Effects Of Non-periodized And Linear Periodized Combined Exercise Training On Insulin Resistance Indicators In Adults With Obesity: A Randomized Controlled Trial

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Abstract

Background

The aim was to verify the effect of non-periodized and linear periodized combined (aerobic more resistance) exercise training on insulin resistance markers in adults with obesity.

Methods

Was conducted a blinded randomized controlled trial with three groups of individuals with obesity (BMI, 30–39.9 kg/m²): control group (CG, n = 23), non-periodized group (NG, n = 23), and periodized group (PG, n = 23). The NG and PG performed aerobic and resistance exercises in the same session in aerobic-resistance order for 16 weeks. Both intervention groups trained three sessions weekly, with total duration of 60 minutes each. The aerobic training of the NG had duration of 30 min always between 50–59% of the reserve heart rate (HRres), while resistance part was compost of 6 exercise, performed always in 2 × 10–12 maximum repetitions (RM). The PG progressed the aerobic and resistance training from 40–49% to 60–69% (HRres) and from 2 × 12–14 to 2 × 8–10 RM, respectively, along intervention period. The evaluated indicators of insulin resistance included fasting glucose, fasting insulin, and homeostasis model assessment-estimated insulin resistance (HOMA-IR) collected pre and post intervention. The analyses to verify the exercise training effect were performed using generalized estimating equations.

Results

After 16 weeks of training, per protocol analysis (n = 39) showed significant reductions in HOMA-IR only in the training groups (NG: Δ=-1.6, PG: Δ=-0.6; p = 0.094). Intention-to-treat analysis demonstrated significant reductions in fasting insulin levels (NG: Δ=-1.4, PG: Δ=-1.0; p = 0.004) and HOMA-IR (NG: Δ=-5.5, PG: Δ=-3.8; p = 0.002).

Conclusion

Periodized and non-periodized combined exercise training reduces similarly insulin resistance markers in adults with obesity.

Key Points

* Combined exercise training promotes significant reductions in insulin resistance indicators in obese adults.

* Starting training at low or moderate intensity, promotes similar results in inactive obese.

* Even with low weekly frequency, combined physical exercise improves glycemic metabolism.

* Obese adults have low adherence to treatment with physical exercise.

Background

Obesity is considered a global health problem affecting 13% of the world population [1], with estimates indicating that 18.9% of the Brazilian population has obesity [2]. According to the Central Intelligence Agency of the United States of America, in 2016, 61% of the population of Nauru was considered obese, occupying the first position in the world ranking. The country with the lowest rate was Vietnam, with about 2% of the population in this condition. Excessive accumulation of ectopic fat is associated with metabolic disorders, where adipose tissue hypertrophy increases the secretion of adipokines, which favors insulin resistance[5] and greatly increases the chances of developing type 2 diabetes mellitus(T2DM) [6]. Indeed, the term "diabesity" has been used in view of the close relationship between these diseases. Corroborating this, individuals with obesity tend to have higher insulin resistance values, with a higher incidence of dysglycemia, hypertriglyceridemia and high blood pressure [3, 4]. Moreover, even individuals with obesity, considered metabolically healthy in the long term, have aggravated insulin resistance status and are more likely to develop other comorbidities and are more prone to all-cause mortality [7].

Regarding glycemic metabolism in individuals with obesity, an important strategy to prevent the occurrence of T2DM and associated complications is the practice of exercise training, which is an effective and low cost tool, recommended worldwide [8]. Among the types of training, it has been observed that a combination of aerobic and resistance exercises, called combined training, generates a sum of benefits from both modalities, and is recommended for health promotion and longevity of adults with and without obesity and diabetes [9, 10]. Acutely, a combined training session has superior results in β-cell function, insulin sensitivity, and glucose levels compared to aerobic and resistance training alone [11], in addition, these benefits can be extended or consonant chronically with such practice [12–14].

