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Research article

A Randomized Controlled Trial to Determine the Impact of Resistance Training versus Aerobic Training on the Management of FGF-21 and Related Physiological Variables in Obese Men with Type 2 Diabetes Mellitus

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Abstract
Fibroblast growth factor 21 (FGF-21) has been suggested as a potential therapeutic target for insulin resistance in health-related metabolic disorders such as type 2 diabetes. Despite the metabolic effects of resistance (RT) and aerobic training (AT) on diabetes symptoms, uncertainty exists regarding the superiority of effects manifested through these training approaches on FGF-21 and biochemical and physiological variables associated with metabolic disorders in men diagnosed with type 2 diabetes. This study aimed to investigate the impact of a 12-week RT and AT on FGF-21 levels and symptoms associated with metabolic disorders in male individuals diagnosed with type 2 diabetes. Thirty-six sedentary obese diabetic men (40 to 45 years old) were matched based on the level of FGF-1. They and were randomly divided into two training groups (RT, n = 12 and AT, n = 12) performing three days per week of moderate-intensity RT or AT for 12 weeks and an inactive control group (n = 12). Both training interventions significantly improved FGF-21, glucose metabolism, lipid profile, hormonal changes, strength, and aerobic capacity. Subgroup analysis revealed that RT had greater adaptive responses ($p < 0.01$) in fasting blood sugar (ES = -0.52), HOMA-IR (ES = -0.87), testosterone (ES = 0.52), cortisol (ES = -0.82), FGF-21 (ES = 0.61), and maximal strength (ES = 1.19) compared to AT. Conversely, AT showed greater changes ($p < 0.01$) in cholesterol (ES = -0.28), triglyceride (ES = -0.64), HDL (ES = 0.46), LDL (ES = -0.73), and aerobic capacity (ES = 1.18) compared to RT. Overall, both RT and AT interventions yielded significant moderate to large ES in FGF-21 levels and enhanced the management of biochemical variables. RT is an effective method for controlling FGF-21 levels and glucose balance, as well as for inducing hormonal changes. On the other hand, AT is more suitable for improving lipid profiles in overweight men with type 2 diabetes mellitus.

Key words: Exercise, lipid profile, insulin resistance, metabolism.

Introduction

The World Health Organization (WHO) has observed a substantial rise in global obesity rates since 1975, resulting in the classification of obesity as a pandemic (Boutari and Mantzoros, 2022). The increase in obesity rates has led to a rise in the prevalence of type 2 diabetes mellitus (T2DM), a condition strongly associated with visceral obesity and insulin resistance (Jorge et al., 2011). Metabolic diseases caused by T2DM can significantly impair liver function, especially regarding glucose regulation (Snowling and Hopkins, 2006). In T2DM, insulin resistance involves distinct circulating proteins, such as fibroblast growth factor-21 (FGF-21), which play a role in insulin regulation and are associated with lipid and glucose metabolism (Chavez et al., 2009). Studies indicate that FGF-21 plays a significant role in improving human glucose uptake (Matuszek et al., 2010). Additionally, there seems to be a connection between circulating hepatokines (i.e., FGF-21) and metabolic indicators in diabetes patients, including blood glucose levels, HbA1c, LDL and HDL cholesterol, and HOMA-IR (Oh et al., 2016). While dietary intervention stands out as the most effective method for weight loss, acknowledging the crucial role of exercise training in both weight management and overall well-being is essential (Cox, 2017). Various exercise training strategies have proven effective in enhancing physical performance, fostering improved health outcomes, and reducing body fat in both men and women (Cox, 2017). For optimal glycemic control and reduction of cardiovascular risk factors in individuals with T2DM, the American Diabetes Association (ADA) advises engaging in at least 150 minutes of aerobic exercise weekly (Colberg et al., 2010). Previous studies have indicated that various forms of aerobic training (AT), such as continuous running or walking training and high-intensity interval training, are effective methods for managing lipid profiles, insulin resistance, and the levels of circulating hepatokines (i.e., Fetuin A and B, FGF-21) (Tjønna et al., 2008; Kang et al., 2009; Tan et al., 2012; Shabkhiz et al., 2021; Rasouli Mojez et al., 2021; Sayevand et al., 2022; Rejeki et al., 2023; Kim et al., 2023).

Over the past few years, resistance training has become increasingly popular for enhancing physical fitness and reducing the risk of injuries (Sheykhlouvand et al., 2022; Behm and Colado, 2012). RT offers increased glucose transporter protein (GLUT) quantity, enhanced muscle mass, and elevated insulin receptor numbers in muscle cells (Holten et al., 2004). The American College of Sports Medicine (ACSM) suggests that engaging in at least three RT sessions per week, targeting all major muscle groups, and performing three sets of 10 repetitions may be an effective training regimen for managing T2DM symptoms (Colberg et al., 2010).

