

## Original Article



# The effects of personalized sprint interval training and combined aerobic endurance and resistance training on insulin resistance and glycated hemoglobin in women with type 2 diabetes

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## Abstract

**Background and aims:** Exercise training is a well-established therapeutic tool for treating type 2 diabetes. The purpose of this study is to examine the beneficial effects of personalized sprint interval training (SIT) and combined aerobic endurance and resistance training (Com) on insulin resistance and glycated hemoglobin A1c (HbA1c) concentration in women with type 2 diabetes.

**Methods:** Fifty-two overweight female type 2 diabetic patients (age 45-60 years and body mass index [BMI] > 30) with HbA1c value of 6.5% or higher and fasting blood glucose (FBG)  $\geq$  126 mg/dL (7.0 mmol/L) were selected. Participants were recruited from patients filed in the outpatient department of Shahrekord Hospital (Shahrekord, Iran) in 2016. The participants were assigned to SIT (n=17), Com (n=17), and control groups (n=18) according to HbA1c levels. The exercises included 10 weeks of Com and SIT.

**Results:** HbA1c concentrations decreased significantly in SIT ( $P=0.002$ ) and Com ( $P=0.006$ ) groups. The dependent *t*-test revealed that differences were significant for the FBG in the SIT groups ( $P<0.001$ ). Serum insulin levels showed significant increases in the SIT ( $P<0.001$ ) and Com ( $P<0.001$ ) groups. Data showed significant differences in homeostasis model assessment-estimated insulin resistance (HOMA-IR) in SIT ( $P<0.001$ ) and Com ( $P<0.001$ ) groups. The analysis of covariance (ANCOVA) test showed significant differences in serum insulin ( $F=3.622$ ,  $P=0.02$ ) and HOMA-IR ( $F=5.511$ ,  $P=0.0001$ ) levels and no significant difference in HbA1c ( $F=0.597$ ,  $P=0.556$ ) and FBG concentrations ( $F=1.853$ ,  $P=0.171$ ).

**Conclusion:** Results highlight that individualized exercise training, independent of the mode of training, is effective in improving glycemic control in overweight patients with type 2 diabetes.

**Keywords:** Personalized SIT, Combined training, Resistance training, HbA1c, Diabetes

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## Introduction

Type 2 diabetes (T2D) as a global health issue is related to various severe medical problems such as cardiovascular disease (CVD), neuropathy, retinopathy, and kidney disease (1). While there is a lot of scientific evidence to support that exercise training interventions such as resistance and aerobic training or combined aerobic and resistance exercises within the same exercise session could improve glycemic index compared to sedentary individuals, comparatively little information is available to determine the optimum frequency, intensity, time, or type of exercise (2-5). Traditional exercise training is difficult to sustain due to lack of time (6). The manipulation of variables following exercise training has created different types of training. High-intensity interval training (HIIT) which is typically defined as exercise at 85%-100% maximum

heart rate (MHR) (7) has potential to improve glycemic control. There seems to be accumulating evidence that glycemic control is improved by HIIT in type 2 diabetic individuals (8, 9).

It has been shown that 15%–20% of patients with type 2 diabetes fail to improve their glucose homeostasis following exercise training (10). Some studies demonstrated that despite using homogeneous populations, there were heterogeneous responses to exercise program (11). Recently, it has been demonstrated that 10%–20% of people are nonresponders to exercise programs, meaning that some exercise training protocol may not have beneficial effects on metabolic syndromes (11). The existence of nonresponders to exercise program demonstrates the need for an individualized exercise program as personalized medicine for the maintenance of

normal glucose homeostasis. Buford et al concluded that tailored exercise strategies must be considered in exercise interventions (12). In addition, because of the prevalence of adverse responses to regular exercise training, exercise prescription should be personalized (13).