However, changes resulting from training are subject to strategies that aim to modulate training variables such as intensity, volume, recovery interval, and exercise order in programs; thus, periodization is employed for this purpose[15–17]. Although health benefits in the population with obesity are enhanced through the use of periodization [15, 16], caution is needed when stating the superiority of periodization, and further research is needed to understand the effectiveness of periodization and the feasibility of implementing flexible methods [18]. However, improvements in glycemic metabolism are often investigated in the T2DM population, and further understanding of the effect of periodic combined training in the population with obesity is required due to the early presentation of significant changes in glucose metabolism, especially insulin resistance, which may collaborate to trigger diabetes mellitus. Moreover, the effects of different periodization possibilities on clinical outcomes in special populations, such as individuals with obesity, are still embryonic.

Thus, the present study aimed to verify the effect of non-periodized and linear periodized combined exercise training on insulin resistance markers in adults with obesity. We hypothesized that both forms of training would benefit insulin resistance markers but that training combined with linear periodization would be superior to non-periodized training.

Methods

2.1 Study design

This study was a blind randomized controlled trial that included three groups of individuals with obesity, conducted in parallel over the course of 16 weeks. The present study is part of a larger project, entitled "Effects of different protocols of adult health training on obese people, which was approved by the Ethics Committee and Research on Human Beings of the institution of origin (protocol 2.448.674) and registered in the Brazilian Registry of Clinical Trials (RBR-3c7rt3). The methodological details of the larger project of this study are described in its protocol [19].

2.2 Participants

The initial disclosure of the study was made in electronic and printed media. Interested volunteers contacted the researchers via an online form to be filled in order to verify their eligibility. Following were the eligibility criteria: age between 20 and 50 years, obesity grade I and II in terms of body mass index (BMI) ($30-34.9$ kg/m² and $35-39.9$ kg/m², respectively), and no physical exercise with a weekly frequency of more than twice a week in the past 3 months. In addition, participants could not present with any cardiometabolic disease and/or use continuous medications, as well as not using medications to control and / or treat obesity, nor having performed any surgical procedure aimed at weight reduction. Those who met all the criteria and consented to participate were included in the study and provided written informed consent.

2.3 Randomization

All participants underwent a series of evaluations before being randomly allocated to three groups: control group (CG), non-periodized training group (NG), and linear periodization group (PG). Randomization was stratified by sex, age, and BMI, collected at baseline, with a ratio of 1:1:1 by the program www.randomizer.com. This process was conducted by independent researchers who were not involved in the evaluations or the intervention process. The allocation list was only unveiled to trainers on the start date of the intervention.

2.4 Interventions

The NG and PG participated in 16 weeks of combined training (including aerobic and strength exercises in the same session). Aerobic training was performed continuously through walking and/or running, with intensities prescribed by percent reserve heart rate ranges (%HRres). Strength training was performed in multiple sets, using six exercises, all performed with weight training equipment, with prescription for

maximal repetition ranges. The established weekly frequency was three times, with an average duration of 60 minutes; the first 5 minutes for warm-up, 30 minutes for aerobic training, 20 minutes for strength training, and the final 5 minutes for stretching. The first week was used as training familiarization for both groups. Afterwards, the PG participated in training with increasing linear periodization, which was divided into three mesocycles, while the NG remained at moderate intensity throughout the study. At the end, the training volume of both groups was equivalent. The CG did not receive any intervention and the participants were instructed to maintain routine activities. Figure 1 shows the prescribed intensities according to the groups at different times of the study. Additional methodological details can be found in the study protocol [19].

2.5 Assessment for sample characterization and exercise prescription

Participants completed an online questionnaire on the Question Pro Platform, containing sociodemographic information. For the body composition evaluation, a tetrapolar bioelectrical impedance In Body 720 (Ottoboni, Rio de Janeiro, Brazil) was used and manipulated by experienced evaluators who followed the recommended protocol to use the equipment. To prescribe physical training, the maximum and resting heart rates were used to calculate the ideal training zone; these were obtained using Polar® portable heart rate monitors, model S810i. The maximum heart rate was measured by exercise test until voluntary treadmill exhaustion (ImbramedMillenium Super ATL, Porto Alegre, Brazil), according to the protocol previously validated by Jones and Doust [20], with a 1% success rate for reproducing race conditions outdoors. The resting heart rate was recorded with the participant lying down with a heart rate monitor strap positioned. Three notes were taken over 5 minutes (minutes 3, 4, and 5), and the average was recorded as a reference value. Strength heart rate reassessments were performed at the end of each mesocycle to adjust the intensity.

