprotein lipase (LPL), lecithin-cholesterol acyltransferase (LCAT) and hepatic lipase (HL) [58, 59].

Type 2 diabetes is associated with increased levels of many inflammatory biological markers, depending on the level of glycemic control, HbA1c%, lipid profile, degree of insulin resistance, and body composition, in different human populations of both sexes [60, 61]. Among these markers, high-sensitivity CRP (hs-CRP) was found to be the gold standard marker of innate immunity associated with increased levels of HbA1c% in individuals with diabetes [62, 63].

In the present study, we observed that type 2 diabetes patients with higher glycemic control levels (HbA1c% ≤ 6.5%) had higher hs-CRP levels than did subjects with lower HbA1c% values (≥6.5%). These results are consistent with other studies that reported higher levels of hs-CRP among hypertensive patients with type 2 diabetes [64] and that significant increases in the levels of CRP were also linked with higher rates of cardiovascular mortality among diabetic patients [65, 66]. Thus, hs-CRP and CRP are significant markers that can predict the severity of diabetes [66].

The data of the present study revealed a significant correlation between hs-CRP levels, glycemic control, and lipid profiles in prediabetes and diabets subjects. The levels of hs-CRP correlated positively (p=0.01) with higher levels of HbAc1, T-cholesterol, TG, and LDL-C and negatively (p=0.01) with lower levels of HDL-C. Like our results, diabetic patients with higher HbAc1% levels [67–69] presented a significant increase in lipid profile parameters, especially LDL-C. The increase in lipids among diabetic patients, such as those with T2DM, was shown to activate a series of local inflammatory events due to increased levels of cellular hs-CRP, which may be related to obesity and a low grade of systemic inflammation in DM patients [70].

Many studies have reported that the reduction in inflammation and hs-CRP levels is significantly related to the physical activity status of diabetic patients [70, 71], whereas aerobic fitness is generally inversely associated with CRP levels [72, 73], and exercise aerobic training has been reported to decrease the levels of CRP and hs-CRP inflammatory markers in individuals with type 2 diabetes [71].

In this study, we showed that 6 months of aerobic training significantly improved all glycemic control parameters in both prediabetes and diabetes patients. The data revealed that in prediabetic patients, the HbA1c % level was lower than 6.5 (4.96 was reduced to 4.56) and that the fasting serum sugar level (113–86.1) significantly improved, with HbA1c % levels greater than 6.5 (7.9–6.3) and fasting serum sugar levels (172.6–135.2).

In addition, hs-CRP significantly improved in prediabetes and diabetes patients following participation in an aerobic training exercise intervention for six months. The data obtained showed that hs-CRP was significantly positively correlated with a decrease in (p=0.01) HbA1c, T-Cholest, TG, and LDL and negatively correlated (p=0.01) with higher HDL-C concentrations in prediabetes and diabetes patients. The data agree with those of others, who reported a significant reduction in hs-CRP, CRP, and other inflammatory markers in type 2 diabetes patients [74–76] and that the improvements may be related to a reduction in body composition following exercise training. Our results also matched those of others [71], who reported that a combined programme of aerobic and resistance exercise for one year could significantly decrease CRP, with percentages of 28% and 54%, respectively, in individuals with type 2 diabetes.

In addition, in this study, the improved VO_2max following 6 months of moderate aerobic training significantly correlated with lipid profile parameters, such as T-Cholest, TG, and LDL-C, and negatively correlated with HDL-C in the prediabetes (P<0.01) and diabetes groups (P<0.01). An improved VO_2max has been linked to better lipid profiles, including reductions in LDL cholesterol and increases in HDL cholesterol. This relationship is crucial for managing cardiovascular risk, which is elevated in diabetic populations. Exercise appears to improve endothelial function and insulin sensitivity, which collectively contribute to better cardiovascular health [76–79].

Finally, these findings highlight the importance of maintaining or improving cardiorespiratory fitness through regular moderate exercise as a nonpharmacological strategy to reduce inflammation and improve lipid metabolism in prediabetic and diabetic individuals.

