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Original Article

Concurrent training improves the body composition of elderly type 2 diabetic patients treated with insulin

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Abstract

Problem Statement: Different drug therapies like insulin and oral hypoglycemic agents help maintain normal glycemic levels and avoid clinical complications of type 2 diabetes mellitus (T2D). Concurrent training (CT – aerobic plus resistance training) is a nonpharmacological tool for T2D treatment that decreases body fat, increases lean body mass, and improves functional capacity. However, it is unknown whether the positive alterations on body composition and cardiometabolic parameters induced by CT occur in different magnitudes for those with T2D who are treated with insulin or not as drug therapy. **Purpose:** to evaluate the effects of 12 weeks of CT on the body composition of elderly individuals with T2D treated with insulin or not. **Approach:** Sixteen subjects (age, 65 ± 7 years; T2D length, 11 ± 7 years) were divided into two groups: insulin-treated (IT; n = 9) and noninsulin-treated (NIT; n = 7), who participated in the same incremental-load CT protocol. **Results:** CT decreased fat body mass (30.5 ± 3.8 kg post-training vs. 32.5 ± 4.5 kg pretraining; $p < 0.01$; effect size (d) = 0.47) and increased lean body mass (45.6 ± 5.5 kg post-training vs. 43.7 ± 4.4 kg pretraining; $p < 0.01$; $d = 0.4$) only in the IT group. CT increased muscle strength (IT: $d = 1.71$; NIT: $d = 1.48$; $p < 0.05$) and the distance traveled during the 6-minute walk test (IT: 519 ± 43 m post-training vs. 499 ± 45 m pretraining, $p < 0.05$; NIT: 546 ± 94 m post-training vs. 488 ± 58 m pretraining, $p < 0.05$) for both groups. **Conclusion:** CT leads to positive body compositions for those with T2D treated with insulin.

Key Words: **Aging; physical exercise; concurrent training; insulin treatment; muscle strength.**

Introduction

Current estimates suggest that 8.8% of the global adult population (20-79 years) have diabetes mellitus (IDF, 2017). Type 2 diabetes mellitus (T2D) is the most common form of the disease, accounting for 90-95% of cases (IDF, 2017). The diagnosis is established by the progressive loss of insulin secretion with a background of insulin resistance because of genetic susceptibilities, sedentary habits, and inadequate diet (Hu, 2011). Moreover, excess weight, obesity, and aging are associated with an increased prevalence of T2D (IDF, 2017).

Two types of T2D treatment have been proposed: drug therapy and nondrug therapy (Dodds, 2017). Metformin has been adopted as the first line of drug therapy for T2D treatment. However, physicians could use other oral hypoglycemic agents, like sulfonylureas, as the second line of treatment. Insulin therapy is suggested in a few cases (Gross et al., 2011). Insulin replacement is associated with better glycemic control and excessive weight gain (Gross et al., 2011); however, the benefits for microvascular prognoses outweigh this fact (Stratton et al., 2000).

It has been shown that people with diabetes have less lower muscle strength and muscle quality (Park et al., 2006), aerobic capacity, flexibility, functional capacity (Milech et al., 2016), and muscle mass per body weight (Kim et al., 2014) and more major cardiovascular disorders (IDF, 2017) compared to subjects without T2D. Therefore, inclusion of these individuals in exercise programs is essential for improving health-related parameters.

There is much evidence of multiple health benefits provided by physical exercise, especially combined aerobic training (AT) and strength training (ST), also referred to as concurrent training (CT), for people with T2D (Balducci et al., 2012; Colberg et al., 2016). The main short-term benefits provided by CT are increased glucose uptake and increased insulin sensitivity (Colberg et al., 2016). The main long-term benefits are improvement in glucose control (Umpierre et al., 2011), blood pressure (Figueira et al., 2014), lipid profile, fat mass, muscle mass strength, and functional or aerobic capacity (Colberg et al., 2016).

