Short-Term High-Intensity Interval Training for Reducing Advanced Glycation End Product Accumulation and Cardiovascular Disease Risk in Female College Students with Normal-Weight Obesity: A Randomized Controlled Trial Postprint

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Abstract

Background: Individuals with normal weight obesity (NWO) are prone to cardiovascular disease during middle and older adulthood. High-intensity interval training (HIIT) has been proven to improve cardiovascular health, yet research on the efficacy of HIIT in improving cardiovascular risk in NWO populations remains limited.

Objective: To investigate the effects of 4-week HIIT on advanced glycation end-products (AGEs) and blood glucose in female college students with NWO, and to clarify the efficacy of HIIT in reducing cardiovascular disease risk.

Methods: Among 137 female college students, 40 individuals with NWO were screened via InBody-770 and randomly assigned to a control group (n=13) or an HIIT intervention group (n=17). Following a 1-week acclimation period, the HIIT group completed 4 weeks of HIIT training at 5 days/week. Both groups underwent pre- and post-intervention assessments of body weight, BMI, body fat percentage (BF%), visceral fat level (VFL), visceral fat area (VFA), and waist circumference using InBody-770; non-invasive AGEs measurement using AGE Reader mu; fasting blood glucose from fingertip blood using a glucose analyzer; four blood lipid ratios calculated via a lipid analysis system; and lifetime cardiovascular risk evaluation using the China-PAR model.

Results: Compared with the control group, the HIIT intervention group exhibited significant reductions after 4 weeks in: (1) BMI, BF%, VFA, VFL, and waist circumference ($p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$, $p<0.01$); (2) AGEs and blood glucose (p<0.01, p<0.01); and (3) TC/HDL, LDL/HDL, TG/HDL ratios, and cardiovascular risk (p<0.01, p<0.01, p<0.01, p<0.01).

Conclusion: Four weeks of HIIT significantly reduces body fat, improves AGEs and blood glucose levels, and decreases cardiovascular disease risk in female college students with NWO.

Full Text

Short-Term High-Intensity Interval Training Reduces Advanced Glycation End-Product Accumulation and Cardiovascular Disease Risk in Normal-Weight Obese Female University Students: A Randomized Controlled Trial

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Abstract

Background: Individuals with normal-weight obesity (NWO) are prone to cardiovascular disease during middle and old age. While high-intensity interval training (HIIT) has been demonstrated to improve cardiovascular health, its effects on cardiovascular risk reduction in NWO populations remain unclear.

Objectives: To investigate the effects of four weeks of HIIT on advanced glycation end-products (AGEs) and fasting blood glucose in NWO female university students, and to elucidate the role of HIIT in reducing cardiovascular disease risk.

Methods: Forty NWO subjects were screened from 137 female university students using InBody-770 analysis and randomly divided into a control group (n=13) and an HIIT intervention group (n=17). Following one week of adaptive training, the HIIT group completed four weeks of training five days per week. Body weight, BMI, body fat percentage (BF%), visceral fat level (VFL), visceral fat area (VFA), and waist circumference were measured using InBody-770. AGEs were assessed non-invasively using an AGE Reader mu. Fingertip blood samples were collected to measure fasting blood glucose using a glucose analyzer, and blood lipid ratios were calculated using a lipid analysis system. Cardiovascular lifetime risk was evaluated using the China-PAR model.

Results: Compared with the control group after four weeks: (1) The HIIT group showed significant reductions in BMI, BF%, VFA, VFL, and waist circumference ($p<0.01$ for all); (2) AGEs and blood glucose decreased significantly ($p<0.01$ for both); (3) TC/HDL, LDL/HDL, TG/HDL ratios, and cardiovascular risk decreased significantly ($p<0.01$ for all).

Conclusion: Four weeks of HIIT can effectively reduce body fat, improve AGEs and blood glucose levels, and decrease cardiovascular disease risk in NWO female university students.