Conclusions

In conclusion, moderate aerobic training for 6 months favourably affects glycemic parameters, lipid profiles, and inflammatory hs-CRP indicators and improves VO_2max, an indicator of physical fitness, in prediabetes and diabetes patients. In addition, both HbA1c % and hs-CRP are vital indicators in the management of prediabetes and diabetes patients. HbA1c% is indispensable for monitoring long-term glucose control and predicting dyslipidaemia, whereas hs-CRP serves as a crucial marker of inflammation, offering insights into cardiovascular risk. Together, these markers help healthcare providers assess the multifaceted risks associated with diabetes, enabling a more targeted approach to prevention and treatment.

The data obtained also suggest the positive effect of moderate exercise training as a protective modulator of cardiovascular disorders, including the dyslipidaemic profile, glycaemic control, and hs-CRP inflammatory markers, in prediabetes and T2DM patients. Thus, regular exercise, owing to its anti-inflammatory effects and ability to improve cardiorespiratory fitness, lipid profiles, blood glucose levels, and insulin resistance, may help reduce the severity of cardiovascular diseases in prediabetes and T2DM patients as well as healthy controls.

Acknowledgements
The authors are grateful to the Researchers Supporting Project number (RSP2024R382), King Saud University, Riyadh, Saudi Arabia, for funding this research.

Author contributions
A.H.A. S.A.G. and A.I. proposed the study's research ideas, conception, and design. A.H.A. and S.A.G. completed practical work and collected the data. A.H.A., S.A.G. and A.I. analysed and interpreted the data. A.H.A. S.A.G. and A.I. prepared the manuscript's initial drafts. A.H.A. S.A.G. and A.I. reviewed the manuscript critically for its intellectual content. All authors reviewed, understood, and approved the manuscript's final version to be submitted or published.

Funding
This study was funded by the Researchers Supporting Project number (RSP2024R382), King Saud University, Riyadh, Saudi Arabia. The funding body played no role in the study design, manuscript writing, or decision to submit the manuscript for publication.

Data availability
The analysed data used to support the findings of this study are included within the article.

Declarations

Ethics approval and consent to participate
The Ethics Subcommittee at King Saud University, Riyadh, Saudi Arabia, reviewed and approved this study, recorded under file ID: RRC-2014-010. Additionally, the study was registered online with the ClinicalTrials.gov Protocol Registration and Results System (PRS) and assigned the identifier ID NCT06246435 dated 30/01/2024. This study followed all the research procedures per the ethical standards of the local Institutional Ethics Review Board and with the Helsinki Declaration of 2010. A signed informed consent was obtained from each participant as a proof of consent to participate before the start of this study.

Consent to publish
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Rehabilitation Sciences, College of Applied Medical Sciences, King Saud University, P.O. Box 10219, Riyadh 11433, Saudi Arabia

Received: 21 January 2024 / Accepted: 26 September 2024
Published online: 09 October 2024

