

# The Effects of Two Exercise Modalities on Novel Cardiovascular Risk Factors in Overweight Women with Type 2 Diabetes: a Randomized Controlled Trial

Ebrahim Banitalebi (✉ [banitalebi.e@gmail.com](mailto:banitalebi.e@gmail.com))

Shahrekord University <https://orcid.org/0000-0001-8386-6608>

Mohammad Faramarzi

Shahrekord University

Majid Mardaniyan Ghahfarrokhi

Shahrekord University

Samira Nasiri

Shahrekord uniiversity

---

## Research article

**Keywords:** Exercise, Cardiovascular Risk Factors, Type 2 Diabetes

**Posted Date:** August 9th, 2019

**DOI:** <https://doi.org/10.21203/rs.2.11408/v1>

**License:**  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

---

# Abstract

**Background:** The purpose of this study was to examine the effects of different exercise modalities (short sprint interval training (SIT) and combined aerobic + resistance training (A+R)) on novel cardiovascular risk factors (lipid accumulation product (LAP), Framingham risk score (FRS), atherogenic index of plasma (AIP), the metabolic syndrome severity scores (Mets score), visceral adipose index (VAI), body adipose index (BAI), triglyceride-glucose index (TyG index), triglyceride glucose-waist circumference (TyG-WC), triglyceride glucose-waist circumference (TyG-BMI), HOMA  $\beta$ -cell, and estimated glucose disposal rate (eGDR)) in overweight women with type 2 diabetes. **Methods:** Fifty-two overweight females with type 2 diabetes (T2D) (aged 45-60 years, BMI > 30, hemoglobin A1c (HbA1c)  $\geq$  6.5 %) were assigned to either SIT (n = 17), combined training (n = 17), or control groups (n = 18). Intervention consisted of SIT or combined aerobic-strength training for 10 weeks. **Results:** There were no significant changes in Mets in the SIT group after 10 weeks (p = 0.187). In addition, there were significant changes (improvements) in LAP (p < 0.001) and VAI (p = 0.002), FRS (p = 0.001), TyG index (p = 0.005), TyG-BMI (p = 0.012), TyG-WC (p < 0.001), AIP (p < 0.001), and eGDR (p = 0.001) in the combined training group after 10 weeks, as compared to the baseline. **Conclusions:** The results highlight that exercise training independent of the mode of training could be an effective strategy to improve some novel cardiovascular risk factors in women with type 2 diabetes.

## Background

Type 2 diabetes (T2D) is a strong independent risk factor for cardiovascular disease (CVD). Adults with diabetes have 2–4 times increased risk of developing CVD and stroke [ 1], and diabetes-related cardiovascular complications are a major cause of morbidity and mortality, in comparison to metabolic dysregulation [ 2]. In addition, the prevalence of obesity increases in the middle of life and decreases upon aging; women are more likely to be overweight than men [ 3]. There is strong evidence suggesting that T2D confers a stronger excess CVD risk in women than in men. There are sex-specific pathophysiological differences in metabolic syndrome that could be potentially due to their adverse risk-factor profile [ 4].

Many researchers have focused on identifying and introducing a large number of novel combined biomarkers to predict the risk scores of CVD, aiming at evaluating and monitoring responses to therapeutic strategies. Several risk prediction equations useful in the primary prevention of CVD at the individual and clinical level have been developed in recent years. It has been shown that lipid accumulation product (LAP), Framingham risk score (FSI), atherogenic index of plasma (AIP) [ 5], the metabolic syndrome severity scores (Mets score) [ 6], visceral adipose index (VAI) [ 7], body adipose index (BAI) [ 8], triglyceride-glucose index (TyG index) [ 9], triglyceride glucose-waist circumference (TyG-WC) [ 10], triglyceride glucose-BMI (TyG-BMI) [ 10], HOMA  $\beta$ -cell [ 11] and estimated glucose disposal rate (eGDR) [ 12] are strong markers predicting the risk of coronary heart diseases. It has also been found that only controlling changeable risk factors (such as age, sex, smoking, blood pressure and total

cholesterol, triglyceride, and waist and hip circumferences) can be efficient for preventive treatments in patients with diabetes [ 13 ].

Exercise has long been recognized as an important management strategy in T2D patients [ 14]. However, adequate support is not still available to show the influence of exercise interventions on other CVD-related risk factors. According to Canadian Diabetes Association (CDA) guidelines, the main lifestyle interventions for reducing the risk of CVD must include improvements in glycemic control, blood lipid levels reduction, blood pressure control, quality of life, and other diabetes-related coexisting complications [ 15]. A sprint interval training (SIT) protocol is 4-6 repeated cycling Wingate tests (4-6 × 30 s WT), interspersed by 2 minutes of recovery. Recent researches have shown that very brief SIT bouts (less than 10 min/session) have similar adaptations compare to longer SIT protocols and moderate-intensity training. Several studies that have compared several weeks of SIT to moderate-intensity training have demonstrated that SIT is equally or more effective than moderate-intensity continuous training for improving many health-related factors such as  $VO_2$ max, altered used substrate during exercise [ 16], resting metabolic rate [ 17], mitochondrial function capacity [ 18], insulin resistance [ 18], and body composition [ 18, 19] and cardiorespiratory fitness [ 20] in obese subjects. In addition, some researchers illustrated that high intensity training may improve resting energy expenditure greater than moderate-intensity training [ 21, 22]. In contrast, high intensity training has 24 hours energy expenditure similar to continuous exercise despite reduced time commitment [ 22].

There is not enough study has directly compared these types of training (very brief SIT protocol vs combined training) and measured changes in cardiovascular risk scores. There is not enough information, however, regarding these novel cardiovascular risk scores and exercise training in individuals with type 2 diabetes. Therefore, the purpose of this study was to compare the effects of two exercise modalities on novel cardiovascular risk factors in overweight women with type 2 diabetes. The two training program differed markedly with respect to volume and time (SIT involved 15 minute of intense intermittent exercise within a session, whereas combined training consisted of 50 minutes exercise per session. We hypothesized that compared to control group, SIT and combined training would similarly improve in cardiometabolic risk factors based on novel equations.