American Diabetes Association (ADA) defined partial remission as sub-diabetic hyperglycemia (fasting plasma glucose of 100-125 mg/dL and HbA1c of 6.5%) of at least 1 year duration in the absence of active pharmacologic therapies (14). Numerous studies that focused on exercise interventions for type 2 diabetic patients utilized standard-based exercise programs and did not address the issue of remission and improvement in overall glycemic control typically observed in type 2 diabetic patients (15-17). It seems that even the exercise guidelines recommended by ADA could not improve glycemic status to prediabetic and normal levels (18). On the other hand, even HIIT which has better effects on diabetic patient fails to change glycemic control and improve it to normal levels (19). Because of complexity and variability in physiological and molecular responses to various exercise treatments, we considered evaluating sprint interval training (SIT) because it induces more robust fitness adaptations compared to moderate-intensity aerobic training (20). Secondly, we hypothesized that both SIT and combined aerobic and resistance training would be associated with metabolic/physiological parameters, body composition, and physical fitness benefits compared to the control group.

## Objectives

In the present study, the patients completed one of two

different personalized training regimes: SIT or Com. We hypothesized that the two different training regimes would produce beneficial effects in diabetic patients. Therefore, the purpose of this study is to examine the effects of personalized SIT and Com on insulin resistance and HbA1c concentration in diabetic female patients.

## Materials and Methods

### Experimental Design

The experimental design consisted of familiarization period (2 weeks), baseline testing, and an 8-week exercise training intervention. This program was done three times a week for 45 minutes per session. This study was a quasi-experimental research with pre-test and post-test design. Purposive sampling with random assignment was used. Participants were randomly assigned to the three groups following pre-testing.

### Patients and Methods

This study was a single-blind randomized clinical trial conducted in Shahrekord University (2016), on the basis of the CONSORT Statement (Figure 1). Participants were recruited from patients filed in the outpatient department of Shahrekord Hospital (Shahrekord, Iran) in 2016. Among 150 patients screened, 52 overweight female type 2 diabetic patients (age: 45-60 years, body mass index [BMI] > 25) with an HbA1c value of 6.5% or above and fasting blood glucose (FBG)  $\geq$  126 mg/dL (7.0 mmol/L) were selected. A total of 27 subjects were treated with oral drugs (metformin and Glibenclamide), 20 were treated with insulin injections, and 5 were treated

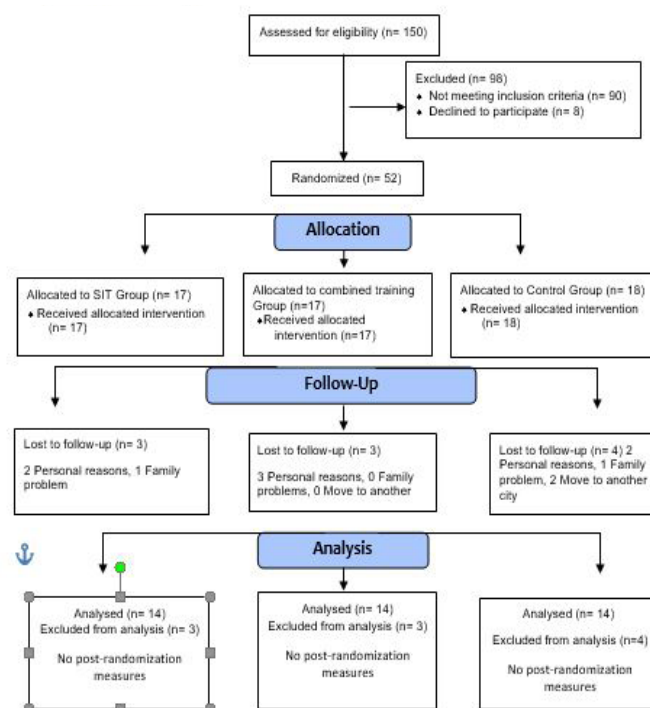


Figure 1. CONSORT 2010 Flow Diagram.

with combination therapy of insulin injection and oral drugs. The main criteria for exclusion were BMI < 25, age >60 years, having uncontrolled high blood pressure, severe CVDs or cancer. In addition, in accordance with previous studies (21-23), a sample size of 10 to 20 participants could clinically provide a statistical power of 80% for finding the effect of SIT protocol versus combined training regimes and a potential difference of 2% following a 10-week exercise training program. Based on the power and sample size calculation, 17 subjects were determined to be included per group based on a predicted dropout rate of 20% in this study.