Keywords: high-intensity interval training; normal-weight obese female university students; advanced glycation end-products; cardiovascular disease

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Introduction

Karelis et al. introduced the concept of normal-weight obesity (NWO) in 2004 to describe the relationship between normal body weight, high fat content, and metabolic abnormalities [1]. NWO is defined as individuals with normal weight and body mass index (BMI) but body fat percentage (BF%) exceeding 30% [2]. Differences in body fat distribution and fat mass may represent cardiovascular disease risk factors. Clinical studies indicate that NWO is characterized by excessive visceral fat, predisposing individuals to insulin resistance, dyslipidemia, and hypertension [3], thereby increasing the risk of diabetes and cardiovascular disease [4]. Previous research has shown a high prevalence of NWO among Chinese university students, particularly females, suggesting a strong association between NWO in women and future cardiovascular disease [5]. Therefore, effective intervention during young adulthood for NWO females not only improves current physical fitness but also reduces future cardiovascular disease risk.

Advanced glycation end-products (AGEs) are stable end-products formed through non-enzymatic glycation reactions between reducing sugars and free amino groups on proteins, lipids, and nucleic acids [6]. Under pathological conditions, excessive AGEs that are not degraded or neutralized by detoxification mechanisms bind to the receptor for AGE (RAGE), triggering inflammation [7] and oxidative stress responses [8]. Research demonstrates that AGEs promote chronic inflammation and insulin resistance, forming the pathological basis for obesity and metabolic syndrome [9]. Furthermore, recent studies indicate that AGE accumulation in blood is closely related to cardiovascular disease (CVD) progression [10], potentially representing an important factor linking obesity to CVD and serving as a biomarker for the transition from obesity to multiple sclerosis [11]. Although serum AGEs levels are significantly elevated in obese patients [12], it remains unclear whether AGEs levels are altered in NWO. Given that excessive visceral fat is a key factor increasing cardiovascular risk in NWO compared to other metabolic obesity types [13], understanding AGEs level changes would facilitate predicting cardiovascular disease risk in NWO.

High-intensity interval training (HIIT) has proven to be an efficient and time-saving exercise modality that produces beneficial physiological effects and promotes physical and mental health across diverse populations (e.g., fitness enthusiasts, obese patients, diabetics, post-stroke rehabilitation patients, and elderly individuals). HIIT' s effectiveness stems from its exercise pattern, which involves several short bouts of high-intensity exercise ($ $80% HRmax, typically reaching anaerobic threshold) interspersed with low-intensity recovery or rest periods (65-80% HRmax). This approach accelerates metabolism, induces excess post-exercise oxygen consumption (EPOC), enhances oxygen uptake rate, promotes fat oxidation, and improves fitness in relatively short timeframes [14]. Additionally, HIIT offers varied formats and is not restricted by location, making it suitable for multiple populations. Studies show that compared to conventional aerobic training, HIIT more effectively reduces abdominal and visceral fat, improves dyslipidemia [15], lowers blood pressure [16], and enhances cardiopulmonary and vascular function [17]. Our previous clinical research demonstrated that short-term HIIT improved arterial velocity pulse index (AVI) and arterial pressure volume index (API) while reducing arterial stiffness in NWO female university students [18]. However, whether HIIT produces favorable physiological effects on AGEs in NWO populations remains unknown. This study investigated the effects of four weeks of HIIT on body composition, AGEs, blood glucose, and blood lipid parameters in NWO female university students to provide experimental evidence for HIIT' s role in reducing cardiovascular risk in this population.

Methods

1.1 Study Subjects and Inclusion Criteria Between November and December 2020, 137 female university students with normal BMI (18.5-24.9 kg/m^2) aged 18-21 years were recruited from Shanghai University of Medicine and Health Sciences. Using the Asian female NWO criterion (BF% > 30%) [19], 40 eligible NWO subjects were screened via InBody body composition analysis (Biospace Co., Seoul, Korea) after exercise risk assessment and randomly divided into two groups: a sedentary control group (n=20) and an HIIT intervention group (n=20). All participants underwent health screening and personal data collection. Exclusion criteria included: (1) limited exercise capacity preventing high-load training, such as skeletal muscle injury, osteoarticular disease, or pain history; (2) history of cardiovascular disease, hypertension, or diabetes; (3) respiratory diseases; (4) family history of sudden death, medication history, or current drug use. Participants unable to guarantee training time or who were not actively engaged were also excluded. Ten subjects withdrew during the intervention due to personal reasons (7 from the control group, 3 from the HIIT group). General characteristics of both groups are detailed in , with no statistically significant between-group differences (p>0.05). All participants provided informed consent after understanding the experimental procedures and risks. This study was approved by the Shanghai University of Medicine and Health Sciences Ethics Committee (2020-20YJCZH001-03) and registered internationally (ChiCTR2100050711).