Numerous research studies have explored the impact of RT and AT on different aspects of T2DM (Snowling and Hopkins, 2006; Tjønna et al., 2008; Jorge et al., 2011; Shabkhiz et al., 2021; Rejeki et al., 2023; Kim et al.,

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2023). However, there is an ongoing debate regarding the effects of resistance or aerobic training on FGF-21 levels and health-related outcomes in obese individuals with T2DM (Holten et al., 2004; Jorge et al., 2011; Kim et al., 2023). Moreover, the available data on the effects of longitudinal RT still needs to be more conclusive (Shabkhiz et al., 2021; Rejeki et al., 2023; Kim et al., 2023). Since different types of exercise training result in varying exercise adaptations, further studies are needed to determine the superiority of each training method in terms of biochemical and health-related performance in T2DM populations. Therefore, the objective of this study was to examine the effects of a 12-week resistance and aerobic training on FGF-21 levels and other symptoms associated with metabolic disorders in men diagnosed with type 2 diabetes.

Methods

Study design

The study utilized a randomized controlled design consisting of two training groups (AT and RT) and a control group (CG). The duration of the study spanned 15 weeks, encompassing a one-week familiarization period, a one-week pretest phase, a 12-week training period, and a one-week posttest phase. All participants were familiarized with the study's design and objectives during the initial week. They also participated in trial exercises to become accustomed to the testing and training protocols (Gharaat et al., 2020; Barzegar et al., 2021). Anthropometric measurements were taken during a laboratory familiarization session. One week later, the participants' lower body maximal strength performance was assessed using the 5-repetition maximum of the leg press exercise. Following a 72-hour interval, an incremental exercise test was conducted to evaluate the subjects' aerobic capacity (i.e., peak oxygen consumption [$\dot{V}O_{2peak}$]). Biochemical variables were evaluated by collecting a blood sample 48 hours before and after the training regimen. Training sessions for all groups were conducted on Monday, Wednesday, and Friday afternoons from 5:00 to 7:00 P.M.

Participants

The sample size was determined following the methodology of Shabkhiz et al. (2021), with an alpha level of 0.05 and a power of 0.80. A priori power analysis was conducted using G* Power (Version 3.1.9.2, University of Kiel, Germany). The analysis indicated that a sample size of N = 10 for each group would be sufficient to detect significant effects of RT on FGF-1 response in men with T2DM. However, the sample size was subsequently increased to 12 participants per group to account for potential subject dropout during data collection. Initially, 58 diabetic men agreed to participate in the study. After meeting specific criteria, 22 subjects were excluded, and 36 were included in the study.

Exclusion and inclusion criteria:

1. Experience with T2DM for at least four years
2. Having a sedentary lifestyle with age between 40 to 45 years old
3. HbA1c level of 6.5% or higher with resting blood sugar ranging from 150 to 200 mg/dL
4. Body mass index greater than 30 kg/m^2
5. No history of musculoskeletal injuries or orthopedic problems affecting training efficiency

The subjects were matched based on the level of FGF-1 and then were randomly divided into two training groups (RT, n = 12 and AT, n = 12) and an inactive control group (CG, n = 12) (Table 1). The study employed the short form of the International Physical The Physical Activity Questionnaire (IPAQ) assessed the participants' physical activity level (Craig et al., 2003). The results revealed that the participants exhibited low levels of physical activity or were predominantly sedentary (McKay et al., 2022) and did not engage in structured physical activity before being included in the study. They relied solely on medication to manage their diabetes. The CG comprised diabetic men who did not engage in any physical activity program and depended exclusively on their medication. The groups were allocated based on a random process using a computer-generated random number. The randomization process was conducted using R software (version 2.14, Foundation for Statistical Computing). All subjects were fully informed about the research procedures, requirements, benefits, and risks prior to the study, and they provided their *written* consent and *voluntarily participated*. The Sichuan Normal University approved the study design and adhered to the ethical guidelines outlined in the Declaration of Helsinki for research involving human subjects.

Measurements

Anthropometry

A wall-mounted stadiometer (± 0.5 cm, Butterfly, Shanghai, China) measured the subjects' height. A digital scale (± 0.1 kg, BC-554 Ironman Body Composition Monitor, TANITA, IL, USA) was utilized for body mass measurement. The body mass index (BMI) was then calculated by dividing the body mass by the square of the subject's height, resulting in a value expressed in kg/m2.

Maximal strength

The strength of the lower body was assessed using the horizontal leg press exercise device (DHZ, FITNESS EQUIPMENT, UK). The strength measurement followed a method previously described by Kraemer and Fry (1995). Subjects underwent a general warm-up before being tested for their maximum strength. The load was gradually increased during consecutive trials until the subjects were unable to perform a proper lift with a complete range of motion and correct technique for five repetitions.

Table 1. Subjects' characterists (mean ± SD).

Groups	Age (y)	Height (cm)	Body mass (kg)	BMI (kg/m^2)	Time since diagnosis (y)	Fasting blood sugar (mg/dL)	Medication (Metformin) (mg/daily)
Resistance training	42.4 ± 2.8	178.6 ± 6.2	97.1 ± 8.6	30.8 ± 0.7	5.7 ± 2.2	175.2 ± 23.1	1875 ± 376
Aerobic training	42.2 ± 1.9	177.2 ± 8.4	98.2 ± 7.7	31.1 ± 0.9	6.1 ± 1.9	173.6 ± 24.7	1916 ± 358
Inactive control group	43.5 ± 1.8	175.4 ± 7.6	97.8 ± 8.9	31.5 ± 1.1	5.5 ± 2.3	170.3 ± 22.8	1958 ± 334

Subsequently, the subjects' 1RM was estimated using the equation provided by Brzycki (1993): 1RM = weight (kg)/1.0278 - (5RM × 0.0278). This method was chosen due to the intense nature of the 1RM test, which could pose a risk to untrained participants in resistance training. During the testing process, spotters and researchers were present to offer support and ensure the safety of the subjects.