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Recent studies have suggested that CT comprising AT and ST during the same training session or alternate training sessions is the preferred exercise modality because it promotes organic adaptations (Schwingshackl, Missbach, Dias, König, & Hoffmann, 2014). AT increases insulin sensibility, and ST increases glucose uptake by increasing muscle mass (Colberg et al., 2016). Furthermore, synergy between the two types of exercise occurs.

Despite the recognized benefits of exercise training for the metabolic profile, some studies have failed to find reductions in fat mass in subjects with T2D after exercise training (Lambers, Van Laethem, Van Acker, & Calders, 2008; Tan, Li, & Wang, 2012). These results may have been influenced by the type of treatment (no insulin or insulin) used during the training protocol. However, these aspects are not completely understood, especially for elderly individuals with T2D. Therefore, the aim of the present study was to evaluate the effects of CT on the body composition of elderly individuals with T2D treated or not treated with insulin.

Materials and Methods

Subjects

For this interventional trial, 16 sedentary subjects with T2D aged 56-78 years volunteered to participate in the study. All experimental procedures were approved by the Ethics Committee of the Universidade Federal de Minas Gerais and were performed in accordance with their policies. Subjects provided their written informed consent. Volunteers were instructed to not change their food and medication routines during the intervention period. Subjects who met the following criteria were included in the present study: age older than 50 years; T2D for more than 3 years; and physically inactive for at least 3 months before initiation of the study. Exclusion criteria adopted were as follows: any complication caused by diabetes or another condition that restricted exercise training; smoking; alcohol use; and narcotic drug use. Thirty subjects started the training protocol, but only 16 completed the training (Table 1 and Figure 1).

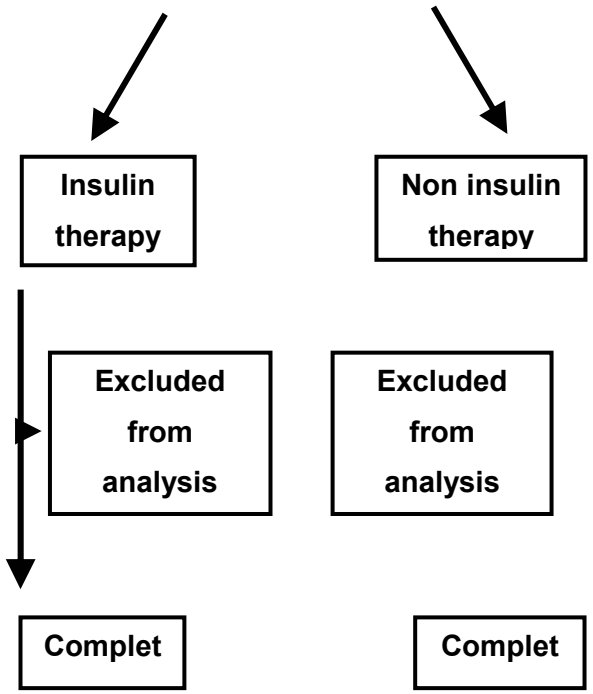
Table 1. Baseline group characteristics

Parameters	NIT Group (n= 7)	IT Group (n= 9)
Age (yr)	63 ± 7	66 ± 6
Sex (M/W)	2/5	2/7
Diagnosis time (yr)	8 ± 6	14 ± 8*
Body mass (kg)	73.8 ± 17	75.7 ± 8.7
BMI ($kg \cdot m^{-2}$)	27.9 ± 6.1	30.2 ± 2.6
Waist girth (cm)	96 ± 11	94 ± 10
Fat percent (%)	39.4 ± 4.7	42.6 ± 2.4
Glycaemia (mg/dL)	122 ± 19	151 ± 32*
SBP (mmHg)	115 ± 9	130 ± 15*
DBP (mmHg)	69 ± 7	76 ± 6*
Heart rate (bpm)	72 ± 14	77 ± 14
Hypertension (%)	71	89
Dyslipidemia (%)	57	78
Medications		
Insulin (%)	0 (0/7)	100 (9/9)
Biguanides (%)	86 (6/7)	89 (8/9)
Anti-hypertensive (%)	71 (5/7)	89 (8/9)
Statin (%)	57 (4/7)	55 (5/9)
Sulfonylurea (%)	29 (2/7)	22 (2/9)
NSAIDs (%)	43 (3/7)	44 (4/9)

BMI = body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; NSAIDs = non-steroidal anti-inflammatory drugs. Values are mean ± SD. *p<0.05 in Student's T test comparison NIT vs. IT groups.