## Methods

### Subjects

In current study, we conducted a single-blind randomized clinical trial according to CONSORT statement [ 23]. This trial was registered in the Iranian Clinical Trial Registry, IRCT: 2017090419995N9. After obtaining ethical approval for the study from the ethics committee of Shahrekord University, 150 potential voluntary participants are invited to take part in this study according to the following inclusion criteria such as diagnosed T2D by a physician based on the American Diabetes Association criteria (hemoglobin A1c (HbA1c)  $\geq$  6.5%, fasting blood glucose  $\geq$  126 mg/dl (7.0 mmol/l)) [ 24], being sedentary (being sedentary defined as no more than 20 min exercise per week over the past 6 months) [ 25], 45–60 year

old pre-menopausal women with a body mass index (BMI) between 25 and 35 kg/m<sup>2</sup>, no diagnosed type I diabetes, and had not lost or gained more than 5 kg in weight during the previous 6 months. The exclusion criteria were as follows: blood pressure  $\geq$  160/100 mmHg, fasting triglyceride  $\geq$  500 mg/dl, had serious cardiovascular, musculoskeletal, thyroid, hormonal, kidney and liver disorders. We concluded that a sample size between 10- 20 could provide the statistical power of 80 % into the effect of SIT versus combined training clinically and detect the potential difference in the means of 2 % after a 10-week training. Power and sample size calculation of this study determined 17 subjects per groups based on a predicted expected dropout rate of 20%. Every participant provided the written informed consent.

Thus, only 54 subjects out of a population of 150 met the study criteria (Fig.1). Eligible subjects were told about study procedure and 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.

A concealed randomization (block size of four) was conducted by an independent research assistant not involved in this trial by using a computer-generated random number sequence. Participants were stratified according to age, baseline BMI and HbA1c levels. Sequential treatment allocations were enclosed in numbered, opaque, sealed envelopes, and distributed by this research assistant to the groups after the baseline assessment. Participants were randomly assigned to the SIT group (n = 17), the A+R group (n = 17), or the control group (n = 18) (Fig.1).

### *Fig.1*

#### Exercise training program

Both exercise training interventions (10- week combined aerobic and resistance training and SIT training) were performed in the morning 2 hours after eating breakfast. Subjects exercised three times per week for 50 minutes, according to [American College of Sports Medicine \(ACSM\)](#) guidelines [ 26], and trainings progressed in duration and intensity. Trainings were supervised by expert exercise physiologists at a clinical gym. Postprandial glucose levels were tested before and after exercise sessions to see whether the subjects could safely begin exercising. Because blood glucose levels could also run high during or after SIT through increasing glucose-raising hormone levels, when blood glucose level before exercise was less than 5.5 mmol/l (in subjects receiving insulin) or less than 6.6 mmol/l (in non-insulin users), subjects could eat a meal with 25 g carbohydrate and 7 g protein [ 27].

*Supervised combined aerobic and resistance trainings:*Through supervised aerobic training program, participants were free to exercise on a treadmill or ergometer. Aerobic training progressed from 20 min/session at 60% maximum heart rate (HR) in the weeks 1-2 to 30 min/session at 70% Max HR in the weeks 3-10. Hear rate was monitored (Polar T31, Oy, Kempele, Finland) to adjust workload to achieve the mentioned target heart rate. The aerobic training was personalized by individualized increments. Supervised resistance training was performed at one set of 15 max reps with 15 repetitions for the first two weeks. Then intensity was increased from 2-3 sets of 12 to 10 max reps with 12 to 10 repetitions between the weeks 3-10 (Table 1) [ 28]. All resistance trainings were performed on weight machines and

included bench pressing, leg pressing, bending over the lateral pull down, bilateral biceps curling, and bilateral triceps pushing down.

*Supervised sprint interval training:* The supervised SIT training consisted of exercising on cycle ergometers (Ergomedic 894E Peak Bike, Monark EB; Varberg, Sweden). Each session consisted of a 5-minute warm-up, with 4×30 second maximum intensity intervals at the breaking wattage of the individual; this was followed by 2 minutes of recovery and 4 minutes of cool-down. Wattage was adjusted upward by 10% based on the performance and the perceived effort in participants who had completed the three intervals on the first SIT session. However, wattage was adjusted down by 10% based on the same criteria for those who were not capable of maintaining the required 120 rpm for any interval. In addition, during the 10 weeks of SIT, wattage was adjusted upward in 10% increments to ensure that the maximum intensity was being exerted during each session if a patient had completed three intervals by maintaining more than 120 rpm on two consecutive sessions [ 29].

*Control group:* The control group continued their usual medical care and received Farsi-translated diabetes recommendations for self-management. They were not given exercise counselling and were asked to maintain baseline activity levels during the study period.

## Blood Analysis

Blood samples (10 cc) from the antecubital vein in a sitting position were collected 24 hours before the exercise protocol and 48 hours after the last session of the training program within 12 hours of the fasting state.

Fasting blood glucose was measured using the glucose oxidase method kit (Pars Azmoon, Tehran, Iran), through auto-analyzer devices (Hitachi®, model 704, 902 made in Japan). Serum insulin concentrations were determined by ELISA technique using a microplate reader. HOMA-IR was calculated by computing the following equation: (fasting glycemia [mmol/l] × fasting insulin [mIU/l]) / 22.5 [ 30]. Participants who used insulin injection were excluded for the HOMA-IR analysis.

## *Novel cardiovascular risk scores*

Lipid accumulation product (LAP) = (waist circumference [cm] - 58) × (triglyceride concentration [mM]) [ 31 ].

Athrogenic index of plasma (AIP) = [Log (Triglycerides/HDL-Cholesterol)] [ 32 ].

Visceral adipose index (VAI) = (WC/ [36.58 + (1.89×BMI)]) × (TG/0.81) × (1.52/HDL-C) [ 33].