References

1. Mukhamedova M, Orziev DZ, Uzokov JK, Abdullaev AX. Optimization of antiplatelet therapy in patients with coronary artery disease and type 2 diabetes mellitus after percutaneous coronary interventions. Eur J Cardiovasc Nurs. 2023;22(Supplement1):zvad064–111.
2. Farag YM, Gaballa MR. Diabesity: an overview of a rising epidemic. Nephrol Dial Transpl. 2011;26(1):28–35.
3. Tao B, et al. Estimating the cost of type 1 diabetes in the U.S.: a propensity score matching method. PLoS ONE. 2010;5(7):e11501.
4. World-Health-Organization. Saudi Arabia: health profile, 2012, World-Health-Organization May 2012.
5. Sultan A, Thuan JF, Avignon A. Primary prevention of cardiovascular events and type 2 diabetes: should we prioritize our interventions? Diabetes Metab. 2006;32:559–67.
6. Arshag D, Mooradian. Dyslipidaemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metabolism. 2009;5(3):150–59.
7. Ayaz KM, Ravindra M, Vivek R, Joshi P, Gopalakrishna, Bhat. A study on APO B100/APO A-I ratio in uncontrolled type 2 diabetes mellitus. Int J Appl Biol Pharma Tech. 2011;2(1):379–84.
8. Asegaonkar SB, Marathe A, Tekade ML, Cherekar L, Bavikar J, Bardapurkar J, Ajay R. High-sensitivity C-reactive protein: a novel cardiovascular risk predictor in type 2 diabetics with normal lipid profile. J Diabetes Complications. 2011 Nov-Dec;25(6):368–70. 10.1016/j. jdi acomp.2011.10.001. Epub 2011 Nov 4.
9. Selvin E, Marinopoulos S, Berkenblit G, Rami T, Brancati FL, Powe NR. Meta-analysis: glycosylated hemoglobin and cardiovascular disease in diabetes mellitus. Ann Intern Med. 2004;14:421–31.
10. Khaw KT, Wareham N, Bingham S, Luben R, Welch A, Day N. Association of hemoglobin A1c with cardiovascular disease and mortality in adults; the European prospective investigation into cancer in Norfolk. Ann Intern Med. 2004;141:413–20.
11. Hu FB. Sedentary lifestyle and risk of obesity and type 2 diabetes. Lipids. 2003;38(2):103–8.
12. Alghadir AH, Gabr SA, Iqbal ZA. Television watching, diet, and body mass index of school children in Saudi Arabia. Pediatr Int. 2016;58(4):290–4.
13. Alghadir AH, Gabr SA, Iqbal ZA. Effects of sitting time associated with media consumption on physical activity patterns and daily energy expenditure of Saudi school students. J Phys Ther Sci. 2015;27(9):2807–12. Epub 2015/10/28.
14. Carvalhal MM, Padez MC, Moreira PA, Rosado VM. Overweight and obesity related to activities in Portuguese children, 7–9 years. Eur J Public Health. 2007;17(1):42–6.
15. Aly FA, Alghadir AH, Gabr SA. Adiponectin response to supervised aerobic training in type II. Diabet Patients Asian Biomed. 2014;8(5):597–602.
16. Li G, Zhang P, Wang J, Gregg EW, Yang W, Gong Q, et al. The long-term effect of lifestyle interventions to prevent diabetes in the China Da Qing diabetes Prevention Study: a 20-year follow-up study. Lancet. 2008;371(9626):1783–9.
17. Lindström J, Ilanne-Parikka P, Peltonen M, Aunola S, Eriksson JG, Hemiö K, Diabetes Prevention Study Group, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish diabetes Prevention Study. Lancet. 2006;368(9548):1673–9.
18. Hayashino Y, Jackson JL, Fukumori N, Nakamura F, Fukuhara S. Effects of supervised exercise on lipid profiles and blood pressure control in people with type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. Diabetes Res Clin Pract. 2012;98(3):349–60. https://doi.org/10.1016/j.diabres.2012.10.004. Epub 2012 Oct 29.
19. American Diabetes Association. Standards of medical care in diabetes. Diabetes Care. 2009;32:S13–61.
20. Aly FA, Alghadir AH, Gabr SA. Adiponectin response to supervised aerobic training in type II diabetic patients. Asian Biomed. 2014;8(5):597–602.
21. Alghadir AH, Gabr SA, Anwer S, Al-Eisa E. Fatigue and oxidative stress response to physical activity in type 2 diabetic patients. Int J Diabetes Developing Ctries. 2016;36:59–64.
22. Otten JJ, Hellwig JP, Meyers LD. Dietary reference intakes: the essential guide to nutrient requirements. Washington, DC: National Academy; 2006.
23. Karvonen M, Kentala K, Mustala O. The effects of training heart rate: a longitudinal study. Ann Med Exp Biol Fenn. 1957;35:307–15.
24. Skinner JS, Wilmore KM, Krasnoff JB, Jaskolski A, Jaskolska A, Gagnon J, Province MA, Leon AS, Rao DC, Wilmore JH. Bouchard C.Adaptation to a standardized training program and changes in fitness in a large, heterogeneous population: the HERITAGE Family Study. Med Sci Sports Exerc. 2000;32:157–61.
25. Hefnawy MA, Fadlallah SA, El-Sherif RM, Medany SS. Competition between enzymatic and nonenzymatic electrochemical determination of cholesterol. J Electroanal Chem. 2023;930:117169.
26. Jalalvand AR. A novel amperometric biosensor for multienzymatic biosensing of triglycerides. Sens Int. 2023;4:100206.
27. Kalfaoglu ME. Could serum uric acid to HDL cholesterol ratio predict sacroiliitis? PLoS ONE. 2023;18(10):e0289624.
28. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of LDL-cholesterol. Clin Chem. 1972;18(6):499–15.
29. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, et al. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. Lancet. 2011;378(9785):31–40.
30. Zanuso S, Jimenez A, Pugliese G, Corigliano G, Balducci S. Exercise for the management of type 2 diabetes: a review of the evidence. Acta Diabetol. 2010;47:15–22.
31. Kanaley JA, Colberg SR, Corcoran MH, Malin SK, Rodriguez NR, Crespo CJ, Kirwan JP, Zierath JR. Exercise/physical activity in individuals with type 2 diabetes: a consensus statement from the American College of Sports Medicine. Med Sci Sports Exerc. 2022;54(2):353.