1.2 Exercise Intervention Protocol The HIIT group underwent one week of pre-adaptive training to learn HIIT movements and familiarize themselves with the training protocol with gradually increasing intensity. From week 2, they completed four weeks of HIIT training five days per week. Each session began with 10 minutes of warm-up (dynamic lower limb stretches, "world' s greatest stretch," rotator cuff activation), followed by 30 minutes of HIIT consisting of nine exercises (jumping jacks, high knees with arm raises, squat jumps, burpees, high plank, lateral jumps, alternating knee tucks, mountain climbers, and lunges). Each exercise lasted 40 seconds with 20 seconds rest, with 60 seconds rest between circuits, repeated for three circuits. Heart rate and fingertip oxygen saturation were monitored in real-time using wrist-worn pulse oximeters, with exercise intensity reaching 90% of maximum heart rate (HRmax = 220 - age). Each session concluded with 10 minutes of static stretching for upper and lower limbs. Training occurred daily from 16:30-17:30 in an exercise classroom under professional supervision to prevent injury or adverse events. To ensure intervention effectiveness, the control group did not exercise during the HIIT training period. Dietary and other lifestyle habits were not intervened in either group.

1.3 Body Composition Analysis Before and after HIIT intervention, BMI, BF%, visceral fat level (VFL), visceral fat area (VFA), and waist circumference were measured using InBody-770. Participants removed shoes, socks, hats, and heavy outerwear, and were instructed not to carry electronic devices or wear rings or bracelets. They grasped the handles with arms extended and abducted 30° during measurement.

1.4 AGEs Measurement AGEs levels in skin tissue were measured non-invasively using an AGE Reader mu device (Diagnoptics Technologies B.V., Groningen) before and after HIIT intervention. After entering the participant' s age, the forearm was placed on the reader in a relaxed position, and measurement was initiated.

1.5 Blood Glucose Measurement Fingertip blood samples were collected after HIIT intervention to measure fasting blood glucose using a glucose analyzer (BeneCheck, Taiwan).

1.6 Blood Lipid Parameters Fingertip blood was collected before and after HIIT using a disposable lancet. The second blood drop (35 L) was collected via capillary tube and applied to a disposable 3-in-1 lipid test card (Model

CCS-114, China). The card was inserted into a lipid analysis system (Model CCM-111, China) using dry chemistry to measure total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). TC/HDL, LDL/HDL, and TG/HDL ratios were calculated to assess cardiovascular disease risk.

1.7 Cardiovascular Risk Assessment Cardiovascular lifetime risk was assessed before and after HIIT according to the *Chinese Guidelines for Cardiovascular Disease Risk Assessment and Management* [20]. The China-PAR model, based on large Chinese cohort data, incorporates factors including sex, age, residence, region, waist circumference, TC, HDL, blood pressure, antihypertensive medication use, diabetes status, smoking, and family history of cardiovascular disease [21, 22].

1.8 Statistical Methods All data are expressed as mean $\pm$ SE. SPSS 26.0 was used for statistical analysis. Repeated measures ANOVA and simple effects tests were applied to analyze measured parameters, with significance level set at $\alpha = 0.05$. Spearman correlation analysis was used to examine the relationship between AGEs and cardiovascular risk, with p<0.05 considered statistically significant.