Body adipose index (BAI) = [hip (cm) / height (m)<sup>1.5</sup>] - 18 [ 34].

MET syndrome Z-Score = waist Z score + BP Z score + glucose Z score + HDL - C Z score + triglycerides Z score [ 35].

Triglyceride-glucose index (TyG index) = (fasting TG [mg/dL] × fasting glucose [mg/dL]/2) [ 9 ].

Triglyceride glucose-waist circumference (TyG-WC) = TyG-WC: TyG index × WC (cm) [ 10 ].

Triglyceride glucose-waist circumference (TyG-BMI) = TyG index × BMI [ 10 ].

HOMA β-cell = [20 × fasting insulin (μIU/MI)] / [fasting glucose (mmol/l) -3.5] [ 11 ].

eGDR (mg/kg/min)= 21.158 + (-0.09 × WC)+ (-0.551 × HbA1C) [ 12].

To estimate cardiovascular risk factor score, we applied the Framingham risk score equation [ 36]. This equation considers gender, age, systolic blood pressure, smoking status, total cholesterol, HDL-C, and diabetes mellitus status to calculate the percentage likelihood of a coronary disease over a 10-year period [ 37].

### *Statistical analyses*

Data from 10 participants who did not attend the post-test assessment was excluded and only the available data of 42 participants who had completed the pre and post assessment was analyzed. Sample size was calculated based on previous researches to examine the difference in effect between SIT and A+R trainings. We concluded that a sample size between 10- 20 could provide the statistical power of 80 % into the effect of SIT versus A+R training clinically and detect a difference in the means of 2 % after 10 weeks of training. Power and sample size calculation of this study determined 17 subjects per groups based on the predicted dropout rate of 20%. A Kolmogorov-Smirnov test was used for checking the normality of data. Baseline characteristics of the groups were compared by one-way Analysis of Variance (one-way ANOVA) or Kruskal-Wallis test when data was not normally distributed. The paired t-test was conducted to compare baseline versus post-training measures and one-way ANOVA followed by a Fisher's Least Significant Difference (LSD) *post hoc* test was used to find the differences between various groups. Statistical significance was accepted when  $p < 0.05$ .

## **Results**

10 participants were excluded from the final analysis as they did not take part in the post-test assessment. Thus, only the available data of 42 participants with the mean age of  $55.07 \pm 5.92$  (drop out 19.2%) who had completed the pre and post assessment was analyzed.

An average adherence rates of 78% in SIT and 82% in A+R groups were for the training sessions.

27 participants were treated with oral diabetes medications, 20 with insulin injections, and 5 with the combination therapy of insulin injection and oral drugs. One-Way ANOVA was used to show that there were no significant differences in terms of the baseline factors between the groups except FBS ( $p= 0.021$ ) and HbA1c ( $p= 0.005$ ) (table 1).

Adverse events

Non-serious medical adverse events were identified and reported during interventions and testing sessions. However, most patients reported muscle soreness in the legs during SIT (76%) and A+R trainings (82%).

#### *Table 1*

At the baseline, One-Way ANOVA showed no differences between the combined, the SIT and the control groups for body mass, % body fat, BMI, WHR, FBG, and HbA1c (Table 1).

#### *Table 2*

In addition, one way-ANOVA test showed there were not statistically significant differences in body mass, BMI, body fat, and WHR between groups. Conducting paired t-test and comparing p values in within groups, however, revealed significant differences in body fat ( $p=0.0001$ ). But there were no significant differences in body mass ( $p= 0.483$ ), BMI ( $p= 0.680$ ), WHR ( $p= 0.202$ ), and body fat percentage ( $p= 0.347$ ) in the combined group after conducting a paired t-test. In addition, paired t-test showed that there were significant differences in body fat ( $p=0.0001$ ). But there were no significant differences in body mass ( $p= 0.372$ ), BMI ( $p= 0.368$ ), WHR ( $p= 0.148$ ), and % body fat ( $p= 0.317$ ) in the SIT group (table 2).

#### *Table 3*

Comparing within-group changes showed significant improvements in LAP ( $p = 0.001$ ) and VAI ( $p < 0.001$ ), FRS ( $p < 0.001$ ), TyG index ( $p < 0.001$ ), TyG-BMI ( $p = 0.001$ ), TyG-WC ( $p < 0.001$ ), AIP ( $p = 0.003$ ), and eGDR ( $p < 0.001$ ) in the SIT group after 10 weeks, as compared to the baseline. In addition, there were significant changes (improvements) in LAP ( $p < 0.001$ ) and VAI ( $p = 0.002$ ), FRS ( $p = 0.001$ ), TyG index ( $p = 0.005$ ), TyG-BMI ( $p = 0.012$ ), TyG-WC ( $p < 0.001$ ), AIP ( $p < 0.001$ ), and eGDR ( $p = 0.001$ ) in the combined training group after 10 weeks, as compared to the baseline. However, there were no significant changes in Mets in the SIT group after 10 weeks ( $p = 0.187$ ). In addition, there were no significant changes in Mets in the combined training group after 10 weeks ( $p = 0.279$ ).

#### *Table 4*

In addition, one- way ANOVA test showed that there were significant differences between the groups in LAP ( $F = 3.408, p = 0.043$ ), VAI ( $F = 8.740, p = 0.001$ ), FRS ( $F = 8.861, p = 0.001$ ), TyG index ( $F = 3.810, p = 0.031$ ), TyG-WC ( $F = 8.600, p = 0.001$ ), and eGDR ( $F = 8.269, p = 0.001$ ). Moreover, there were significant differences between groups in insulin ( $F = 3.622, p = 0.036$ ), and HOMA-IR ( $F = 5.511, p = 0.008$ ).

In addition, there was a significant reduction in fasting blood glucose in the SIT ( $p < 0.001$ ) after 10 weeks. Furthermore, paired *t* tests showed that there was a significant decrease in the insulin level in combined training ( $p < 0.001$ ) and SIT ( $p < 0.001$ ) groups after the 10 week intervention

Furthermore, ANOVA test showed that there were no significant differences in fasting blood glucose concentrations ( $F = 1.853, p = 0.171$ ). However, there were significant differences between groups in

insulin ( $F = 3.622, p = 0.036$ ) and HOMA-IR ( $F = 5.511, p = 0.008$ ).