Aerobic capacity

An incremental exercise test on a treadmill (T676, Sport Art Fitness, UK) determined the participants' aerobic capacity ($\dot{V}O_{2peak}$). The test commenced at an intensity of 3 km/hr and gradually increased by 2.5% every 2 minutes until the subjects reached volitional exhaustion. The time taken by the subjects was then recorded to estimate $\dot{V}O_{2peak}$ using the formula: $\dot{V}O_{2peak}$ = 1.444 (Time) + 14.99 (Hanson, 1984).

Blood sampling and analyses

Blood sampling was conducted 48 hours before the initiation of the training program and 48 hours after the final training session. To ensure consistency, subjects were instructed to arrive at the laboratory between 8 - 9 A.M. after a 12-hour fast and 8 hours of sleep. Compliance was confirmed through a personal interview before the measurements. Blood samples (15 mL) were drawn from the antecubital vein into plain evacuated test tubes. After allowing the blood to clot at room temperature for 30 minutes, the samples were centrifuged at 1500 g for 10 minutes. The resulting serum was separated and stored at -20°C in multiple aliquots for subsequent analysis. The photometric End Point method was employed to measure cholesterol, HDL, LDL, and triglyceride by available kits (Novus Biologicals, USA) using auto-analyzer devices (Hitachi®, model 704, 902, Japan). In addition, HbA1c was determined using the HPLC method with the assistance of a similar device to assess lipid profile. The ELISA kit (Eagle Biosciences, USA) measured glucose levels. Lastly, the insulin level was measured using a radioimmunoassay (RIA). Insulin resistance in the fasting state was assessed using a homeostasis model assessment (HOMA-IR) before and after the 12-week training intervention according to this formula: HOMA-IR = [fasting glucose (mmol/l) × fasting insulin (mU/l)/22.5]. Previous studies have confirmed the validity and reliability of HOMA-IR, showing a strong correlation between HOMA-IR and the glucose clamp technique in both pre- and post-treatment evaluations of type 2 diabetic patients (Katsuki et al., 2001; Ahmadizad et al., 2007). The FGF-21 levels were measured in commercially available ELISA kits (BioVendor, R&D, Czech Republic). In addition, serum testosterone and cortisol levels were measured using ELISA kits (Monobind, Inc. Lake Forest, USA). The coefficient of variation for the measurements was less than 7%.

Training program

Participants of training groups engaged in their training programs three times weekly on Monday, Wednesday, and Friday for 60 to 70 minutes in the afternoon between 5:00 to 7:00 P.M. for 12 weeks (Colberg et al., 2010). Each training session initiated with a 15-minute warm-up consisting of 5 minutes of walking and jogging, 5 minutes of dynamic stretching, and 5 minutes of moderate-intensity ballistic movements. Following the warm-up, participants engaged in either RT or AT interventions for approximately 30 to 45 minutes. The session concluded with a 10-minute cool-down, incorporating stretching exercises.

The AT program involved continuous running at 70 to 75% of maximal heart rate (HR_{max}), calculated using the formula 207 - (0.7 × age in years). The training duration progressively increased from 30 minutes in week 1 to 42 minutes in week 12, with a weekly increment of 1 minute. The authors controlled the exercise intensity using a heart rate monitor (Polar S610i, FIN, 90440, Finland), ensuring it remained between 70 and 75% of HR_{max} throughout the trial.

The RT program included full-body, multi-joint exercises using machines and dumbbells at 70 to 75% intensity, emphasizing lower-body exercises, similar to the AT group. These exercises included leg press, knee extension, knee flexion, dumbbell calf raise, bench press machine, and Lat pull down for 30 minutes at week 1 to 42 minutes at week 12 with increasing repetitions. For instance, each exercise began with 2 sets of 10 repetitions in week one and gradually progressed to 3 sets of 10 repetitions. These methods were implemented to regulate the intensity and volume load of the training programs in both the RT and AT interventions. Rest periods of 1 to 2 minutes were permitted between sets and exercises for recovery.

Additionally, the Borg 0-10 RPE Scale (Foster, 1998) was employed to assess the session rating of perceived exertion (sRPE) 10 minutes following each training session. Moreover, the RPE and the duration of the training (in minutes) were documented to clarify the workload parameters (Foster, 1998). Throughout the study period, the CG refrained from engaging in any additional physical exercise or activity beyond their initial declaration. Their sole involvement during the study was the consistent use of the prescribed medications. A certified strength and conditioning specialist provided direct supervision during the training sessions, guiding the subjects on the correct execution of each exercise.

Statistical analyses

The data were presented as the mean ± standard deviation (SD). Pre- and post-intervention values for the dependent variables were assessed for normal distribution using the Shapiro-Wilk Normality test. A 3 (group) x 2 (time) analysis of variance (ANOVA) was conducted to compare group differences. The effect size (ES) with a 95% confidence interval (CI) was used to evaluate the training effects, calculated using Hedge's g for all measures. According to Hopkins et al. (2009), effect sizes below 0.2 were considered trivial, 0.2 -0.6 small, 0.6 - 1.2 moderate, 1.2 - 2.0 large, 2.0 - 4.0 very large, and above 4.0 nearly perfect. Statistical significance was set at $\alpha \leq 0.05$.