2.6 Outcome assessments

Outcomes were obtained by venipuncture, where 20ml samples were collected in dry bottles with separating gel and another in parallel with anticoagulant (EDTA). Collections took place between 7am and 9am, and the participants fasted for 12 hours prior to collection. Post-treatment collections were made between 48 and 72 hours after the last exercise session. Blood samples were processed and centrifuged to obtain plasma and serum, before storing in a -80ºC bio freezer. The evaluated indicators of insulin resistance were fasting glucose, fasting insulin, and insulin resistance (HOMA-IR). An enzymatic-colorimetric kit (Trinder) was used according to the manufacturer's recommendations for the determination of fasting glucose values. The serum insulin concentration values in mU/L were measured by chemiluminescence immunoassay using the ADVIA CentaurXP ™ Automated Chemiluminescence System. Both analyses were performed at the Clinical Analysis Laboratory of the University Hospital of the Federal University of Santa Catarina. Insulin resistance was estimated using the insulin resistance homeostasis model (HOMA-IR) using the formula: HOMA-IR = [fasting glucose (mmol/L) * fasting insulin (uU/ml)] / 22.5.

2.7 Statistical analysis

The sociodemographic variables, sex (male or female), marital status (with and without a partner), ethnicity (white or brown), and schooling (high school and college) were used to characterize the sample. Continuous variables were expressed as mean and standard deviation, and categorical variables were expressed as relative frequency and percentage. Data distribution was verified using the Shapiro-Wilk test. Differences between the groups at baseline were tested by one-way analysis of variance for independent samples (one-way ANOVA) and Chi-square test.

Outcomes were analyzed by per protocol analysis in those who participated until the end of the study and had complete post-evaluation data. Outcomes were also analyzed by intention-to-treat analysis, in which all randomized participants were included, and the missing values were imputed by regression predictive factors by the maximum likelihood estimator given by generalized estimating equations (GEE). Intra and intergroup analyses were also performed by GEE with the adoption of the Bonferroni post-hoc test. Data are expressed as mean and standard error. The level of significance adopted for the interaction was $p<0.10$, while for the isolated effect of time and/or group was $p<0.05$. All analyses were performed using IBM SPSS version 21.0 (IBM Corp., Armonk, NY, USA). The intra-group effect sizes (ES) were calculated by Cohen's d-test [21]; for this, the value of dividing the mean difference between each intragroup assessment was considered by grouping the standard deviation between the same assessment period. According to Cohen (1988), it was agreed that d values are considered small if ($0.20 \leq d <0.50$), medium if ($0.50 \leq d <0.80$), and large if ($d \geq 0.80$).

For fasting glucose data, the results of the individual responses (Δ=post intervention data − pre-intervention data) of the participants analyzed per protocol are presented.

Results

More than 500 volunteers applied for the study; however, after the initial evaluation processes, 69 participants remained, and were randomized into three equal groups (NG, PG, and CG). After sixteen weeks of training, part of the sample was lost for reasons such as unavailability, work or study and even health problems (Fig. 2).

A total of 39 people completed all phases of the trial and were included in the per-protocol analyses. The frequency of sessions was 64% and 61% for NG and PG, respectively, with no differences in aerobic ($p = 0.350$) and strength training volume ($p = 0.987$). The overall average weekly frequency was 2.0 sessions in the first mesocycle, while in the third mesocycle it was 1.6, with no significant differences between training groups. However, the intensity proposed during the sessions was met by 90% of the participants. There were no adverse events during the exercises during the study.

Table 1 shows the baseline comparison of the sociodemographic characteristics and nutritional status of adults with obesity participating in the study. No significant differences were found between the groups for age, BMI, sex, marital status, skin color, and educational level.

Table 1. Characteristics of study participants (n=69).