Post hoc Tukey analysis test showed significant differences in LAP between SIT and control groups ( $p = 0.05$ ), VAI between SIT and combined training groups ( $p = 0.035$ ) and SIT and control groups ( $p = 0.001$ ), FRS between SIT and combined training groups ( $p = 0.018$ ) and SIT and control groups ( $p = 0.001$ ), TyG index between SIT and control groups ( $p = 0.035$ ), TyG-WC index between SIT and control groups ( $p = 0.001$ ), and eGDR between SIT and control groups ( $p = 0.001$ ).

## Discussion

To our knowledge, this study could be regarded as the first randomized controlled trial (RCT) comparing the effects of different modes of exercise modalities on novel cardiovascular risk factors among women with diabetes type 2. The major novel finding from this study was that 10 weeks of SIT in previously inactive women with diabetes type 2 improved WC, HbA1c, MetS, FRS, LAP, VAI, TyG index, TyG-BMI, eGDR to the same extent as and combined resistance and endurance, despite a 10-fold lower exercise time commitment.

This study demonstrated that sprint interval training was a more potent stimulus than combined aerobic and resistance training in improving some cardiovascular factors (LAP, VAI, FRS, TyG, TyG-WC and eGDR), though it failed to significantly improve Mets, TyG-BMI and AIP, as compared with combined training. Additionally, SIT and combined training did not lead to more powerful significant changes in body composition in terms of body mass, BMI, WHR, and body fat percentage in women suffering from diabetes.

In the present study, the LAP index was significantly improved after two exercise interventions. The association between exercise training and LAP index has not been studied before. The LAP index is an accurate index for predicting the risk of developing diabetes type 2 [31]; SIT and combined training in our study could contribute to reducing LAP in women with diabetes type 2. The improvement of LAP index after two exercise interventions reflected the possible reduction of ectopic fat deposition which could be responsible for the improvement of insulin resistance (HOMA-IR) in diabetes type 2 [38], as seen in our study. However, as observed, women' body composition did not change in this study. There have been no similar studies testing the effects of exercise modalities on the LAP index in patients with diabetes mellitus. A previous study, however, had shown that isocaloric diet lowered the LAP index in healthy non-obese non-diabetic subjects [39].

The different improvements of interventions on VAI, a reliable marker of visceral fat distribution, can be gender dependent, reflecting that fat distribution associated with cardiovascular risk in this study was independent of body composition changes. Furthermore, the independence of body composition change from -improvement in VAI could be associated with the increased physical activity volume and also, the improvement of physical fitness parameters [40], as seen in this study (data not shown). Thus, exercise training led to a significant reduction in VAI, which pointed out the potential additive effect of exercise training on WC in T2D women. It seems that exercise program that is aerobic, in contrast to resistance

training and/or combined interventions, could alter adipose tissue metabolism and regional visceral adipose tissue depot loss, possibly by mobilizing free fatty acids from visceral adipose tissue at different abdominal regions [ 41]. Several inconsistent findings have been found regarding how interval training can reduce abdominal fat mass in T2D men [ 42, 43]. Comparison with our results in women participating in this shows that there are some gender differences in the effects of exercise modalities on some biomarkers of CVD risk factors. For examples, women had greater reductions in body fat than men; women could decrease hsCRP level more than men by following exercise intervention through sex differences in body fat distribution and sex hormones [ 44]; women could also reduce sympathetic nervous activity more than men, showing that there are greater changes in arterial stiffness and endothelial function in women than in men [ 44]. No differences were found in MetS Z-score changes between SIT and combined training. In addition, there were also no significant changes in MetS Z-score from the baseline to post-exercise training in all groups. Furthermore, the beneficial effects of exercise on the MetS Z-score were achieved without concomitantly altering body composition. It has been shown that fat mass changes are not correlated to MetS Z-score [ 45]. Interestingly, we did not see any significant reduction in body composition in all groups. It seems that exercise-dependent changes in body composition or more precisely, changes in body mass, body fat percentage and WHR are not important factors in reducing the cardiovascular risk score [ 45].

In this study, we showed that no significant change in the MetS Z-score would be possible in the absence of change in body composition. The strengths of present study were the use of the novel MetS Z-score to evaluate the effects of different exercise modalities. Confirming the present results, Gates illustrated that 16 weeks of aerobic training did not change the MetS Z-score [ 35]. In addition, Johnson et al. did not show the superiority of SIT, as compared with moderate intensity training, in overweight/obese subjects [ 46]. Furthermore, Earnest et al. [54] showed similar reductions in the MetS Z-score in high intensity training and moderate training in overweight males [ 47]. Because of methodological differences across studies, such as differences in gender, age, health, weight and physical fitness status, medication, mode and intensity of exercise and duration of the training program [ 48], drawing general conclusions is difficult [ 49]. It could be speculated that both trainings might not induce improvements in the metabolism, metabolic capacity, and body composition [ 49, 50]. The hypothesis of the study was that the regular SIT and combined training could reduce the risk of CVD in type 2 diabetes. It has also been proven that both exercise modalities could be recommended for type2 diabetes patients. This finding is consistent with the results obtained by Ramos et al, who found that low-volume HIIT could be as effective as moderate-intensity continuous training in the reduction of the MetS Z-score [ 51]. In addition, Fisher and colleague demonstrated that both high intensity interval training and continuous moderate intensity training are associated with improvements in cardiovascular risk factors (body fat percent, cholesterol, VLDL, HDL, triglycerides and VO<sub>2</sub>peak) in overweight men [ 52]. Furthermore, the results of the present study showed that applying regular SIT and combined training could reduce risks of CVD for 10 years. This improvement may result from the decreased systolic and diastolic blood pressure and improvements of lipid profile [ 53], as shown in our study. Significant improvements in systolic and diastolic blood pressure and lipid profile might be because of these reductions in FRS [ 53]. The FRS

reduction results were in agreement with those obtained by [Amin-Shokravi et al., \[ 53\]](#) and [Tulley et al., \[ 54\]](#). It seems that the severity of applied exercise training in this study was sufficient to bring about changes in FRS.