Results

During the study, each subject exhibited full compliance, leading to a remarkable achievement of reaching a success rate of 100%. Moreover, no injuries were linked to the

training and testing methods. Furthermore, no statistically significant differences ($p > 0.05$) were observed between the groups at the baseline. Both the AT and RT groups resulted in significantly greater changes in all measured variables than the CG ($p = 0.001$). Both training interventions significantly ($p < 0.05$) decreased FBS (RT: *ES* = -1.78, 95% CI = -2.73 to -0.84; AT: *ES* = -1.11, 95% CI = -1.97 to -0.25) (Figure 1), HbA1C (RT: *ES* = -1.25, 95% CI = -2.12 to -0.37; AT: *ES* = -1.06, 95% CI = -1.91 to -0.20) (Figure 1), insulin (RT: *ES* = -1.37, 95% CI = -2.25 to -0.45; AT: *ES* = -0.97, 95% CI = -1.81 to -0.12) (Figure 1), HOMA-IR (RT: *ES* = -1.75, 95% CI = -2.69 to -0.81; AT: *ES* = -1.05, 95% CI = -1.90 to -0.20) (Figure 1), and cortisol (RT: *ES* = -1.24, 95% CI = -2.12 to -0.37; AT: *ES* = -1.01, 95% CI = -1.86 to -0.16) (Figure 2) from pre to post-intervention.

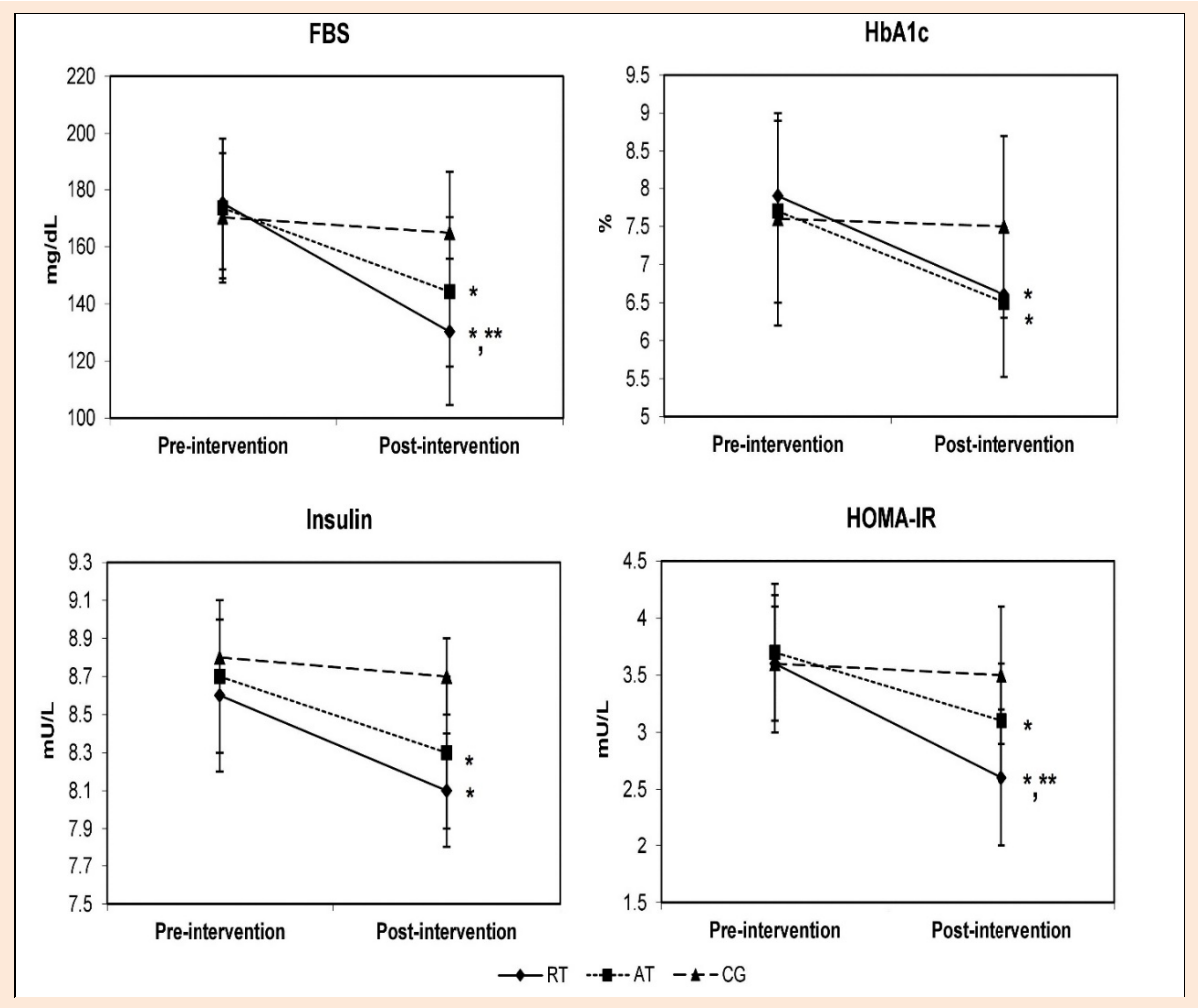

Figure 1. Changes in glucose homeostasis from pre to post-intervention in the groups (mean ± SD). * Significant differences vs. pre-intervention and CG ($p < 0.05$). ** Significant differences vs. AT ($p < 0.05$).