Variables	CG (23)	NG (23)	PG (23)	p-value
	(±sd)	(±sd)	(±sd)	
Age (years)	34.2 (±7.6)	34.2 (±6.7)	35.6 (±7.4)	0.740
BMI (kg/m²)	33.2 (±2.4)	33.7 (±3.0)	33.5 (±3.1)	0.129
	n (%)	n (%)	n (%)	
Sex				1.000
Female	14 (60.9)	14 (60.9)	14 (60.9)	
Marital status				0.442
With a partner	17 (73.9)	14 (60.9)	13 (56.5)	
Skin color				0.910
White	19 (82.6)	19 (82.6)	18 (78.3)	
Educational level				0.914
High-school	18 (78.3)	18 (79.7)	18 (78.3)	

Note: n = absolute frequency; % = relative frequency.

X = average; ± dp = standard deviation.

CG: control group; NG: non-periodized group; PG: periodized group.

BMI = body mass index.

Table 2 shows the insulin resistance indicators with analysis per protocol and intention-to-treat. In the per protocol analysis, HOMA-IR was reduced in the training groups with medium effect size. The intention-to-treat analysis demonstrated that the fasting insulin and HOMA-IR decreased in all groups with medium and high effect size for training groups.

Table 2. Blood glucose, insulin and insulin resistance for control group (CG), non-periodized group (NG) and periodized group (PG) before and after 16 weeks of intervention.

Group	Pré-Intervention (±se)	Post-Intervention (±se)	Mean difference	Cohen d	P-value group	P-value time	P-value group*time
Per protocol (n=39)							
Blood glucose (mg/dL)							
CG(n=14)	95.0 (±1.0)	101.0 (±4.0)	6.0	0.58	0.584	0.788	0.102
NG(n=11)	97.1 (±2.7)	91.9 (±3.6)	-5.2	0.54			
PG(n=14)	97.0 (±3.4)	94.7 (±3.2)	-2.3	0.20			
Insulin (mU/L)							
CG(n=14)	15.3 (±2.1)	16.1 (±2.1)	0.8	0.11	0.438	0.072	0.141
NG(n=11)	16.8 (±3.4)	10.8 (±1.6)	-6.0	0.75			
PG(n=14)	13.8 (±1.2)	11.6 (±1.5)	-2.2	0.46			
HOMA-IR							
CG(n=14)	3.6 (±0.5)	4.0 (±0.9)	0.4	0.15	0.441	0.130	0.094
NG(n=11)	4.1 (±0.9)	2.5 (±0.4)*	-1.6	0.76			
PG(n=14)	3.3 (±0.3)	2.7 (±0.4)*	-0.6	0.49			
By intention to treat (n=69)							
Blood glucose (mg/dL)							
CG(n=23)	99.8 (±4.1)	99.6 (±3.4)	-0.2	0.01	0.426	0.124	0.614
NG(n=23)	96.2 (±1.8)	92.4 (±3.1)	-3.8	0.31			
PG(n=23)	97.5 (±2.1)	94.3 (±3.1)	-3.2	0.25			
Insulin(mU/L)							
CG(n=23)	16.8 (±2.1)	15.2 (±1.8)	-1.6	0.17	0.536	0.002	0.430
NG(n=23)	16.4 (±1.8)	10.9 (±1.3)	-5.5	0.74			
PG(n=23)	16.0 (±1.4)	12.2 (±1.7)	-3.8	0.52			
HOMA-IR							
CG(n=23)	4.1 (±0.5)	3.8 (±0.5)	-0.3	0.12	0.405	0.004	0.447
NG(n=23)	3.9 (±0.4)	2.5 (±0.3)	-1.4	0.84			
PG(n=23)	3.9 (±0.3)	2.9 (±0.4)	-1.0	0.60			

Note: X = average; ±se = standard error;

CG: control group; NG: non-periodized group; PG: periodized group;

Generalized estimated equation (GEE); Bonferroni post-hoc test. * Significant difference intra groups (p <0.05).

In Fig. 3, we present the fasting glucose individual responsiveness data according to the groups. This descriptive information allows the visualization of positive results predominantly in the groups that participated in the training, even without statistical significance.

Discussion

In the current study, the goal was to determine the effect of 16 weeks of training combined with linear periodization and non-periodization on insulin resistance indicators in adults with obesity. The markers investigated included blood glucose, insulin, and HOMA-IR. Clinical and statistical improvements were observed for insulin and insulin resistance outcomes for both training groups, refuting the initial hypothesis of superiority to the GP.