Results

2.1 Effects of HIIT on Body Composition in NWO Subjects As shown in , significant time × group interactions were observed for body weight (F(1,28)=21.348, p<0.001, ^{2}=0.433). Simple effects tests revealed no significant pre-intervention differences between groups (HIIT: 58.61\$±1.03*kgvs.control* : 58.34±1.18*kg*; *F*(1, 28) = 0.031, *p* = 0.862, *η*{2}= 0.001).*Afterfourweeks,HIITgroupweightwassignificantlylowerthancontrol*(57.56±1.08*kgvs.*59.85±1.24*kg*; *F*(1, 28) = 1.

BMI showed significant time × group interaction (F(1,28)=11.249, p=0.002, ^{2}=0.287). No pre-intervention differences existed (HIIT: 21.93\$±0.28*kg/m*^{2}\$ vs. control: 22.15\$±0.31*kg/m*{2}; *F*(1, 28) = 0.270, *p* = 0.607, *η*{2}= 0.010).*Post − interventionBMIwassignificantlylowerintheHIITgroup*(21.03±0.41*kg/m*^{2}\$ vs. 23.21\$±0.46*kg/m*{2}; *F*(1, 28) = 12.560, *p* = 0.001, *η*{2}\$=0.310).

BF% demonstrated significant time × group interaction (F(1,28)=46.558, p<0.001, ^{2}=0.624). Pre-intervention values were similar (HIIT: 33.52\$±0.63±0.72{2}= 0.007).*Afterfourweeks,HIIT* indicating effective weight and body fat reduction.

VFA showed significant time × group interaction (F(1,28)=15.575, p<0.001, ^{2}=0.357). Pre-intervention VFL values were 95.07\$±3.69*and*104.36±4.22(*F*(1, 28) = 2.746, *p* = 0.109, *η*{2}= 0.089).*Post − interventionVFAwassignificantlylowerintheHIITgroup*(66.40±3.12*vs.*93.28±3.56; *F*(1, 28) = 0.535).*Within−groupcomparisonsshowedsignificantVFAreductionsinbothcontrol*(*F*(1, 28) = 10.919, *p* = 0.003, *η*{2}= 0.281)*andHIITgroups*(*F*(1, 28) = 95.529, *p* < 0.001, *η*{2}\$=0.773).

VFL exhibited significant time × group interaction (F(1,28)=16.330, p<0.001, ^{2}=0.368). Pre-intervention VFL values were 9.92$±0.42and8.94±0.37(F(1,28) = 3.114, p = 0.089, η{2}= 0.100).Post − interventionVFLwassignificantlylowerintheHIITgroup(8.85±0.37vs.6.18±0.33; F(1,28) = 29 0.511).Within−groupcomparisonsrevealedsignificantVFLdecreasesinbothcontrol(F(1,28) = 11.732, p = 0.002, η{2}= 0.295)andHIITgroups(F(1,28) = 101.116, p < 0.001, η{2}= 0.783).Theseresultssuggestthatdespitepre−interventionVFAapproaching100cm^{2}$, VFL remained within the normal range (1-9), and HIIT effectively reduced abdominal visceral fat content.

Waist circumference showed non-significant time × group interaction (F(1,28)=3.107, p=0.089, ^{2}=0.100). Simple effects tests revealed no pre-intervention differences (HIIT: 81.63$±1.10cmvs.control : 79.31±0.96cm; F(1,28) = 2.531, p = 0.123, η{2}= 0.083).Post − interventionwaistcircumferencewassignificantlylowerintheHIITgroup(80.16±0.94cmvs.75. 0.325).Within−groupcomparisonsshowednosignificantchangeinthecontrolgroup(F(1,28) = 2.353, p = 0.136, η{2}= 0.078)butasignificantreductionintheHIITgroup(F(1,28) = 19.640, p < 0.001, η{2}= 0.412).Thesefindingsindicatethatwhilepre−interventionwaistcircumferenceapproached80cm(nearthe85cm cm.