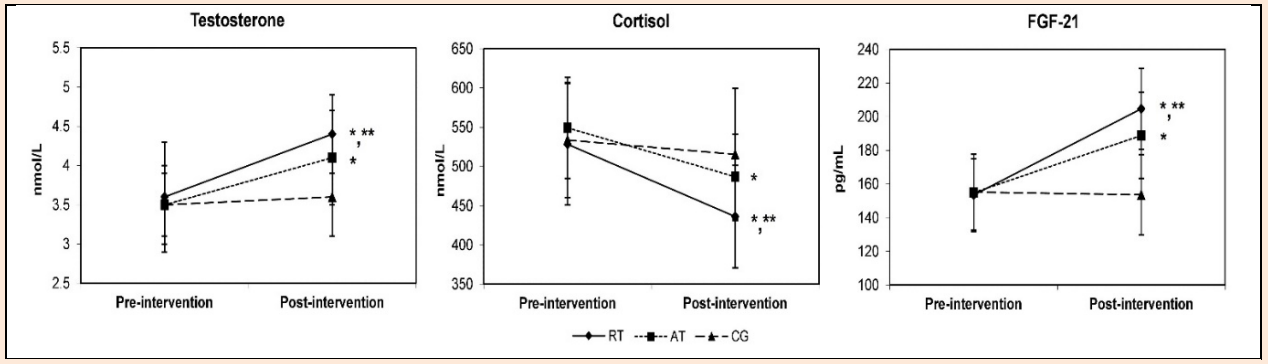

Figure 2. Changes in testosterone, cortisol and FGF-21 from pre to post-intervention in the groups (mean ± SD). * Significant differences vs. pre-intervention and CG ($p < 0.05$). ** Significant differences vs. AT ($p < 0.05$).

Table 2. Lipid profile changes form pre to post-intervention in the groups (mean ± SD).

	Pre-intervention	Post-intervention	MD	Hedge's g (95% CI)	
Cholesterol (mg/dL)					
RT	185.7 ± 20	163.7 ± 22.1*	-22	-1.01 (-0.16 to -1.86)	Moderate
AT	191.2 ± 27.8	156.9 ± 24.9*,**	-34.1	-1.25 (-0.38 to -2.13)	Large
CG	188.5 ± 21.1	184.6 ± 19.8	-3.9		
Triglyceride (mg/dL)					
RT	213.8 ± 25.9	189.6 ± 27.7*	-24.2	-0.87 (-0.03 to -1.71)	Moderate
AT	208.3 ± 28.9	171.7 ± 26.4*,**	-36.6	-1.28 (-0.40 to -2.15)	Large
CG	210.6 ± 27.5	208.5 ± 25.3	-2.1		
HDL (mg/dL)					
RT	31.5 ± 6.1	36.3 ± 5.8*	4.8	0.78 (-0.05 to 1.61)	Moderate
AT	32.2 ± 4.8	39.6 ± 5.6*,**	7.4	1.37 (0.48 to 2.26)	Large
CG	33.1 ± 3.9	33.3 ± 4.6	0.2		
LDL (mg/dL)					
RT	107.1 ± 6.3	98.8 ± 7.4*	-8.3	-1.17 (-0.30 to -2.03)	Moderate
AT	105.7 ± 6.3	93.8 ± 5.7*,**	-11.9	-1.91 (-0.95 to -2.88)	Large
CG	103.8 ± 7.1	99.2 ± 8.8	-3.6		

*significant differences vs. pre-intervention and CG ($p < 0.05$). **significant differences vs. RT ($p < 0.05$).