Perhaps the most striking and novel finding from the present work was the similar improvements in TyG, TyG-BMI and TyG-WC indices. Although few studies have investigated the relationships between TyG indices and CVD risk [[10](#), [55](#)], none of them has yet explored the effects of different exercise modalities on TyG indices. It has been shown that TyG index is a reliable predictor to identify insulin resistance and diabetes type 2 [[9](#), [56](#)]. One major advantage of the TyG index is the use of fasting glucose and triglyceride parameters. It seems that the TyG index predominantly shows muscle insulin resistance, while HOMA-IR mainly reflects liver insulin resistance [[57](#)]. Several candidate mechanisms have been suggested to explain the effect of exercise training on TyG indices in patients with diabetes type 2. It might be postulated that improvement in insulin resistance, as seen in our study, may explain improvements of TyG-indices in women with diabetes type 2 [[9](#)]. Our results demonstrate that a surprisingly small amount of SIT can be as effective as a large volume of moderate combined training for improving TyG, TyG-BMI and TyG-WC indices.

As shown by the previous studies, exercise training is an effective anti-atherosclerosis intervention [[58](#), [59](#)]. Some novel findings from the present study were the similar improvements in atherogenic index of plasma in SIT and combined training. Both training protocols were capable of reducing AIP in women with diabetes type 2. As AIP was calculated based on TG and HDL-C levels, it was expected that any changes in TG and HDL-C following exercise training would result in the change in AIP. But, the findings also showed that vigorous intensity interval training and combined aerobic plus resistance training did not significantly change the levels of HDL and TG. The present study showed that even without changes in HDL and TG levels, both modalities could serve as an appropriate stimulus to reduce the atherogenic risk. It could be speculated that LDL particle size may explain the exercise training related mechanisms involved in the reduction of the atherogenic risk [[58](#), [59](#)].

Several studies recently have shown that SIT appears to be a very time-efficient exercise regime that shares many of the metabolic adaptations as traditional endurance exercise training does [[60-62](#)].

However, combined exercise training had a more considerable total duration of exercise and calorie consumption, as compared with the time when each type of training was done alone [[63](#)]. Despite the fact that such patients tolerate this exercise mode, it seems that by following this exercise prescription, more calories could be consumed.

It has been shown that lower eGDR score was associated with the prevalence of T2D and increased diabetes-related vascular complications (the use of the Estimated Glucose Disposal Rate as a Measure of Insulin Resistance in an Urban Multiethnic Population with Type 1 Diabetes). This study showed that eGDR was decreased by following two exercise modalities in 2DM patients. This effect of exercise intervention on eGDR has not been described previously. It seems that the decrease of eGDR by following exercise training could be caused by the reduction of HbA1C. Decline in HbA1C reflects an adaptation in

glucose hemostasis. The novel aspect of our study was that we investigated the utility of eGDR in the assessment of exercise-induced training effects on insulin sensitivity in the patients with T2DM. The results of this study showed that both protocols had a positive effect on eGDR in the patients with type 2 diabetes, and the change in HbA1c levels at the exercise program. The most important was the fact that subjects receiving the SIT training program showed significantly greater improvement in eGDR levels over the 10 week period, as compared to the control group. One limitation of the present RCT was that SIT protocols had also to be evaluated in terms of safety in women living with T2D though exercise training, though it was generally quite safe [ 64].

Study limitations:

The randomized controlled trial design, the inclusion of two different training programs in the same study, the direct personalized exercise training for all training sessions, and the use of a novel cardiovascular risk score to evaluate the effects of different exercise modalities on the risk of cardiovascular diseases, which provided an increased level of accuracy and sensitivity, were amongst the strengths of the present study. As for the limitations of this study, the small size, significant dropout rate, and supervised exercise only in the experimental groups can be mentioned. Moreover, the non-significant reductions of body composition parameters, which can be attributed to the lack of diet control could be taken one other limitation. This study could yield some insight in selecting the type of exercises that can be more helpful for cardiovascular risk reduction. However, this exercise schedule may not be suitable for real-life setting as adequacy of exercise cannot be quantified and many patients with type 2 diabetes may not be having the facilities for such exercises. This is also is another limitation of this study.

## Conclusions

Taken together, the results of the present study supported the importance of SIT and combined training program in improving T2D and novel cardiovascular risk scores, despite the fact that some studies had shown that combined training (aerobic and resistance) and SIT interventions could improve glucose homeostasis in overweight women with type 2 diabetes. Results highlighted that much lower exercise volume involved with SIT, these data also seemingly suggest that training intensity, rather than volume, may be the more critical determinant of the improvement in some novel cardiometabolic-related scores. Results highlighted that exercise training independent of the mode of training (SIT vs. combined training) could be an effective training method to improve some novel cardiovascular risk scores in overweight women with type 2 diabetes. Furthermore, even without weight loss during the course of the 10-week exercise, there was a significant reduction in anthropometric variables, suggesting that weight loss is not mandatory for the healthy body composition.

## Abbreviations

SIT: Short sprint interval training; combined training: resistance and aerobic training; Control group: subjects who did not participate in exercise training; MetS: Metabolic syndrome scores; FRS: Framingham

Risk Score; LAP: Lipid Accumulation Product; VAI: Visceral adipose index; TyG index: Triglyceride-glucose index; TyG-BMI: Triglyceride Glucose-Body Mass Index; eGDR: Estimated Glucose Disposal Rate; BMI: body mass index; HDL: high density lipoprotein; TG: triglyceride; WC: waist circumference; MAP: Mean arterial pressure; WHR: Waist-hip ratio; BMI: body mass index. WHR: circumference waist of hip ratio. HOMA-IR: Homeostatic Model Assessment-Insulin Resistance; RPE: rating of perceived exertion; ELISA: enzyme-linked immunosorbent assay.