2.2 Effects of HIIT on Blood Lipid Parameters in NWO Subjects

As shown in , TC/HDL demonstrated significant time × group interaction (F(1,28)=81.708, p<0.001, ^{2}=0.745). Simple effects analysis revealed no pre-intervention differences (F(1,28)=5.824, p=0.023, ^{2}=0.172). Post-intervention TC/HDL was significantly lower in the HIIT group (F(1,28)=16.505, p<0.001, ^{2}=0.371). Within-group comparisons showed an increasing trend in the control group (F(1,28)=2.376, p=0.134, ^{2}=0.078) but a significant decrease in the HIIT group (F(1,28)=160.189, p<0.001, ^{2}=0.851).

LDL/HDL showed significant time × group interaction (F(1,28)=90.098, p<0.001, ^{2}=0.763). Pre-intervention TG/HDL values were not significantly different (F(1,28)=0.394, p=0.535, ^{2}=0.014). Post-intervention TG/HDL was significantly lower in the HIIT group (F(1,28)=116.868, p<0.001, ^{2}=0.807). Within-group comparisons revealed an increasing trend in the control group (F(1,28)=2.376, p=0.134, ^{2}=0.078) and a significant reduction in the HIIT group (F(1,28)=160.189, p<0.001, ^{2}=0.851), indicating HIIT effectively reduced TG/HDL.

TG/HDL exhibited significant time × group interaction (F(1,28)=70.763, p<0.001, ^{2}=0.716). Pre-intervention values were similar (F(1,28)=0.501, p=0.485, ^{2}=0.018). Post-intervention TG/HDL was significantly lower in the HIIT group (F(1,28)=113.689, p<0.001, ^{2}=0.802). Within-group comparisons showed an increasing trend in controls (F(1,28)=3.250, p=0.082, ^{2}=0.104) and a significant decrease in the HIIT group (F(1,28)=114.86, p<0.001, ^{2}=0.804). These results demonstrate that HIIT effectively improved blood lipid ratios and reduced cardiovascular disease risk in NWO female university students.

2.3 Effects of HIIT on Cardiovascular Risk in NWO Subjects

To further clarify HIIT' s impact on cardiovascular risk, we assessed cardiovascular disease risk before and after intervention. Since the risk assessment tool applies to individuals aged 20+ years, only nine HIIT group subjects were eligible. As shown in , significant time × group interaction was observed for cardiovascular risk (F(1,20)=7.838, p=0.011, ^{2}=0.282). Simple effects tests revealed significant pre-intervention differences between groups (F(1,20)=7.618, p=0.012, ^{2}=0.276). After four weeks, cardiovascular risk was significantly lower in the HIIT group (6.93$±1.17±0.97{2}= 0.530).Within − groupcomparisonsshowednosignificantchangeinthecontrolgroup(F(1, 20) = 3.827, p = 0.065 0.161)andanon − significantreductionintheHIITgroup(F(1, 20) = 4.057, p = 0.058, η^{2}$=0.169).

2.4 Effects of HIIT on AGEs and Blood Glucose in NWO Subjects As shown in , AGEs demonstrated significant time × group interaction (F(1,28)=47.929, p<0.001, ^{2}=0.631). Simple effects analysis revealed no pre-intervention differences (HIIT: 1.82$±0.05vs.control : 1.71±0.07; F(1, 28) = 1.560, p = 0.222, η{2}= 0.053).Afterfourweeks, AGEsweresignificantlylowerintheHIITgroup(1.11±0.05vs.1.59±0.06; F(1, 28) = 10 0.795).Within−groupcomparisonsshowednosignificantchangeincontrols(F(1, 28) = 3.215, p = 0.084, η{2}= 0.103)butasignificantreductionintheHIITgroup(F(1, 28) = 71.683, p < 0.001, η{2}$=0.719), indicating that four weeks of HIIT effectively reduced AGEs levels.

Blood glucose showed significant time × group interaction (F(1,28)=33.614, p<0.001, ^{2}=0.546). Pre-intervention values were similar (HIIT: 6.11$±0.20mmol/Lvs.control : 6.22±0.23mmol/L; F(1, 28) = 0.138, p = 0.713, η{2}= 0.005).Post − interventionglucosewassignificantlylowerintheHIITgr 0.533).Within−groupcomparisonsrevealedsignificantglucoseelevationincontrols(F(1, 28) = 6.030, p = 0.021, η{2}= 0.177)andsignificantreductionintheHIITgroup(F(1, 28) = 35.991, p < 0.001, η{2}$=0.562), demonstrating HIIT' s effectiveness in reducing blood glucose.