Of 150 recruited participants, 54 subjects met the inclusion criteria (Figure 1). Eligible participants were informed about study program, the possible risks, and benefits involved in the trial. Participants were assured that all answers would be kept strictly confidential.

The block randomization method (6 blocks) was conducted by a research assistant who was not involved in this research using a computer-generated random number sequence. The participants were assigned to three different groups (SIT group (n = 17), the A+R group (n = 17), or the control group (n = 18)) according to HbA1c level. Sequential treatment allocations were enclosed in numbered, opaque, sealed envelopes, and distributed by the research assistant to the groups after the baseline testing (Figure 1).

After baseline assessments, the participants were assigned to SIT group (n = 17, age: 55.35±5.94 years, height: 162.93±67.97 cm, body mass: 73.06±21.62 kg, BMI: 29.57±2.77 kg.m<sup>-2</sup>, HbA1c: 9.64±1.08 %, FBG: 210.07±32.90 mg/dL), Com group (n = 17, age: 54.14±5.43 years, height: 160.57±4.98 cm, body mass: 76.30±9.58 kg, BMI: 30.57±2.97 kg.m<sup>-2</sup>, HbA1c: 9.49±0.86 %, FBG: 214.64±27.67 mg/dL), and control group (n = 18, age: 55.71±6.40 years, height: 156.42±12.82 cm, body mass: 71.44±13.20 kg, BMI: 29.70±4.17 kg.m<sup>-2</sup>, HbA1c: 9.10±0.51 %, FBG: 200.86±46.88 mg/dL) according to HbA1c levels. The inclusion criteria were being sedentary and not having exercised for more than 20 minutes a week over the past 6 months. The subjects were familiarized with study procedures and were informed about the possible risks and benefits involved in this study both verbally and in writing. They were assured that all answers would be

kept strictly confidential. Patients were asked to sign an informed consent form.

Patients received no dietary intervention, but they were instructed not to change their dietary habits during the study. In order to minimize diet-induced variability in glycemic indexes and other tests, they were instructed to consume the same dietary intake for two days before pretest and posttest.

During the experimental period, 10 patients dropped out of the study (3 in the combined training group, 3 in the SIT training group, and 4 in the control group) due to illness and failure to follow up.

Forty-two females with stable type 2 diabetes, all free of exercise limiting or diabetes-related complications such as musculoskeletal impairment, vascular disease or orthopedic limitations that could cause interference effects on their participation in the exercise program or laboratory test results, were eligible to participate in this study and enroll in a 30-session rehabilitation program. Body mass, BMI, body fat, and waist circumference (WC) are presented in Table 1.

### Exercise training protocols

The two different exercise interventions included 10 weeks of either combined (resistance plus aerobic) training or SIT.

Each combined training session consisted of 10 minutes of general warm-up (50% HRR) and 50 minutes of exercise training, and 10 minutes of cooling down (40% HRR). All participants attended a familiarization session for becoming familiar with training procedures, intensity, and equipment.

In weeks 1–2, aerobic training was performed at 60% heart rate reserve (HRR) calculated by Karvonen formula (24) (exercise heart rate = % 60 (MHR – resting heart rate) + resting heart rate) for 20 minutes on a cycling ergometer, three times a week. During weeks 3–10, the intensity increased by 10 % HRR. The aerobic training was personalized by increments, when the subjects could complete exercise while maintaining target heart rate, the time was increased by 10 %.