## Declarations

### Acknowledgements

The authors would like to thank all participants of this study. This study was supported by a grant from Shahrekord University (Code No: 97GRN1M895).

### Availability of data and materials

The datasets used and/or analyzed during the this study available from the corresponding author on reasonable request.

### Author's contributions

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

### Competing interests

The authors declare that they have no competing interests.

### Funding

No funding was obtained for this study.

### Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Shahrekord University (Shahrekord, Iran). Informed consents were signed by the women that participated in the study. The researcher explained the research purposes to the subjects. Researcher assured subjects of their right to refuse to participate or withdraw from the study at any time.

## References

1. Collaboration, E.R.F., *Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies*. The Lancet, 2010. 375(9733): p. 2215-2222.
2. Shah, A.D., et al., *Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1·9 million people*. The lancet Diabetes & endocrinology, 2015. 3(2): p. 105-113.
3. Yip, Y., S. Ho, and S. Chan, *Tall stature, overweight and the prevalence of low back pain in Chinese middle-aged women*. International Journal of Obesity & Related Metabolic Disorders, 2001. 25(6).
4. Kanaya, A.M., D. Grady, and E. Barrett-Connor, *Explaining the sex difference in coronary heart disease mortality among patients with type 2 diabetes mellitus: a meta-analysis*. Archives of internal medicine, 2002. 162(15): p. 1737-1745.
5. Hosseinpanah, F., et al., *Lipid accumulation product and incident cardiovascular events in a normal weight population: Tehran Lipid and Glucose Study*. European journal of preventive cardiology, 2016. 23(2): p. 187-193.
6. Wiley, J.F. and M.J. Carrington, *A metabolic syndrome severity score: a tool to quantify cardio-metabolic risk factors*. Preventive medicine, 2016. 88: p. 189-195.
7. Han, L., et al., *Visceral adiposity index score indicated the severity of coronary heart disease in Chinese adults*. Diabetology & metabolic syndrome, 2014. 6(1): p. 143.
8. Bannasar-Veny, M., et al., *Body adiposity index and cardiovascular health risk factors in Caucasians: a comparison with the body mass index and others*. PloS one, 2013. 8(5): p. e63999.
9. Lee, E.Y., et al., *Triglyceride glucose index, a marker of insulin resistance, is associated with coronary artery stenosis in asymptomatic subjects with type 2 diabetes*. Lipids in health and disease, 2016. 15(1): p. 155.
10. Zheng, S., et al., *Triglyceride glucose-waist circumference, a novel and effective predictor of diabetes in first-degree relatives of type 2 diabetes patients: cross-sectional and prospective cohort study*. Journal of translational medicine, 2016. 14(1): p. 260.
11. Ha, C.H., et al., *Effects of combined exercise on HOMA-IR, HOMA  $\beta$ -cell and atherogenic index in Korean obese female*. Sport Sciences for Health, 2015. 11(1): p. 49-55.
12. Epstein, E.J., et al., *Use of the estimated glucose disposal rate as a measure of insulin resistance in an urban multiethnic population with type 1 diabetes*. Diabetes care, 2013. 36(8): p. 2280-2285.
13. Chamnan, P., et al., *Cardiovascular risk assessment scores for people with diabetes: a systematic review*. Diabetologia, 2009. 52(10): p. 2001.

14. Colberg, S.R., et al., *Exercise and type 2 diabetes: American College of Sports Medicine and the American Diabetes Association: joint position statement. Exercise and type 2 diabetes*. *Medicine and science in sports and exercise*, 2010. 42(12): p. 2282-2303.
15. Chudyk, A. and R.J. Petrella, *Effects of exercise on cardiovascular risk factors in type 2 diabetes*. *Diabetes care*, 2011. 34(5): p. 1228-1237.
16. Astorino, T.A., et al., *Effect of two doses of interval training on maximal fat oxidation in sedentary women*. *Medicine and science in sports and exercise*, 2013. 45(10): p. 1878-1886.
17. Schubert, M.M., et al., *Impact of 4 weeks of interval training on resting metabolic rate, fitness, and health-related outcomes*. *Applied Physiology, Nutrition, and Metabolism*, 2017. 42(10): p. 1073-1081.
18. Gillen, J.B., et al., *Interval training in the fed or fasted state improves body composition and muscle oxidative capacity in overweight women*. *Obesity*, 2013. 21(11): p. 2249-2255.
19. Weston, K.S., U. Wisløff, and J.S. Coombes, *High-intensity interval training in patients with lifestyle-induced cardiometabolic disease: a systematic review and meta-analysis*. *Br J Sports Med*, 2014. 48(16): p. 1227-1234.
20. Burgomaster, K.A., et al., *Similar metabolic adaptations during exercise after low volume sprint interval and traditional endurance training in humans*. *The Journal of physiology*, 2008. 586(1): p. 151-160.
21. Hazell, T.J., et al., *Two minutes of sprint-interval exercise elicits 24-hr oxygen consumption similar to that of 30 min of continuous endurance exercise*. *International journal of sport nutrition and exercise metabolism*, 2012. 22(4): p. 276-283.
22. Skelly, L.E., et al., *High-intensity interval exercise induces 24-h energy expenditure similar to traditional endurance exercise despite reduced time commitment*. *Applied Physiology, Nutrition, and Metabolism*, 2014. 39(7): p. 845-848.
23. Pandis, N., et al., *CONSORT 2010 statement: extension checklist for reporting within person randomised trials*. *Bmj*, 2017. 357: p. j2835.
24. Association, A.D., *Standards of medical care in diabetes—2014*. *Diabetes care*, 2014. 37(Supplement 1): p. S14-S80.
25. Bennett, J.A., et al., *Definitions of sedentary in physical-activity-intervention trials: a summary of the literature*. *Journal of aging and physical activity*, 2006. 14(4): p. 456-477.
26. Albright, A., et al., *American College of Sports Medicine position stand. Exercise and type 2 diabetes*. *Medicine and science in sports and exercise*, 2000. 32(7): p. 1345-1360.