During this study, participants were not prescribed any medication. The noninsulin-treated (NIT, n= 7) group and insulin-treated (IT, n= 9) group were created according to the medical prescriptions of each subject. Furthermore, subjects were also asked if they were using the drug therapy proposed by the physician. In the IT group, the mean insulin dose was 40 (range, 15–70) units/day. All subjects used intermediate-acting insulin (NPH) and only one used combined NPH plus ultra-rapid-acting insulin.

Experimental design



The experimental sequence is described in Figure 2. First, all subjects with TD2 completed a questionnaire about the use of medications and their resting blood glucose was evaluated. During the second visit, participants were subjected to anthropometric assessments and were familiarized with both strength tests and aerobic tests (1 session of 10-15 repetitions of all resistance exercises with a low or moderate load and 10 minutes of walking at a comfortable speed). During the third visit, volunteers were subjected to the 6-minute walk test (6-MWT) and maximal repetitions test. After these pretraining evaluations, TD2 subjects performed 12 weeks of CT sessions (ST plus AT), as described in Table 2. At the end of the exercise training period, the anthropometric, metabolic, and performance parameters were re-evaluated according to the same protocol adopted for the initial assessments.

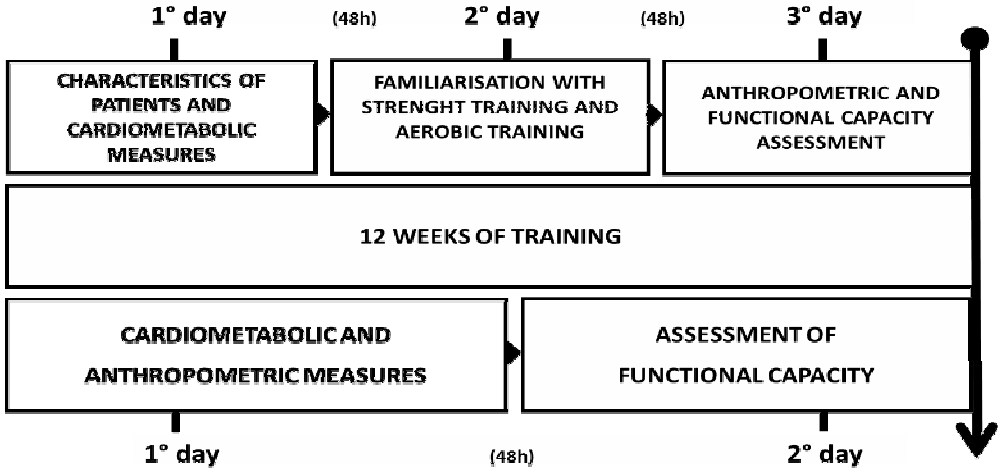


Fig. 2 – Experimental sequence procedures

Anthropometric assessment

Body mass was measured using a calibrated analog scale (Filizola®; Brazil) with a maximum load of 150 kg and precision of 0.1 kg. Height was assessed using a stadiometer (Sanny®; Standard, Brazil) with a measuring field between 0.8 and 2.2 m and precision of 0.5 cm. Body girths were evaluated with inextensible 1.5-m-long anthropometric tape at 14 sites (neck, shoulders, chest, right arm, left arm, right forearm, left forearm, waist, abdomen, hip, right thigh, left thigh, right calf, and left calf). A precision of 0.5 mm was adopted. The skinfolds were measured using the skinfold caliper (Saehan®; SH5020, Korea) at four standardized sites

(triceps, biceps, iliocristale, and medial calf) with a measurement field between 1 and 65 mm and accuracy of 1 mm. All anthropometric measurements were performed by the same trained evaluator. Using the skinfold thickness values and ages of the volunteers, we calculated corporal density using an equation for Brazilian subjects (Filardo & Petroski, 2007) and the Siri's equation (1961) (% fat = [(4.95/corporal density) – 4.50] *100) to obtain the percentage of body fat. Lean body mass and fat body mass were estimated using the percentage of body fat.