Our findings corroborate those of Bonfante et al. 2017, in that 24 weeks of training combined with linear periodization in men with obesity caused improvements in the abovementioned indicators[12]. Obesity is characterized by a state of low grade systemic inflammation[22] due to increased secretion of inflammatory cytokines such as TNF-α and IL-6, which are antagonists of insulin. In addition, promotes increased secretion of leptin, resistin, and plasminogen activation inhibitor-1, which promote insulin resistance[23]. Physical exercise, in turn, decreases the inflammatory condition, reducing the secretion of leptin and TNF-α, which in a metabolic cascade of changes in other adipokines reduces the secretion and cytokines of the insulin antagonist and subsequently improves resistance to insulin. Thus, reductions in insulin resistance indicators are important and affect the improvement of this mechanism, which, in the long term, affect the onset of metabolic syndrome and T2DM[23].

In the per protocol analysis, HOMA-IR showed significant reductions over time only in the combined training groups. However, in the intention-to-treat analysis, in addition to HOMA-IR, fasting insulin also indicated reductions over time, with effect sizes of moderate magnitude for intervention groups. Ahmadizad et al. (2014) and e Inoue et al. (2015) investigated in their respective studies the effect of different forms of periodization on insulin resistance indicators and found no differences[15,24]. This finding supports the importance of structuring physical exercise in modulating these metabolic variables regardless of the form of periodization, especially in people who are inactive or unfamiliar with physical exercise. In the study by Aminilari et al. (2017), fasting blood glucose decreased significantly in all intervention groups (aerobic, strength, and combined), but insulin and HOMA-IR were reduced only in the aerobic and combined exercise groups in overweight adults[25]. In general, these positive effects on glucose metabolism may be effective in preventing and treating obesity, as well as T2DM, by promoting adjustments on adipocytokines and other metabolic markers[26].

With regards to fasting glucose, no significant changes were detected, regardless of group or analysis. Despite this, when analyzing only the participants per protocol, it is possible to perceive a greater amount

of positive responses in this variable in the participants of the intervention groups. Serum values that are already normal at baseline measurement, according to the reference values established by the Brazilian Society of Diabetes(2019)27, minimize the amplitude for improvement. However, these participants, who are already in a state of metabolic abnormality, are able to maintain their glycemic levels within a normal range due to increased insulin secretion. This fact is relevant in this scenario, since physiological changes, such as an increase in pro inflammatory cytokines and circulating free fatty acids as well as reduced insulin sensitivity, increase the need for insulin secretion to maintain glycemic homeostasis. Over time, and with the aggravation of disease, hyperglycemia will be established due to the saturation of insulin production, as well as by resistance mechanisms9. In addition, evidence points to the importance of training volume and intensity for meaningful blood glucose results28,29, which, was weakened in the present study.

Strohacker et al. (2015) understood that it was premature to conclude that periodized training is superior to non-periodized training in terms of improving health indicators in non-athletes subjects18. However, they stated the need for further research to understand the effectiveness of periodization and the feasibility of implementing flexible methods. Until this point, an insufficient number of studies had investigated this theme. Moreover, Inoue et al.(2015) built models of interdisciplinary therapy that included periodized combined training (linear versus undulating) and realized that both forms were effective in improving the lipid profile and insulin sensitivity in adults with obesity24. Still with this population, and with similar comparisons, Foschini et al. (2010) only demonstrated a reduction in insulin and HOMA-IR concentrations in the group that used daily wave periodization30. In addition, the participants in this study were not previously trained, which expands and / or limits training regardless of the periodization model. In the present study, superiority was also not evidenced. Among the possible explanations for this, the fact that the participants in this study were not previously trained, which increases their trainability, regardless of the periodization model. Thus, gaps in the body of evidence on the superiority of training with different forms of periodization are indicated for health outcomes of special populations. Still, clinically the results of periodization are relevant, as they suggest significant reductions in insulin resistance indicators in a population at metabolic risk.