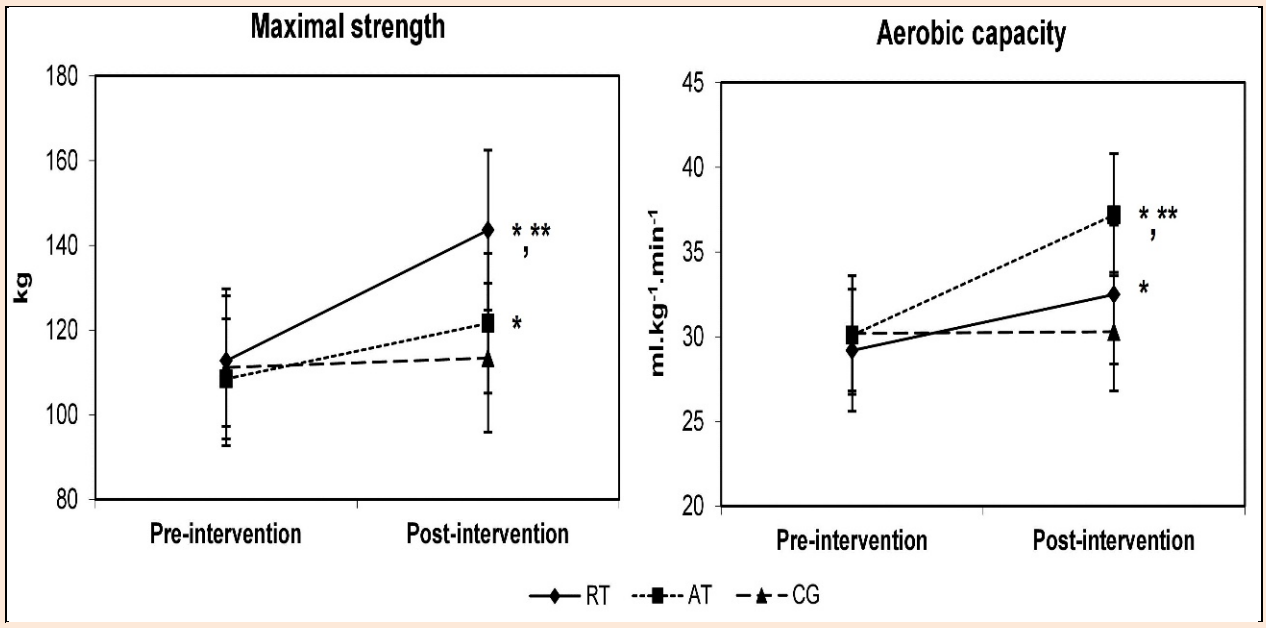

Figure 3. Changes in maximal strength and aerobic capacity from pre to post-intervention in the groups (mean ± SD). * Significant differences vs. pre-intervention and CG ($p < 0.05$). ** Significant differences vs. AT in maximal strength and vs. RT in aerobic capacity ($p < 0.05$).

In the lipid profile, both the training groups indicated significant ($p < 0.05$) moderate to large training effects at post-intervention compared with pre-intervention (Table 2).

In addition, both training interventions significantly ($p < 0.05$) increased testosterone (RT: *ES* = 1.27, 95% CI = 0.39 to 2.15; AT: *ES* = 1.14, 95% CI = 0.27 to 2.00) (Figure 2), FGF-21 (RT: *ES* = 2.16, 95% CI = 1.15 to 3.17; AT: *ES* = 1.36, 95% CI = 0.47 to 2.24) (Figure 2), maximal strength (RT: *ES* = 1.73, 95% CI = 0.79 to 2.67; AT: *ES* = 0.86, 95% CI = 0.02 to 1.70) (Figure 3), and aerobic capacity (RT: *ES* = 0.83, 95% CI = -0.01 to 1.66; AT: *ES* = 1.93, 95% CI = 0.96 to 2.90) (Figure 3) over the training period. There was significant time-regimen interactions ($p < 0.01$), indicating greater adaptive responses in the FBS (*ES* = -0.52, 95% CI = -1.34 to 0.29), HOMA-IR (*ES* = -0.87, 95% CI = -1.71 to -0.04), testosterone (*ES* = 0.52, 95% CI = -0.29 to 1.34), cortisol (*ES* = -0.82, 95% CI = -1.65 to 0.01), FGF-21 (*ES* = 0.61, 95% CI = 1.43 to -0.21), and maximal strength (*ES* = 1.19, 95% CI = 0.32 to 2.06) in RT than the AT over time (Figure 4). Conversely, the AT demonstrated greater adaptive changes ($p < 0.01$) in the cholesterol (*ES* = -0.28, 95% CI = -1.08 to 0.53), triglyceride (*ES* = -0.64, 95% CI = -1.46 to 0.18), HDL (*ES* = 0.46, 95% CI = -0.35 to 1.27), LDL (*ES* = -0.73, 95% CI = -1.56 to 0.10), and aerobic capacity (*ES* = 1.18, 95% CI = 0.31 to 2.04) compared to RT.

In relation to training workload parameters, both the RT and AT groups displayed similar sRPE (RT: 6.5 ± 0.8 scale, AT: 6.3 ± 0.6 scale) and training load (RT: 8420 ± 980 AU, AT: 8125 ± 777 AU) throughout the training period.

Discussion

Despite the documented effects of RT or AT on various aspects of T2DM (Snowling and Hopkins, 2006; Tjønna et al., 2008; Kang et al., 2009; Jorge et al., 2011; Tan et al.,

2012; Keihanian et al., 2019; Shabkhiz et al., 2021; Rejeki et al., 2023; Kim et al., 2023), uncertainty remains regarding the specific effects of these training approaches on managing glucose, lipid levels, and FGF-21 in obese individuals with T2DM over a defined training period. This study aimed to investigate the impact of a 12-week RT and AT on FGF-21 levels and symptoms associated with metabolic disorders in male individuals diagnosed with type 2 diabetes. Our findings indicated that AT was superior to RT in producing notable enhancements in lipid profiles and aerobic capacity. Conversely, participants in the RT group demonstrated greater improvements in glucose metabolism, hormonal changes, maximal strength, and FGF-21 levels compared to those in the AT group throughout the 12-week training period.

Both the AT (moderate ES) and RT (large ES) groups showed significant decreases in glucose metabolism factors such as FBS, HbA1c, insulin, and HOMA-IR over the training period, which aligns with previous studies reporting positive effects of exercise training on managing glucose metabolism and insulin sensitivity in T2DM (Ahmadizad et al., 2007; Keihanian et al., 2019; Shabkhiz et al., 2021). The improvements in insulin sensitivity and blood glucose regulation after the exercise training are generally attributed to improvements in insulin signaling, glucose transportation to working muscle fibers, protein kinase B activation, and the enhancement of GLUT4 protein expression, facilitating glucose uptake in muscle cells for energy production during physical activity (Boulé et al., 2005; Jorge et al., 2011; Oh et al., 2016).