27. Castaneda, C., et al., *A randomized controlled trial of resistance exercise training to improve glycemic control in older adults with type 2 diabetes*. Diabetes care, 2002. 25(12): p. 2335-2341.
28. Larose, J., et al., *Comparison of strength development with resistance training and combined exercise training in type 2 diabetes*. Scandinavian journal of medicine & science in sports, 2012. 22(4).
29. Higgins, T.P., et al., *Heterogeneous responses of personalised high intensity interval training on type 2 diabetes mellitus and cardiovascular disease risk in young healthy adults*. Clinical hemorheology and microcirculation, 2015. 59(4): p. 365-377.
30. Ahmadizad, S., A.H. Haghghi, and M.R. Hamedinia, *Effects of resistance versus endurance training on serum adiponectin and insulin resistance index*. European journal of Endocrinology, 2007. 157(5): p. 625-631.
31. Mirmiran, P., Z. Bahadoran, and F. Azizi, *Lipid accumulation product is associated with insulin resistance, lipid peroxidation, and systemic inflammation in type 2 diabetic patients*. Endocrinology and Metabolism, 2014. 29(4): p. 443-449.
32. Dobiasova, M., *AIP-atherogenic index of plasma as a significant predictor of cardiovascular risk: from research to practice*. Vnitri lekarstvi, 2006. 52(1): p. 64-71.
33. Amato, M.C., et al., *Visceral adiposity index*. Diabetes care, 2010. 33(4): p. 920-922.
34. Barreira, T.V., et al., *Body adiposity index, body mass index, and body fat in white and black adults*. Jama, 2011. 306(8): p. 828-830.
35. Gates, T., *Effect of Exercise Training on Metabolic Syndrome z-score: the Association of C-reactive protein*. 2015.
36. D'Agostino, R.B., et al., *General cardiovascular risk profile for use in primary care*. Circulation, 2008. 117(6): p. 743-753.
37. Mannan, H., et al., *Framingham risk prediction equations for incidence of cardiovascular disease using detailed measures for smoking*. Heart international, 2010. 5(2).
38. Sambataro, M., et al., *Lipid accumulation in overweight type 2 diabetic subjects: relationships with insulin sensitivity and adipokines*. Acta diabetologica, 2013. 50(3): p. 301-307.
39. Briganti, S., et al., *Effect of an isocaloric diet containing fiber-enriched flour on anthropometric and biochemical parameters in healthy non-obese non-diabetic subjects*. Journal of clinical biochemistry and nutrition, 2015. 57(3): p. 217-222.
40. Balducci, S., et al., *Volume-dependent effect of supervised exercise training on fatty liver and visceral adiposity index in subjects with type 2 diabetes The Italian Diabetes Exercise Study (IDES)*. Diabetes

research and clinical practice, 2015. 109(2): p. 355-363.

41. Idoate, F., et al., *Weight-loss diet alone or combined with resistance training induces different regional visceral fat changes in obese women*. International Journal of Obesity, 2011. 35(5): p. 700-713.

42. Boudou, P., et al., *Absence of exercise-induced variations in adiponectin levels despite decreased abdominal adiposity and improved insulin sensitivity in type 2 diabetic men*. European Journal of Endocrinology, 2003. 149(5): p. 421-424.

43. Heydari, M., J. Freund, and S.H. Boutcher, *The effect of high-intensity intermittent exercise on body composition of overweight young males*. Journal of obesity, 2012. 2012.

44. Morita, N. and K. Okita, *Is gender a factor in the reduction of cardiovascular risks with exercise training?* Circulation Journal, 2013. 77(3): p. 646-651.

45. Ramírez-Vélez, R., et al., *Similar cardiometabolic effects of high-and moderate-intensity training among apparently healthy inactive adults: a randomized clinical trial*. Journal of translational medicine, 2017. 15(1): p. 118.

46. Johnson, J.L., et al., *Exercise training amount and intensity effects on metabolic syndrome (from Studies of a Targeted Risk Reduction Intervention through Defined Exercise)*. The American journal of cardiology, 2007. 100(12): p. 1759-1766.

47. Earnest, C., et al., *Interval training in men at risk for insulin resistance*. International journal of sports medicine, 2013. 34(04): p. 355-363.

48. Jelleyman, C., et al., *The effects of high-intensity interval training on glucose regulation and insulin resistance: a meta-analysis*. Obesity reviews, 2015. 16(11): p. 942-961.

49. Batacan, R.B., et al., *Effects of high-intensity interval training on cardiometabolic health: a systematic review and meta-analysis of intervention studies*. Br J Sports Med, 2017. 51(6): p. 494-503.

50. Kessler, H.S., S.B. Sisson, and K.R. Short, *The potential for high-intensity interval training to reduce cardiometabolic disease risk*. Sports medicine, 2012. 42(6): p. 489-509.

51. Ramos, J.S., et al., *Low-Volume High-Intensity Interval Training Is Sufficient to Ameliorate the Severity of Metabolic Syndrome*. Metabolic syndrome and related disorders, 2017. 15(7): p. 319-328.

52. Fisher, G., et al., *High intensity interval-vs moderate intensity-training for improving cardiometabolic health in overweight or obese males: a randomized controlled trial*. PloS one, 2015. 10(10): p. e0138853.

53. Amin-Shokravi, F., R. Rajabi, and N. Ziaee, *Exercise effects on risk of cardiovascular disease among Iranian women*. Asian journal of sports medicine, 2011. 2(1): p. 37.