32. Tuomilehto J, Lindström J, Eriksson JG, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med. 2001;344(18):1343–50.
33. Kumar AS, Maiya AG, Shastry BA, Vaishali K, Ravishankar N, Hazari A, Gundmi S, Jadhav R. Exercise and insulin resistance in type 2 diabetes mellitus: a systematic review and meta-analysis. Annals Phys Rehabilitation Med. 2019;62(2):98–103.
34. Rijal A, Adhikari TB, Dhakal S, Maagaard M, Piri R, Nielsen EE, Neupane D, Jakobsen JC, Olsen MH. Effect of exercise on functional capacity and body weight for people with hypertension, type 2 diabetes, or cardiovascular disease: a systematic review with meta-analysis and trial sequential analysis. BMC Sports Sci Med Rehabilitation. 2024;16(1):38.
35. De Feyter HM, Praet SF, van den Broek, et al. Exercise training improves glycemic control in long-standing insulin-treated type 2 diabetic patients. Diabetes Care. 2007;30(10):2511–3.
36. Sigal RJ, Kenny GP, Boulé NG, et al. Effects of aerobic training, resistance training, or both on glycaemic control in type 2 diabetes: a randomized trial. Ann Intern Med. 2007;147(6):357–69.
37. Ross R, Janssen I, Dawson J, et al. Exercise-induced reduction in obesity and insulin resistance in women: a randomized controlled trial. Obes Res. 2004;12(5):789–98.
38. Lee S, Kuk JL, Davidson LE, et al. Exercise without weight loss is an effective strategy for obesity reduction in obese individuals with and without type 2 diabetes. J Appl Physiol. 2005;99(3):1220–5.
39. Boulè NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a metaanalysis of controlled clinical trials. JAMA. 2001;286:1218–27.
40. Boulè NG, Kenny GP, Hadda E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in type 2 diabetes mellitus. Diabetologia. 2003;46:1071–81.
41. Gregg EW, Chen H, Wagenknecht LE, Look AHEAD Research Group, et al. Association of an intensive lifestyle intervention with remission of type 2 diabetes. JAMA. 2012;308(23):2489–96.
42. Christ-Roberts CY, Pratipanawatr T, Pratipanawatr W, et al. Exercise training increases glycogen synthase activity and GLUT4 expression but not insulin signalling in overweight nondiabetic and type 2 diabetic subjects. Metabolism. 2004;53(9):1233–42.
43. Wang Y, Simar D, Fiatarone Singh MA. Adaptations to exercise training within skeletal muscle in adults with type 2 diabetes or impaired glucose tolerance: a systematic review. Diabetes Metab Res Rev. 2009;25(1):13–40.
44. Vukomanovic V, Suzic-Lazic J, Celic V, Cuspidi C, Petrovic T, Grassi G, Tadic M. The relationship between functional capacity and left ventricular strain in patients with uncomplicated type 2 diabetes. J Hypertens. 2019;37(9):1871–6.
45. Röhling M, Pesta D, Markgraf DF, Strassburger K, Knebel B, Burkart V, Szendroedi J, Müssig K, Roden M. GDS study group. Metabolic determinants of impaired pulmonary function in patients with newly diagnosed type 2 diabetes mellitus. Exp Clin Endocrinol Diabetes. 2018;126(9):584–9.
46. Roberts TJ, Burns AT, MacIsaac RJ, MacIsaac AI, Prior DL, La Gerche A. Exercise capacity in diabetes mellitus is predicted by activity status and cardiac size rather than cardiac function: a case control study. Cardiovasc Diabetol. 2018;17(1):44.