2.5 Correlation Analysis Between AGEs and Cardiovascular Risk As shown in [Figure 1: see original paper], the correlation coefficient between AGEs and cardiovascular risk was r=-0.006 (p=0.979), indicating no significant correlation between AGEs levels and cardiovascular risk in NWO subjects.

Discussion

NWO is diagnosed when BMI is normal but BF% exceeds 30%, with clinical features characterized by excessive visceral fat [3]. Fat deposits form plaques on the walls of large and medium arteries (aorta, coronary arteries, cerebral arteries, carotid arteries). These plaques narrow vascular lumens, reduce blood flow, and increase blood pressure, causing decreased tissue perfusion. Additionally, they secrete pro-inflammatory cytokines (IL-1β, TNF-α, NF- B) and generate free radicals that induce oxidative stress. The combination of chronic inflammation and oxidative stress promotes vascular smooth muscle cell proliferation, reduces vascular compliance, and increases vasoconstrictive factors, further decreasing blood flow [23]. This mechanism underlies the development of hypertension, myocardial infarction, and ischemic stroke in NWO patients during middle and old age [24]. Supporting evidence indicates that NWO doubles the incidence of subclinical atherosclerosis compared to normal-weight lean individuals, with higher rates of soft plaques, pulse wave velocity, and vascular inflammation [25, 26]. Therefore, although TC, HDL, LDL, and TG may remain within normal physiological ranges in NWO patients, they are more susceptible to future atherosclerosis and cardiovascular disease [27]. Notably, because these patients are young with normal weight, metabolic and cardiovascular diseases may not manifest clinically for years, obscuring the need for early detection and treatment [1]. Early screening for cardiovascular risk in NWO and timely intervention are crucial for understanding obesity subtypes, improving clinical guidance, and implementing secondary prevention, holding significant importance for cardiovascular disease prevention. Our results show that NWO subjects had VFL concentrated at 8-10, VFA approaching 100 cm^2, and waist circumference around 80 cm, indicating excessive visceral fat and increased risk for diabetes and CVD [4].

We also measured TC/HDL, LDL/HDL, and TG/HDL ratios to assess cardiovascular disease risk. Lorenzo et al. reported values of 2.56±0.54, 1.29±0.37, *and*0.78±0.33, respectively, in young healthy adults [4]. Our NWO subjects showed significantly higher pre-intervention ratios, indicating substantially increased cardiovascular disease probability. Cardiovascular risk assessment revealed a lifetime risk probability of approximately 10.99%, with control group risk increasing from 11.82% to 14.13%. Although current risk remains low, the potential for NWO to develop cardiovascular disease may have insidious onset and long latency, particularly given our young university student population. Identifying effective screening markers and implementing economical, efficient interventions to improve NWO physical fitness represents an important strategy for reducing future cardiovascular risk.

The role of AGEs in exacerbating metabolic disorders has gained increasing recognition. Recent research shows that chronic hyperglycemia increases AGEs in fibroblast-like synoviocytes of diabetic osteoarthritis patients, accelerating pathological progression [28]. Hyperglycemic environments alter protein structure and function while increasing inflammation and oxidative stress, accelerating AGE precursor formation [41, 42]. AGE-RAGE binding induces insulin resistance [29], inflammation [7], and oxidative stress [8], worsening metabolic disease severity [2]. Thus, increased AGEs represent both a pathogenic mechanism and important pathological feature of obesity and diabetes. Additionally, substantial evidence indicates that AGE-RAGE-mediated internal environment disruption accelerates CVD development [10, 30, 31], while reducing AGE accumulation and RAGE expression can decrease CVD risk [31]. Given the close relationship between AGEs and metabolic obesity/CVD, we hypothesized AGEs might serve as a biomarker for cardiovascular risk in NWO.