RT seems more beneficial than AT in promoting adaptive responses in glucose metabolism. The group that engaged in RT experienced significantly greater decreases in FBS levels and HOMA-IR following the training sessions compared to the AT group. These findings suggest that the mechanical stress induced in muscle fibers during RT may trigger more substantial improvements in the mechanisms involved in glucose metabolism (Colberg et al., 2010), resulting in reduced levels of FBS and HOMA-IR post-training. Additionally, the heightened insulin sensitivity and reductions in FBS levels linked with RT may be predominantly influenced by alterations in FGF-21, as evidenced in this study, and by the AMP-activated protein kinase pathway (Chavez et al., 2009).

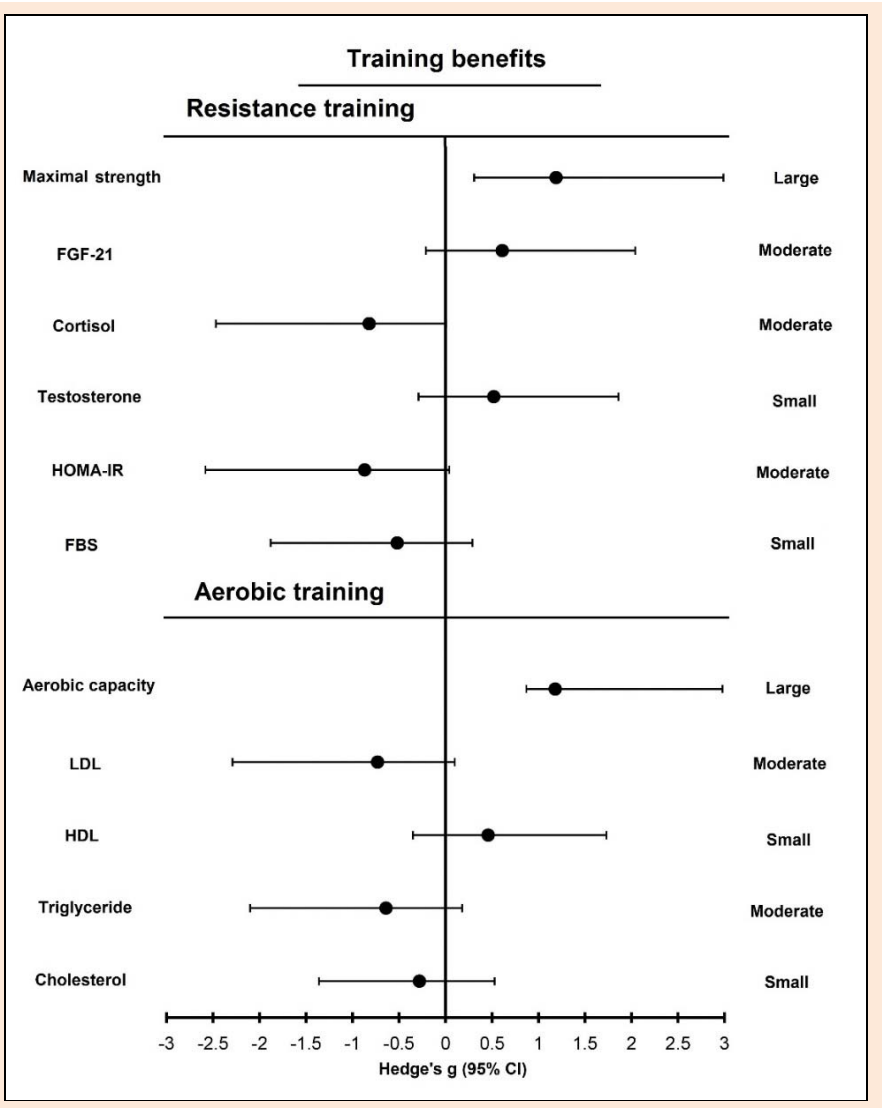

Figure 4. Comparing magnitude of differences in training benefits between resistance and aerobic training groups (ES with 95% CI).

Significant training effects, ranging from moderate to large, were noted for both the RT and AT groups regarding adaptations to lipid profiles post-intervention. Previous studies have reported reductions in cholesterol, LDL, and triglyceride levels, along with increases in HDL, following various types of exercise training (Mann et al., 2014; Keihanian et al., 2019; Franczyk et al., 2023). It seems that the regulation of the lipid profile after physical training may be linked to the increased expression of muscle and adipose tissue PPARγ and PGC-1α messenger RNA, as Ruschke et al. (2010) noted. The findings from the present study indicate that the AT group showed superior adaptive responses in managing lipid profiles compared to the RT group. This implies that the alterations in lipid profiles due to exercise training are probably influenced by the intensity and duration of the training (Mann et al., 2014). Specifically, continuous AT exercises stimulated various aerobic metabolic pathways, facilitating lipids' adaptations. Conversely, incorporating rest intervals during the moderate-intensity RT program led to a metabolic shift toward anaerobic pathways. It is clear that continuous aerobic running training, without interruptions, fosters aerobic metabolic conditioning. This results in the engagement of cellular oxidative metabolic pathways, consequently leading to reductions in lipid profiles following AT (Mann et al., 2014; Keihanian et al., 2019).