47. Kokkinos P, Manolis A, Pittaras A, Doumas M, Giannelou A, Panagiotakos DB, Faselis C, Narayan P, Singh S, Myers J. Exercise capacity and mortality in hypertensive men with and without addition. Hypertension. 2009;53:494–9.
48. Swank AM, Horton J, Fleg JL, Fonarow GC, Keteyian S, Goldberg L, Wolfel G, Handberg EM, Bensimhon D, Illiou MC, Vest M, Ewald G, Blackburn G, Leifer E, Cooper L, Kraus WE, and for the HF-ACTION Investigators. (2012) Modest increase in peak VO_2 is related to better clinical outcomes in chronic heart failure patients: results from heart failurea controlled trial to investigate outcomes of exercise training. Circ Heart Fail,2012; 5(5):579–585.
49. Boulé NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Metaanalysis of the effect of structured exercise training on cardiorespiratory fitness in type 2 diabetes mellitus. Diabetologia. 2003;46(8):1071–81.
50. Fujimoto N, Moriwaki K, Takeuchi T, Sawai T, Sato Y, Kumagai N, Masuda J, Nakamori S, Ito M, Dohi K. Effects of sitagliptin on exercise capacity and hemodynamics in patients with type 2 diabetes mellitus and coronary artery disease. Heart Vessel. 2020;35(5):605–13.
51. Tadic M, Grassi G, Cuspidi C. Cardiorespiratory fitness in patients with type 2 diabetes: A missing piece of the puzzle. Heart Fail Rev. 2021;26(2):301–308. https://doi.org/10.1007/s10741-020-10015-3. PMID: 32803640.
52. Teixeira de Lemos E, Reis F, Baptista S, et al. Exercise training decreases pro inflammatory profile in Zucker diabetic (type 2) fatty rats. Nutrition. 2009;25(3):330–9.
53. Berg A, Frey I, Baumstark MW, Halle M, Keul J. Physical activity and lipoprotein lipid disorders. Sports Med. 1994;17(1):6–21.
54. Pi-Sunyer X, Blackburn G, Brancati FL, et al. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. Diabetes Care. 2007;30:1374–83.
55. Krook A, Holm I, Pettersson S, Wallberg-Henriksson H. Reduction of risk factors following lifestyle modification programme in subjects with type 2 (noninsulin dependent) diabetes mellitus. Clin Physiol Funct Imaging. 2003;23:21–30.
56. Lira FS, Yamashita AS, Uchida MC, et al. Low and moderate, rather than high intensity strength exercise induces benefits regarding plasma lipid profile. Diabetol Metab Syndr. 2010;2:31.
57. Winder WW, Hardie DG. Inactivation of acetyl-CoA carboxylase and activation of AMP activated protein kinase in muscle during exercise. Am J Physiol. 1996;270(2 Pt 1):E299–304.
58. Berg AH, Combs TP, Scherer PE. ACRP30/adiponectin: an adipokine regulating glucose and lipid metabolism. Trends Endocrinol Metab. 2002;13(2):84–9.
59. Goldhammer E, Ben-Sira D, Zaid G, et al. Paraoxonase activity following exercise-based cardiac rehabilitation program. J Cardiopulm Rehabil Prev. 2007;27(3):151–4.
60. Romani R, De Medio GE, di Tullio S, et al. Modulation of paraoxonase 1 and 3 expression after moderate exercise training in the rat. J Lipid Res. 2009;50(10):2036–45.
61. Duncan B.B., Schmidt M.I., Pankow J.S., et al. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabetes. 2003;52:1799–805.
62. Spranger J, Kroke A, Mohlig M, et al. Inflammatory cytokines and the risk to develop type 2 diabetes: results of the prospective population-based European prospective investigation into Cancer and Nutrition (EPIC)-Potsdam Study. Diabetes. 2003;52:812–7.