Resistance training consisted of exercising twice a week for 10 weeks. During weeks 1–2, resistance training was performed at 15-RM calculated by the Brzycki equation [1-RM = Weight ÷ (1.0278 – (0.0278 × number of

**Table 1.** Exercise training interventions

Week (No)	Resistance training program					Aerobic endurance training				SIT	
	Set	Repetition (Number)	Rest between (min)	weight	Frequency (days/week)	Duration (min)	Intensity (MHR %)	Frequency (day/week)	Duration (second)	Intensity (MHR %)	Frequency (day/week)
1-2	1	15	2-3	15-RM	2	15-20	60	3	4×30s	75 %	3
3-4	2	15	2-3	15-RM	2	25	60	3	4×30s	75 %	3
5-6	3	12	2-3	12-RM	2	30	70	3	4×30s	75 %	3
7-8	3	12	2-3	12-RM	2	30	70	3	4×30s	75 %	3
9-10	3	10	2-3	10-RM	2	30	70	3	4×30s	75 %	3

RM: Repetition maximum, MHR: Maximum heart rate, SIT: Sprint interval training

repetitions))] (25), three times a week. During weeks 3–10, the intensity increased by 70 % 1-RM. The resistance training was performed as follows: bench press, leg press, bent over lateral pull-down, bilateral biceps curl, and bilateral triceps push down. The strength was measured by 1-RM test. The resistance training was performed at 40 % of 1-RM for 1–2 week. Each patient received their own personalized exercise program in a training diary that had to be completed at each training session. For personalizing resistance training, when the patients could perform more than eight repetitions while maintaining proper form and full range of motions, the load was increased by 2.5–5 kg (26).

SIT protocol was done three times per week on cycle ergometers (Seca cardiostest 100, model 545) for 10 weeks. SIT consisted of a 5-minute warm-up at 50 revolutions per minute (rpm) followed by 4×30 seconds of high-intensity interval cycling sprints, interspersed with a 2-minute recovery and 4-minute cool-down (25 W). Patients who completed the three intervals in the first SIT session had their wattage (cycling with 7.5 % of body weight) (27) adjusted upward by 10% increments based on performance and perceived effort. Furthermore, for patients who were unable to maintain the required >120 rpm for any interval, wattage was adjusted down by 10% increments based on the same criteria. During the 10 weeks of SIT, if a patient completed three intervals maintaining more than 120 rpm on two consecutive sessions, the wattage was adjusted upward by 10% increments to ensure that maximum intensity exerted during each session (11).

### Measurements

Body fat percentage (BF %) was measured to the nearest 0.5 mm at three sites: abdominal, thigh, and suprailiac (Lafayette Skinfold Caliper II).

### Exercise testing protocols

To measure aerobic capacity, a Modified Bruce protocol treadmill test was used (28). To measure the lower limb strength and upper limb strength, a 1-RM leg press test (29) and a 1-RM bench press test were used (30).

### Blood analysis

In order to examine serum glucose, insulin, and HbA1c, blood samples (10 mL) of the subjects were collected 24 hours before exercise training and 48 hours after the last session of the training program in a 12-hour fasting state from the antecubital vein in a sitting position. The blood samples were then centrifuged at 500 g for 10 minutes at 4°C to separate the serum.

The levels of FBG were measured using Glucose Oxidase Assay Kit (Pars Azmoon, Tehran, Iran), with an autoanalyzer device (Hitachi®, model 704, 902 made in Japan). Serum insulin concentrations were determined by ELISA kit. HbA1c levels were measured using commercial

ELISA kits. Insulin resistance (HOMA-IR) was calculated along with blood fasting glucose (mg/dL) and fasting insulin (mU/L) values using the validated calculator (available at <http://www.dtu.ox.ac.uk>) in those participants who were not taking exogenous insulin (n = 22).

### Statistical Analyses

All values are represented as mean ± standard deviation (SD). The Kolmogorov-Smirnov test was used to test the normality of the data. Data were analyzed by dependent *t* test to compare pre-test and post-test values in each group. The analysis of covariance (ANCOVA) test was used to compare the changes in experimental and control training groups after 10 weeks. When a significant *F* value was achieved, Fisher's least significant difference (LSD) test was used to find the differences between groups.