Assessments of muscle strength and aerobic performance

Muscle strength was assessed using a submaximal test for all eight exercises included in the training protocol. Each volunteer performed between 4 and 20 repetitions of each exercise with a predetermined load until voluntary fatigue was achieved. Between each attempt and each exercise, participants were allowed a minimum of 3 minutes of rest. To estimate the maximum repetition (1-RM), the number of repetitions performed with a certain load was included in the following regression equation: 1-RM = w · [1+ (0,025 · r)], where w = weight and r = number of repetitions (O'Connor, O'Connor, Simmons, & O'Shea, 1989).

Aerobic performance was evaluated by the 6-MWT performed in a standardized hall with a length of 30 m (Enright, 2003). Subjects were instructed to walk at their maximal speed during the 6 minutes of the test while they received standardized verbal encouragement during the first minute. The distance walked during the 6-MWT was measured with 1-m precision.

Cardiometabolic parameters

Blood glucose levels were measured after a 12 h fasting period, before and after the training protocol. Glycemia was evaluated by a fresh capillary blood insert on a specific test strip. Then, a calibrated and validated glucometer (Accu-Chek Active®; Roche, Basel, Switzerland) (Dhatt, Agarwal, Othman, & Nair, 2011) was used to quantify blood glucose with a measuring range between 10 and 600 mg/dL.

Concurrent exercise training

Subjects performed AT plus ST two or three times per week for a total of 24 sessions. Subjects performed CT for 12 ± 1 weeks. All sessions were supervised by professional sports scientists or exercise physiologists, and they were performed at the same time of day. The initial order of training was alternated (AT before ST and ST before AT).

AT was performed on a treadmill (model LX160®; Movement, Brazil) at a self-paced walking speed for 20-25 minutes. Then, volunteers provided a rate of perceived effort (RPE) using a scale of 6-20 points (light to somewhat difficult).

ST was performed during eight resistance exercises (Table 2). The exercise order involved alternating the use of the muscle groups of the upper and lower limbs. Two training periods (eight sessions each) were used according to the statement of the American Diabetes Association for diabetic subjects (Colberg et al., 2016). AT progressed only regarding the volume of training (20 min to 22.5 min to 25 min); the intensity was always self-paced. Similarly, the volume of the workloads during ST was increased (2×15 repetitions to 3×15 repetitions to 3×20 repetitions) at the same intensity of 50% 1-RM; 30 to 40 seconds of rest was allowed between sets and exercises. Volunteers were instructed to keep a moderate speed of motion during each repetition, but time was not recorded during each repetition or each session.

After the training session, the subjective perceptions of AT and ST were not different between the first, second, or third progressions of the sessions, and they also were not different between the IT and NIT groups. The RPE values scale remained between 10 and 14 and between all sessions.

Table 2. Summary of exercise training prescriptions

Type of training	Parameter	Training sessions 1 at 8	9 at 16	17 at 24
Strength	Frequency (d/wk)	2	2	2
	Intensity (% of 1-RM)	50	50	50
	Volume	2 sets x 15 rep.	3 sets x 15 rep.	3 sets x 20 rep.
	Duration of repetition	self-controlled	self-controlled	self-controlled
	Pause (sec)	30	30	40
	Number of exercises	8	8	8
Aerobic	Frequency (d/wk)	2	2	2
	Intensity (EPS)	9 at 14	9 at 14	9 at 14
	Duration (min)	20	22.5	25
	Training method	constant-speed	constant-speed	constant-speed

1-RM = 1-repetition maximum; rep. = repetition; EPS = Effort perceived scale.