Both interventions increased testosterone levels and decreased serum cortisol concentrations, aligning with prior research indicating that exercise training exerts anabolic effects in diabetic men (Baillot et al., 2012). Elevated resting testosterone levels and reduced cortisol levels generally signify an anabolic state and improve health outcomes in individuals with T2DM (Khan et al., 2022). Conversely, in diabetic individuals, decreased testosterone, increased cortisol levels, and the advancement of insulin resistance may trigger a catabolic state that results in decreased muscle mass (Khan et al., 2022). Exercise training has been identified as an effective therapeutic approach for regulating catabolic and anabolic hormones by downregulating adrenal gland receptors, which subsequently reduces ACTH and cortisol levels while increasing testosterone levels post-training (Kraemer and Ratamess, 2005). Results from the current investigation indicate that the RT group displayed greater adaptive responses in testosterone and cortisol levels compared to the AT group. The hypothesis suggests that the mechanical stress caused by weight loads during RT might have triggered the downregulation of receptors in the adrenal gland, potentially leading to more pronounced hormonal adaptations (Kraemer and Ratamess, 2005).

Twelve weeks of AT and RT induced large and very large training effects in FGF-21 responses. FGF-21 plays a crucial role in regulating glucose homeostasis, potentially enhancing glucose uptake by up-regulating GLUT4 and serving as a therapeutic option for type 2 diabetes (Chavez et al., 2009; Kim et al., 2023). Exercise training effectively manages T2DM symptoms and hepatokines by increasing natural inhibitors of the insulin receptor tyrosine kinase in the liver, insulin sensitivity, GLUT-4, glucose transporter protein, and mRNA levels, glycogen synthesis, and hexokinase activity, muscle glucose uptake, and changes in muscle composition (Tjønna et al., 2008; Matuszek et al., 2010; Oh et al., 2016).

Following the intervention, RT demonstrated more substantial adaptive responses compared to AT. The impact of chronic exercise training on FGF-21 levels and the particular exercise modality has been discussed, yet the findings remain inconclusive (increase [Keihanian et al., 2019], decrease [Shabkhiz et al., 2021]). Resistance exercise training induces FGF-21 activation, which in turn enhances insulin action in muscles, thereby improving glucose metabolism upstream of AMP-activated kinase activity (Loyd et al., 2016). This occurs because FGF-21 stimulates mitochondrial production and increases the oxidative capacity of myofibrils (Rockl et al., 2007), improving systemic glucose homeostasis (Saltiel and Kahn, 2001). However, these assertions rely on speculation, underscoring the need for further investigations to validate them across diverse populations and analyze the mechanisms responsible for these variations following RT and AT.

The RT group exhibited greater increases in maximal strength, while the AT group demonstrated more adaptive changes in aerobic capacity. This underscores the specificity of training in driving meaningful adaptations. These results are consistent with prior studies showing the positive impact of RT on strength gains and AT on aerobic capacity improvements. Increased maximal strength may result from enhanced motor neuron excitability, increased motor unit firing frequency, elevated efferent motor drive, and muscle hypertrophy following 12 weeks of RT (Elgueta-Cancino et al., 2022). On the other hand, improved aerobic capacity following AT could be attributed to enhancements in muscle fiber capillary density and cardiac function, which facilitate better oxygen delivery (Sheykhlouvand and Gharaat, 2024) and optimize oxygen utilization by the muscles during aerobic exercises (Fereshtian et al., 2017; Sheykhlouvand et al., 2018a; 2018b; Ross et al., 2023).

One potential limitation of this study was the absence of laboratory measurements of resting cytokines, myokines, and other hepatokines relevant to diabetic men. This aspect should be explored in future studies. Lastly, we utilized the HOMA-IR to assess IR and clarify the impact of RT and AT. While the hyperinsulinaemic-euglycaemic clamp is considered the gold standard for assessing IR, financial constraints prevented us from employing this approach. However, previous research (So et al., 2020) has shown a significant relationship between HOMA-IR and the hyperinsulinaemic-euglycaemic clamp, suggesting that HOMA-IR can be a viable method for assessing IR in human studies.

Conclusion

The results of the present study indicate that 12 weeks of both aerobic and resistance training yield significant moderate to large effects on FGF-21 levels, symptoms associated with T2DM, and enhancements in physical attributes. Resistance training seems to be more effective in prompting favorable changes in FBS, HOMA-IR, testosterone, cortisol, maximal strength, and FGF-21 levels. Conversely, aerobic training proves more beneficial for enhancing lipid

profiles and aerobic capacity in obese men with T2DM. In practical terms, resistance training is recommended for controlling glucose homeostasis, while aerobic training is preferred for managing lipid profiles.

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Key points

- The integration of RT and AT could stimulate adaptive mechanisms involved in effectively managing symptoms associated with T2DM.
- Comparative analysis indicates RT is effective for glucose metabolism and hormonal adaptations, whereas AT is better suited for managing lipid profiles.
- Implementing of RT resulted in greater improvement in maximal strength, while AT led to a considerable increase in aerobic capacity.

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