54. Tully, M., et al., *Brisk walking, fitness, and cardiovascular risk: a randomized controlled trial in primary care*. Preventive medicine, 2005. 41(2): p. 622-628.
55. Kim, J.-H., et al., *Triglyceride glucose index predicts coronary artery calcification better than other indices of insulin resistance in Korean adults: the Kangbuk Samsung Health Study*. Precision and Future Medicine, 2017. 1(1): p. 43-51.
56. Lee, E.S., et al., *Predictive value of triglyceride glucose index for the risk of incident diabetes: a 4-year Retrospective Longitudinal Study*. PloS one, 2016. 11(9): p. e0163465.
57. Tripathy, D., et al., *Contribution of insulin-stimulated glucose uptake and basal hepatic insulin sensitivity to surrogate measures of insulin sensitivity*. Diabetes care, 2004. 27(9): p. 2204-2210.
58. Ezeukwu, A.O., E.O. Agwubike, and P.O. Uadia, *Differential Effects of Continuous and Interval Exercise Training on the Atherogenic Index of Plasma in the Non-Obese Young Male*. Acta Cardiologica Sinica, 2015. 31(4): p. 337.
59. Stranska, Z., et al., *Aerobic exercise has beneficial impact on atherogenic index of plasma in sedentary overweight and obese women*. Neuro endocrinology letters, 2011. 32(1): p. 102-108.
60. Burgomaster, K.A., et al., *Six sessions of sprint interval training increases muscle oxidative potential and cycle endurance capacity in humans*. Journal of applied physiology, 2005. 98(6): p. 1985-1990.
61. Whyte, L.J., J.M. Gill, and A.J. Cathcart, *Effect of 2 weeks of sprint interval training on health-related outcomes in sedentary overweight/obese men*. Metabolism, 2010. 59(10): p. 1421-1428.
62. Richards, J.C., et al., *Short-term sprint interval training increases insulin sensitivity in healthy adults but does not affect the thermogenic response to  $\beta$ -adrenergic stimulation*. The Journal of physiology, 2010. 588(15): p. 2961-2972.
63. Sigal, R.J., et al., *Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial*. Annals of internal medicine, 2007. 147(6): p. 357-369.
64. Francois, M.E. and J.P. Little, *Effectiveness and safety of high-intensity interval training in patients with type 2 diabetes*. Diabetes Spectrum, 2015. 28(1): p. 39-44.

## Figures

Fig1. CONSORT 2010 Flow Diagram

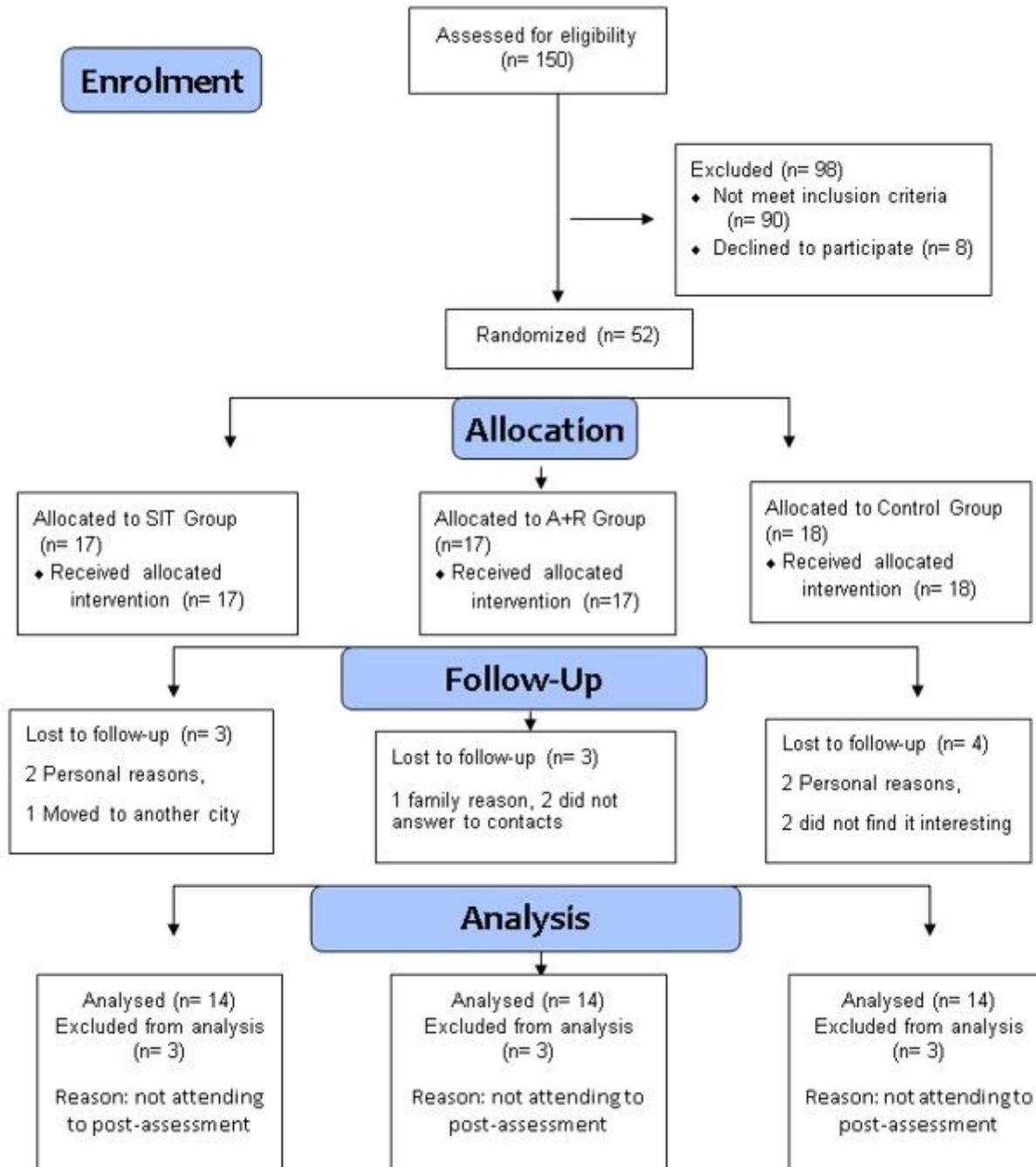


Figure 1

CONSORT 2010 Flow Diagram

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [TablesEdited.pdf](#)