Statistical analyses

In descriptive measures and graphs, data are expressed as mean ± standard deviation. Pre-session and post-session data and pre-training and post-training data are shown as mean and standard deviation. The Shapiro-Wilk and Levene tests were used to verify normality and homoscedastic of the data, which were confirmed for all variables. SigmaPlot version 11.0 (Systat Software Inc., San Jose, CA, USA) was used for data registration and analysis. Baseline descriptive data were compared using the independent two-tailed Student t test. To compare the cardiometabolic, functional, and body composition parameters before and after 12 weeks of CT training, repeated-measures two-way analysis of variance (ANOVA) was performed for groups (insulin vs. noninsulin) and time (pretraining vs. post-training). When differences were found using ANOVA, the Tukey *post hoc* analysis was used to detect the differences. Pearson's correlation coefficient was used for related baseline values of glycemia and their respective variations during each CT session. To improve the clinical relevance of our findings, we calculated the effect size (Cohen's *d*) as follows: mean pretraining – mean post-training / pooled standard deviation. The significance level was set at 5%.

Results

At baseline, the IT group presented higher occasional glycemia levels compared to the NIT group (Table 1). In addition, the time since the T2D diagnosis was higher for the IT group compared to the NIT group. However, significant differences in body composition and hypoglycemic drugs, except insulin, were not observed between the IT and NIT groups.

Effects of CT on body composition

Table 3 shows the effects of CT on body composition for the IT and NIT groups. CT had no significant impact on body mass or body mass index (BMI) for both groups. There was no significant impact on the interaction of group x time ($F < 2$ in all situations; $p > 0.05$). However, decreased fat percentages (F: 6.82, $p = 0.02$) and total fat body mass (F: 7.72, $p = 0.015$) and increased total lean body mass (F: 10.56, $p=0.006$) were found only for the IT group. In addition, the effect size analysis revealed Cohen's *d* values of 1.0, 0.47, and 0.40 for body fat percentage, fat body mass, and lean body mass of the IT group, respectively. We did not find a Cohen's *d* value larger than 0.2 for the NIT group. Figure 3 presents individual data for these three parameters.

3.2 Effects of CT on muscle strength and aerobic performance

Both groups showed differences in the time to predict 1-RM for all eight exercises normalized for body mass (NIT pretraining 4.4 [3.1-5.6] vs. post-training 5.2 [3.7-6.7]; IT pretraining 4.0 [3.32-4.58] vs. post-training 4.5 [3.8-5.3]; F: 38.65; $p < 0.001$), but no differences were found between groups or the interaction of time x group ($F < 2$ for both; $p > 0.05$). CT improved the 6-MWT distance for both groups (NIT pretraining 500 [470-528] vs. post-training 519 [491-548]; IT pretraining 488 [445-531] vs. post-training: 546 [477-616]; F: 12.13; $p = 0.004$), but no differences were found between groups or the interaction of group x time ($F < 2.8$ for both; $p > 0.05$).

Table 3. Anthropometric measures at baseline and after 12 weeks of concurrent training

Parameters	NIT (n = 7)		IT (n = 9)	
	Baseline	Post	Baseline	Post
Body Mass (kg)	73.8 (61.2-83.5)	73.3 (60.4-86.3)	76.1 (70.8-81.5)	76.1 ± (70.7-81.6)
BMI (kg/m²)	28.0 (23.5-32.5)	27.8 (23.1-32.4)	30.7 (28.8-32.6)	30.7 (28.7-32.8)
Fat percentage (%)	39.4 (36.0-42.9)	38.5 ± (33.7-43.2)	42.6 (41.0-44.2)	40.1 (33.4-41.8)*
Lean body mass (kg)	44.6 (37.2-52.0)	44.8 (37.5-52.0)	43.6 (40.7-46.5)	45.6 ± (42.0-49.2)*
Fat body mass (kg)	29.2 (23.2-35.3)	28.6 (21.6-35.5)	32.5 (29.5-35.5)	30.5 ± (28.0-33.0)*

NIT = non-insulin therapy group; IT = insulin therapy group; BMI = body mass index; Post = after 12 weeks of combined strength and aerobic training. Values are mean ± SD. *p<0.01 between baseline vs. post.