### Results

The results were based on the observations of 14 participants in control, 14 participants in SIT and 14 people in combined training groups. The *P* values for comparisons of anthropometric characteristics before and after training within and between groups are reported in Table 2.

The effects of a 10-week combined resistance/ endurance training and SIT program on glycosylated hemoglobin (HbA1c) concentration and insulin resistance in female diabetic patients are shown in Table 3. HbA1c concentrations changed significantly in SIT (*P* = 0.002) and Com (*P* = 0.006) groups.

The dependent *t* test showed that the differences in the FBG in the SIT group were significant (*P* < 0.001) following a 10-week exercise training protocol. Paired *t* tests showed that the serum insulin levels significantly increased in the SIT (*P* < 0.001) and Com (*P* < 0.001) groups following exercise training.

In addition, the results of a paired *t*-test showed significant differences in HOMA-IR in SIT (*P* < 0.001) and Com (*P* = 0.001). Furthermore, the results of ANCOVA test showed that there was no significant difference in HbA1c concentrations (*F* = 0.597, *P* = 0.556) and FBG concentrations (*F* = 1.853, *P* = 0.171). However, the results of ANCOVA test showed that there were significant differences between groups in insulin (*F* = 3.622, *P* = 0.02) and HOMA-IR (*F* = 5.511, *P* = 0.0001).

### Discussion

This study investigated the idea of integrating adaptability and personalization into the exercise treatments for type 2 diabetes patients and investigating to what extent the adaptive personalized training may contribute to successful metabolic improvements. However, for many patients with type 2 diabetes, the presence of non-responders to exercise showed that some people derive less metabolic benefit from exercise training. Patients who need any

**Table 2.** The comparison of changes in the anthropometric variables before and after 10 weeks of exercise training

Variables	Groups	Mean $\pm$ SD		Within group (P value)	Between groups (P value)
		Pre-test	Post-test		
Body mass (kg)	SIT (n=14)	73.06 $\pm$ 21.62	77.00 $\pm$ 12.34	0.377	0.197
	Com (n=14)	76.30 $\pm$ 9.58	75.55 $\pm$ 9.23	0.032*	
	Control (n=14)	71.44 $\pm$ 13.20	71.26 $\pm$ 13.06	0.639	
BMI (kg/m <sup>2</sup> )	SIT (n=14)	29.57 $\pm$ 2.77	28.97 $\pm$ 3.39	0.248	0.603
	Com (n=14)	30.57 $\pm$ 2.97	31.58 $\pm$ 8.61	0.680	
	Control (n=14)	29.70 $\pm$ 4.17	29.13 $\pm$ 4.41	0.189	
Body fat (%)	SIT (n=14)	42.64 $\pm$ 2.23	41.14 $\pm$ 4.34	0.317	0.505
	Com (n=14)	31.32 $\pm$ 4.63	27.99 $\pm$ 2.36	0.347	
	Control (n=14)	43.92 $\pm$ 2.49	42.64 $\pm$ 4.95	0.379	
WC (cm)	SIT (n=14)	102.21 $\pm$ 10.67	95.14 $\pm$ 9.48	0.001**	0.004**
	Com (n=14)	101.14 $\pm$ 10.16	96.00 $\pm$ 6.55	0.001**	
	Control (n=14)	97.42 $\pm$ 11.08	97.27 $\pm$ 9.78	0.901	
WHR	SIT (n=14)	1.01 $\pm$ 0.13	0.93 $\pm$ 0.06	0.001**	0.002**
	Com (n=14)	1.01 $\pm$ 0.25	0.97 $\pm$ 0.07	0.001**	
	Control (n=14)	1.01 $\pm$ 0.018	0.98 $\pm$ 0.07	0.08	

SIT: sprint interval training; Com: resistance and aerobic endurance training; Control: subjects who did not participate in exercise training; BMI: body mass index; WC: waist circumference; WHR: waist-hip ratio.

\* Significant difference between two groups ( $P < 0.05$ ). \*\* Significant difference between two groups ( $P < 0.01$ ).