The strengths of this blinded randomized clinical trial were the control of aerobic training variables, maintenance of relative intensity in the NG and the gradual increase in intensity in the GP along the mesocycles, both of which were adjusted by resting heart rate, and are considered a low cost control method. The pioneering study design, with intensity progression and similarity in training volume is another strength, since it allows verification of the effects of different forms of periodization in the combined training program in an equalized manner. However, limitations, such as the low frequency of participants in the training program and sample loss, are also recognized due to missing data on the outcome variables of this study, which may lead to low sampling power for statistically significant findings. Furthermore, the absence of control of food intake is an important consideration, and lack of glycated hemoglobin may be another limitation. In addition, it is plausible to consider the biological individuality of the participants, their respective routines, and other factors that could not be measured here as determinants in the alterations, whether they have been highlighted or not.

Conclusion

Thus, in 16 weeks, periodized combined training improve similarly to non-periodized combined training the insulin resistance indicators in adults with obesity. The training used, which has practical applicability, even with low adherence, provided a reduction in important risk factors for triggering other comorbidities in a population already considered at risk. For future studies, greater attention is recommended in this health indicators in adults with obesity not yet diagnosed with other comorbidities. In addition, we recommended the implementation of adherence strategies to enhance the results of this study, as well as further exploration of other training methods.

Abbreviations

T2DM: type 2 diabetes mellitus

BMI: body mass index

CG: control group

NG: non-periodized training group

PG: linear periodization group

%HRres: reserve heart rate ranges

GEE: Generalized estimated equation

Declarations

Ethics approval and consent to participate

Ethics Committee and Research on Human Beings at Federal University of Santa Catarina, protocol 2.448.674;

Brazilian Registry of Clinical Trials number RBR-3c7rt3

Consent for publication - Not applicable

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

ARS contributed to literature review, data collection, data analysis and interpretation and writing of the manuscript. LSL and RSD contributed to data analysis and interpretation and writing of the manuscript. CRC and GFDD contributed research concept and study design and draft of manuscript. All authors read and approved the final manuscript.

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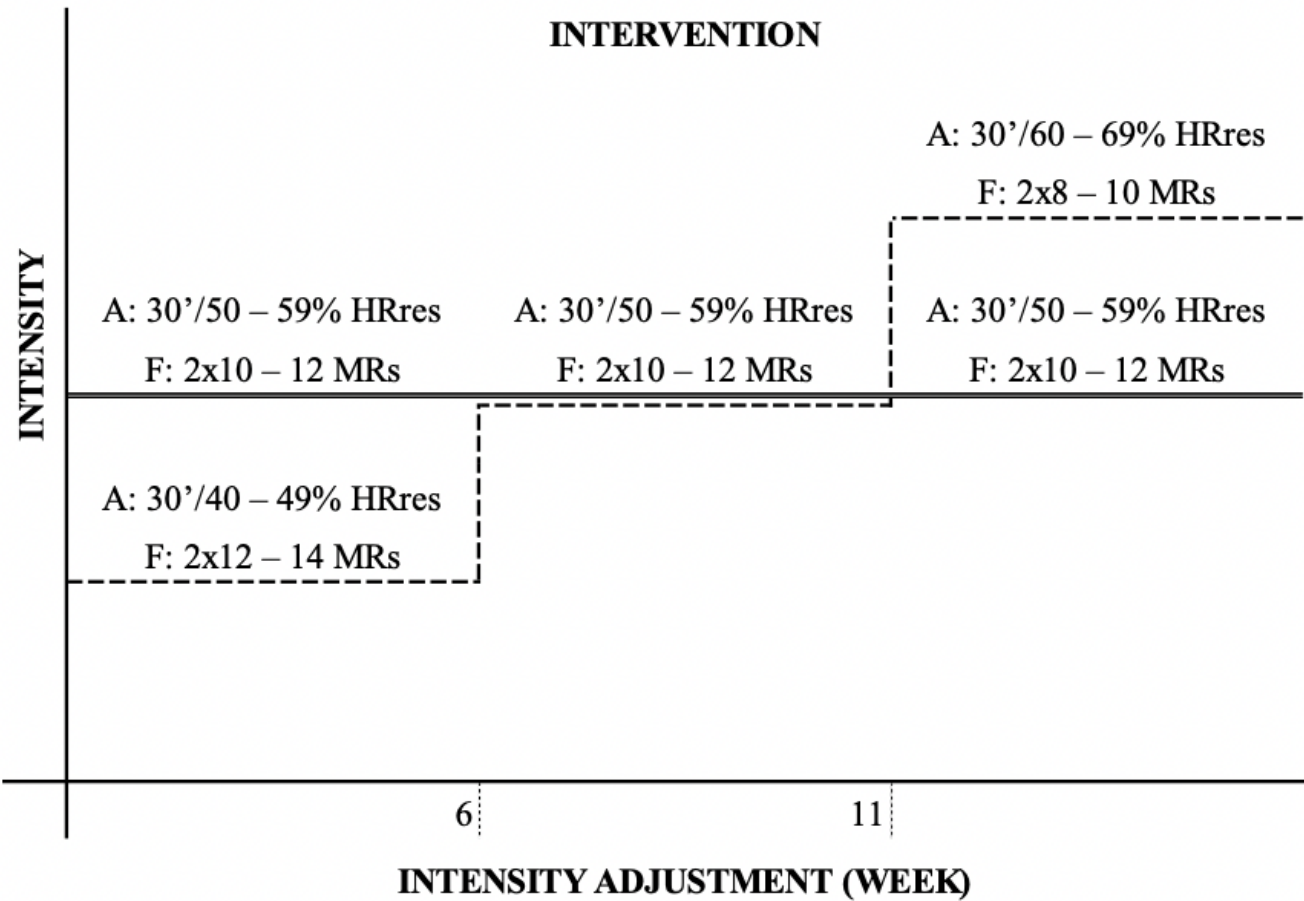
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Figures