63. Martha RM, Fernando GR. Increased levels of CRP in Noncontrolled Type II diabetic subjects. J Diabetes Complicat. 1999;13:211–5.
64. Pradhan AD, Manson JE, Rifai N, Burning JE, Ridker PM. C-reactive protein, interleukin 6 and risk development type 2 diabetes mellitus. JAMA. 2005;286:327–34.
65. Luciana ML, Maria das GC, Anna LS, Adriano de PS, Ana PF, Bethania AN, et al. High sensitivity C-reactive protein in subjects with type diabetes mellitus and/or high blood pressure. J Arg Bras Endocrinol Meta. 2007;51:6.
66. Pfutzner A, Forst T. High-sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. Diabetes Technol Ther. 2006;8(1):28–36.
67. Chiriboga DE, Ma Y, Li W, et al. Seasonal and gender variation of the high sensitivity C-Reactive protein in healthy adults: a Longitudina study. Clin Chem. 2009;55:313–21.
68. Wang X, Bao W, Liu J, et al. Inflammatory markers and risk of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2013;36(2013):166–75.
69. Graham I. European guidelines on cardiovascular disease prevention in clinical practice: executive summary. Atherosclerosis. 2007;194:1–45.
70. Kahn SE, Zinman B, Haffner SM, et al. Obesity is a major determinant of the association of C-reactive protein levels and the metabolic syndrome in type 2 diabetes. Diabetes. 2006;55:2357–64.
71. Balducci S, Zanuso S, Nicolucci A, et al. The 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;20:608–17.
72. Aronson D, Sheikh-Ahmad M, AvizoharO, et al. C-Reactive protein is inversely related to physical fitness in middle-agedsubjects. Atherosclerosis. 2004;176:173–9.
73. McGavock JM, Mandic S, Vonder Muhll I, et al. Low cardiorespiratory fitness is Associated with elevated C-Reactive ProteinLevels in women with Type2 diabetes. Diabetes Care. 2004;27(2):320–5.
74. Stewart LK, Earnest CP, Blair SN, Church TS. Effects of different doses of physical activity on C - reactive protein among women. Med Sci Sports Exerc. 2010;42(4):701–7.
75. Pezhman A, Mohsen T, Akbar AA, Javad A. Serum C-reactive protein and glycosylated hemoglobin in response to aerobic training in diabetic patients. Int J Biosci. 2012;2(8):115–9.
76. Vancea DM, Vancea JN, Pires MI, Reis MA, Moura RB, Dib SA. Effect of frequency of physical exercise on glycemic control and body composition in type 2 diabetic patients. Arq Bras Cardiol. 2009;92(1):23–30.

77. Buzdagli Y, Tekin A, Eyipinar CD, Öget F, Siktar E. The effect of different types of exercise on blood lipid profiles: a meta-analysis of randomized controlled studies. Sci Sports. 2022;37(8):675–87.
78. Martins RA, Neves AP, Coelho-Silva MJ, Veríssimo MT, Teixeira AM. The effect of aerobic versus strength-based training on high-sensitivity C-reactive protein in older adults. Eur J Appl Physiol. 2010;110(1):161–9. https://doi.org/10.1007/s00421-010-1488-5.
79. Abdi H, Bolboli L, Afroundeh R. The effect of 6 weeks of intense interval training on lipid profile, body composition indices and VO_2max in overweight male smokers. J Appl Health Stud Sport Physiol. 2023;10(2):81–92.

Publisher's note

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