**Table 3.** The comparison of changes in the glycemic variables before and after 10 weeks of exercise training

Variables	Groups	Pretest	Posttest	Within group (P-value)	Remission (%)		F	Between groups (P value)
		Mean $\pm$ SD	Mean $\pm$ SD		prediabetes	normal		
HbA1c % (mmol/mol)	SIT (n=14)	9.64 $\pm$ 1.08 (82)	7.82 $\pm$ 0.93 (63)	0.002**	14.25	7.14	0.597	0.556
	Com (n=14)	9.49 $\pm$ 0.86 (83)	8.25 $\pm$ 1.22 (67)	0.006**	7.14	0		
	Control (n=14)	9.10 $\pm$ 0.51 (76)	9.12 $\pm$ 1.41 (80)	0.231	7.14	0		
FBG (mg/dL)	SIT (n=14)	210.07 $\pm$ 32.90	137.36 $\pm$ 32.95	0.001**	42.85	7.14	1.853	0.171
	Com (n=14)	214.64 $\pm$ 27.67	163.86 $\pm$ 71.47	0.062	35.71	7.14		
	Control (N=14)	200.86 $\pm$ 46.88	190.50 $\pm$ 59.71	0.690	0	0		
Serum insulin ( $\mu$ U/mL)	SIT (n=14)	10.08 $\pm$ 5.43	8.18 $\pm$ 5.75	0.001**	35.71	64.28	3.622	0.02*
	Com (n=14)	10.37 $\pm$ 5.35	8.83 $\pm$ 7.60	0.001**	21.42	78.57		
	Control (n=14)	9.55 $\pm$ 4.05	9.16 $\pm$ 3.75	0.378	8.1	0		
HOMA-IR	SIT (n=14)	01.63 $\pm$ 0.83	1.15 $\pm$ 0.74	0.001**	10.02	6.76	5.511	0.0001**
	Com (n=14)	01.13 $\pm$ 0.28	0.95 $\pm$ 0.24	0.001**	8.23	0		
	Control (n=14)	1.39 $\pm$ 0.63	1.42 $\pm$ 0.71	0.732	4.65	0		

SIT: sprint interval training; Com: resistance and aerobic endurance training; Control: subjects who did not participate in exercise training; HbA1c: glycated hemoglobin A1c; FBG: fasting blood glucose; HOMA-IR: homeostasis model assessment for insulin resistance.

\* Significant difference between two groups ( $P < 0.05$ ). \*\* Significant difference between two groups ( $P < 0.01$ ).

kind of exercise therapy are individuals with their own characteristics and needs.

The results of this trial showed that serum HbA1c, insulin, and HOMA-IR changed after 10 weeks of SIT and combined training in diabetic women compared to the baseline values. This study has demonstrated that personalized progressive SIT and combined training program performed 3 days/week for 10 weeks was effective in improving serum insulin, HOMA-IR, and HbA1c levels.

These findings seem to be consistent with the results of studies which found that high intensity training was accompanied by improved glycemic control in obese and/or patients with type 2 diabetes (6,31). Several studies recently have shown that SIT appears to be a time-efficient exercise training that shares many of the metabolic

adaptations with traditional endurance exercise training (31,32).

However, few studies have assessed the impact of HIIT and combined (resistance and aerobic) training on glycemic control in patients with diabetes type 2 (6,33,34). Recent randomized controlled clinical trial studies in patients with type 2 diabetes have reported improved glucose tolerance (35) following low-volume interval training, although most (36), but not all (10), have failed to improve HbA1c level and insulin resistance.

It seems that people with type 2 diabetes respond quite differently to SIT and combined training protocols. The mechanisms for the improvement in glycemic index observed after personalized SIT and combined training in the current study are unclear. It has been suggested that the improvement in HbA1c, insulin, FBG, and HOMA-IR

levels following personalized SIT and combined training occurs via mechanisms different from standard aerobic and resistance training. It is likely that personalized SIT and combined exercise-induced abdominal subcutaneous adipose tissue reduction could be explained by the lowering of HbA1c, insulin, FBG, and HOMA-IR levels (37).