INTERVENTION

A: 30'/60 – 69% HRres
F: 2x8 – 10 MRs

A: 30'/50 – 59% HRres
F: 2x10 – 12 MRs

A: 30'/50 – 59% HRres
F: 2x10 – 12 MRs

A: 30'/50 – 59% HRres
F: 2x10 – 12 MRs

A: 30'/40 – 49% HRres
F: 2x12 – 14 MRs

INTENSITY

6   11

INTENSITY ADJUSTMENT (WEEK)

---: linear periodized training group;
═══: non-periodized training group;
A: aerobic training;
F: resistance training;
HRres: reserve heart rate;
MRs= maximal repetition;
x: series.

Figure 1

Structure of the training protocols performed by the periodized combined training group (PG) and the non-periodized training group (NG).
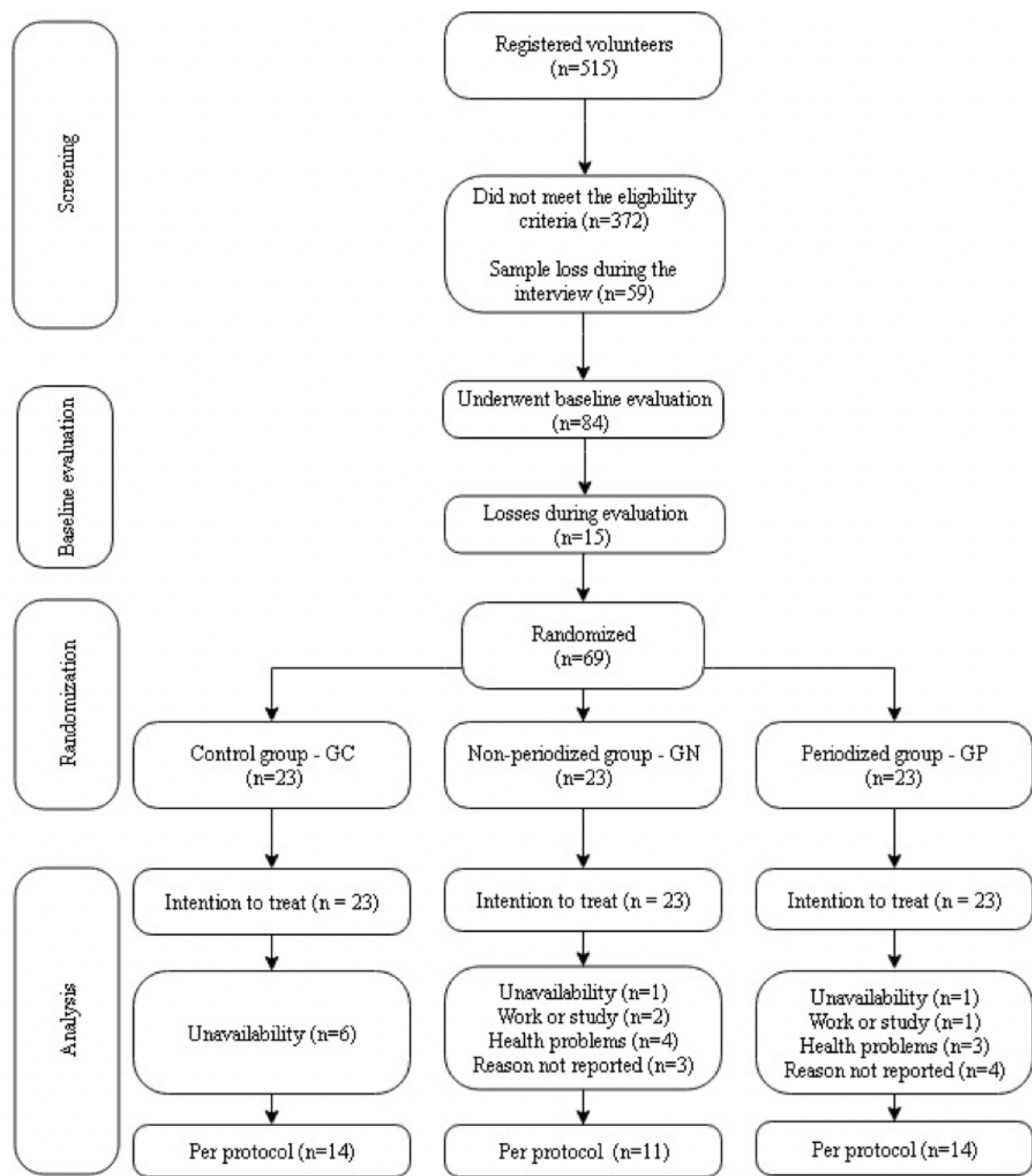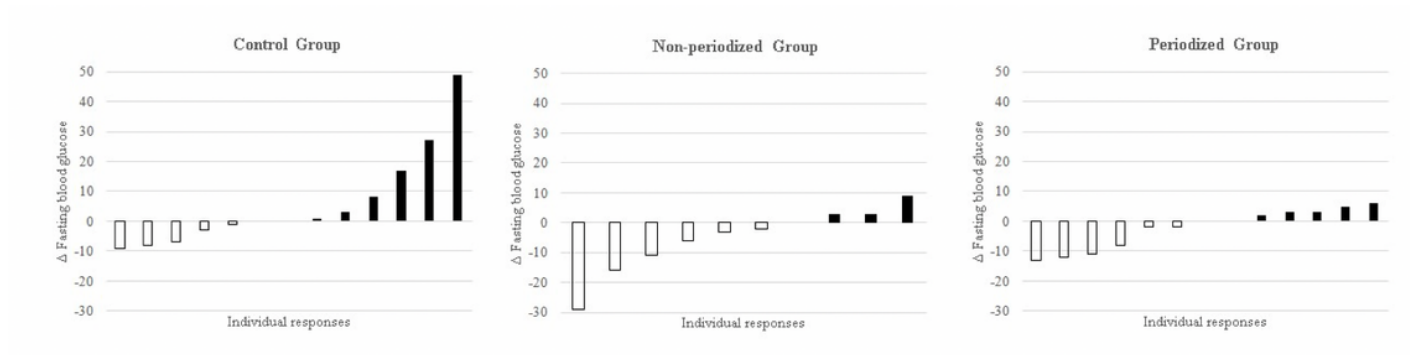

Figure 2

Study Flowchart.

Figure 3

Individual responses of fasting blood glucose according to the groups.