We pioneered non-invasive skin AGEs measurement in China, offering more convenient and accurate detection within 12 seconds compared to traditional methods, facilitating cardiovascular health assessment in NWO populations. Previous studies reported skin AGEs levels of 1.11$±0.20to1.53±$0.30 in healthy 10-30-year-olds [32]. Our subjects showed slightly elevated pre-intervention AGEs levels. Since chronic hyperglycemia accelerates AGEs formation and fasting glucose is an important marker for diabetes development in NWO, we measured fasting glucose levels. Pre-intervention and post-intervention values in the control group slightly exceeded 6.1 mmol/L (normal fasting glucose). Correlation analysis between AGEs and cardiovascular risk revealed low correlation, suggesting that NWO' s impact on cardiovascular risk in youth may not depend on AGEs generation, a hypothesis supported by our blood AGEs and glucose level changes.

HIIT, widely used in competitive sports, has been increasingly applied in public fitness and rehabilitation medicine. Comparative studies demonstrate that HIIT achieves better results than continuous aerobic exercise in weight control, fat reduction (especially visceral fat), and lean mass increase in shorter timeframes, with well-established safety [26]. Meta-analyses show similar effectiveness between HIIT and moderate-intensity continuous training for reducing total body fat and waist circumference in overweight/obese adults, but HIIT requires 40% less exercise time, indicating higher time efficiency [29]. Additionally, research on obese diabetic women found that intermittent exercise produced lower ratings of perceived exertion (RPE) than continuous exercise at the same intensity, with shorter bouts feeling easier and more enjoyable, enhancing adherence [33]. Our previous clinical study found that four weeks of HIIT not only reduced weight and improved body composition but also improved resting heart rate, blood pressure, AVI, and API while reducing arterial stiffness [24]. However, HIIT' s effects on AGEs levels and cardiovascular risk in NWO were previously unknown. Our results demonstrate that four weeks of HIIT significantly reduced AGEs, fasting glucose, BF%, VFL, VFA, waist circumference, and blood lipid ratios, decreasing cardiovascular risk from 9.79% to 6.93% in NWO subjects, indicating that short-term HIIT effectively reduces AGEs accumulation, visceral fat content, and cardiovascular disease risk.

Notably, HIIT' s physiological effects are influenced by exercise mode, load intensity, repetitions, duration, rest intensity, rest duration, sets, inter-set intensity, and inter-set duration [34], suggesting different HIIT protocols may produce varying effects. Future clinical applications require optimal exercise protocols for NWO patients. Additionally, due to HIIT' s high intensity, pre-exercise risk assessment, gradually increasing adaptive training, adequate warm-up and cool-down, and injury prevention measures are essential to ensure safety, scientific validity, and effectiveness.

Outlook and Limitations

Our NWO subjects were exclusively female university students with a small sample size, potentially limiting evaluation of HIIT' s effects on AGEs and cardiovascular risk. Future studies will increase sample sizes across age groups to clarify relationships between NWO stage and cardiovascular risk and HIIT' s role. Additionally, the biochemical mechanisms underlying HIIT' s reduction of AGEs accumulation remain unclear. Future research will establish NWO animal models for molecular-level investigation. Since AGEs can be generated through dietary intake (e.g., Western diets), subsequent studies will consider combining dietary restriction with HIIT intervention to provide theoretical basis for optimal clinical strategies to improve NWO physical fitness and reduce cardiovascular disease risk.

Author Contributions

HU Jingyun conceived the study, established overall objectives, and took responsibility for the manuscript. CAI Ming drafted the manuscript, designed the exercise intervention, analyzed data, and prepared figures. WANG Liyan, YANG Ruoyu, and LIANG Leichao organized subject recruitment, conducted exercise risk assessments, supervised experiments, and analyzed data. REN Yu, YANG Yuanyuan, JIA Shihao, CHEN Ruiyi, and LIU Qianle organized exercise interventions, executed experiments, and entered data.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Note: Figure translations are in progress. See original paper for figures.