The mechanism by which SIT improves HbA1c, insulin, FBG, and HOMA-IR levels may lie in its ability to recruit more skeletal muscle fibers and rapidly deplete muscle glycogen contents, thereby increasing muscle insulin sensitivity (6).

However, combined exercise training had a longer total duration of exercise and caloric use compared to each type of training which was done alone. Although these patients tolerated this exercise mode, it seems that following this exercise protocol more calories were used.

Moreover, this study illustrated that after 10 weeks of exercise training, there were no significant differences between SIT and combined training in some glycemic control, HbA1c, and FBG in type 2 diabetic individuals. However, in the present study, significant differences were found only in insulin and HOMA-IR indices between SIT and combined training protocols. The results support the hypothesis that HIIT can have different effects on insulin resistance. In addition, there are no other trials to compare these findings with their results. Our results are in agreement with previously published studies. In a study, Little et al illustrated that after 2 weeks of SIT, the average 24-h blood glucose concentration reduced in people with type 2 diabetes (19). Recently, Jung et al showed that insulin sensitivity improved in patients who performed HIIT compared with the control sedentary group (38). It has been shown that FBG levels reduced and skeletal muscle GLUT-4 levels increased by approximately 20 % following one week of HIIT and remained elevated over six weeks of training and a subsequent six weeks of detraining (39).

Significant decrease and improvement in HbA1c, insulin, FBG, and HOMA-IR levels in the patient with diabetes type 2 demonstrated clinical importance. These results are notable because it suggests that this kind of exercise may have the potential to alter glycemic indices.

A novel finding of the present study was that following the implementation of personalized training, HbA1c levels reduced among the two experimental groups; however, patients with type 2 diabetes generally did not have a high percentage of improvement in HbA1c in SIT (14.25%) and combined training (7.14%) groups. However, there were acceptable improvements in FBG and insulin concentrations following personalized SIT and combined training. Although we did not find any significant reduction in FBG after combined training compared to SIT with a significant reduction in FBG. We found an acceptable improvement following SIT (42.85 %) and combined training (35.71 %) in FBG in patients with

type 2 diabetes. Previous studies found that approximately more than 15% of patients fail to improve their glucose status and insulin resistance after different exercise training modalities. For example, Gregg et al (40) illustrated that a long-term multi-modal lifestyle intervention including exercise and diet interventions led to complete remission in approximately 9% of the patients.

Lack of long-term post-intervention follow-up is a certain limitation of this study. Another limitation of this study is that improvements in some body composition variables such as waist-hip ratio (WHR), WC, and body mass might not be only due to SIT or combined training, because it is possible that patients alter their diet in this study. It remains unclear whether or not patients altered their diet because we did not quantify the energy intake of them in the present study and there was no information about appetite changes following the interventions. These observations demonstrate that doing a low-volume SIT protocol (three times/week) can improve the health, body composition, and glycemic indexes in patients with type 2 diabetes.

### Conclusion

Taken together, these results support the importance of the personalized exercise program. Some previous studies showed that combined training (aerobic and resistance) and SIT interventions could improve glucose homeostasis in overweight women with type 2 diabetes. Results highlight that individualized exercise training, independent of the mode of training, is an effective training method to improve body composition and glycemic control in overweight individuals with type 2 diabetes.

### Conflicts of interest

Nil.

### Ethical Approval

The study protocol was registered in the Iranian Clinical Trial Registry (IRCT20141118019995N10; <http://www.irct.ir/trial/17753>) and approved by the Research Ethics Committee of Shahrekord University under the code of SKU-94-210.

### Authors Contribution

HG, ST, EB designed the study. HG and EB supervised exercise training protocols. EB, HG, ST supervised laboratory exams and data collection. HG, EB and ST analyzed and interpreted the data. HG, EB wrote the first draft of the manuscript. HG and EB edited the paper. All authors contributed to the writing of the paper. All authors read and approved the final manuscript

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