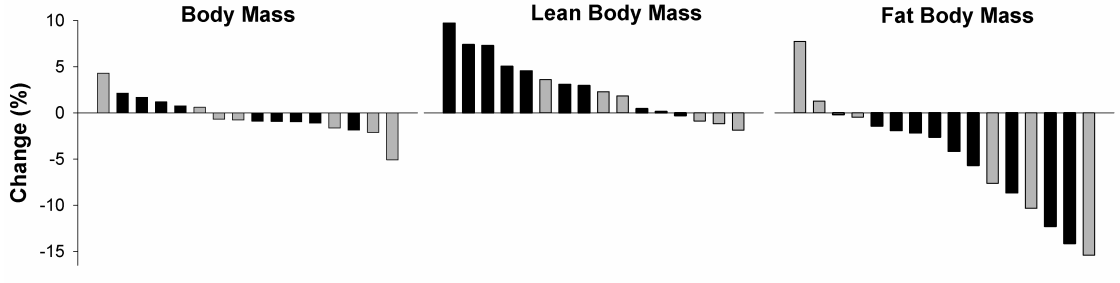


Fig. 3. Effects of concurrent training on body composition. Subjects were sequenced from minor to high responses for body mass, lean body mass, and fat body mass. Black bars: IT ($n = 9$). Grey bars: NIT ($n = 7$). IT: insulin-treated; NIT: noninsulin-treated.

Effects of CT on blood glucose parameters

Concurrent training failed to produce long-term reductions in blood glucose for the IT (Pre = 173.22±49.02 vs. Post = 202.22±61.24 mg/dL, p = 0.17) and NIT groups (Pre = 138.67±41.02 vs. Post = 128.50.22±40.21 mg/dL, p = 0.48).

Discussion

In the present study, we used a CT protocol with great external validity and good reproducibility. The main finding was that IT subjects had more pronounced alterations in body composition in response to exercise training than did NIT subjects. However, improvements in muscle strength and aerobic performance induced by CT were not dependent on IT. These findings have great significance for the health of subjects with T2D because it is very important to understand the interaction between pharmacological and nonpharmacological tools for diabetes treatment.

Anabolic effects on skeletal muscle and adipose tissue are induced by the effects of insulin on different systems. Insulin influences the metabolism of carbohydrates, lipids and proteins. These effects combined may increase muscle mass and fat mass using different mechanisms (Dimitriadis, Mitrou, Lambadiari, Maratou, & Raptis, 2011). Therefore, we speculated that IT subjects would have different body composition responses after CT than subjects treated with hypoglycemic oral drugs. Additionally, adiposity may blunt the anabolic effects of insulin (Murphy, Chevalier, Gougeon, Goulet, & Morais, 2015). Therefore, as observed in the IT group, the reduction in body fat may have recovered the anabolic effect of insulin, thus allowing the gain of lean mass in this group.

Decreases in body fat percentage and increases in lean body mass have great importance for improving the clinical conditions of elderly TD2 individuals because they have low muscle mass indices, strength and quality (Kim et al., 2014) when compared with subjects without TD2. Finally, it is important to emphasize that muscle mass increases would promote greater uptake of postprandial glucose, thus helping to increase the daily energy expenditure of TD2 individuals and, consequently, improve glycemic control.

CT did not efficiently decrease body mass or BMI. Previous studies of TD2 individuals who performed 8 and 24 weeks of exercise training also did not display decreases in these parameters (De Feyter et al., 2007; Lambers et al., 2008; Maiorana, O'Driscoll, Goodman, Taylor, & Green, 2002; Tan et al., 2012). Studies with longer interventions periods (e.g., 12 months) resulted in observed reductions in BMI (Balducci et al., 2012), suggesting that longer interventions are necessary to reduce BMI. In fact, although exercise training improves glycemic control after a few sessions, significant impacts on body weight are often not exhibited (Boulé, Haddad, Kenny, Wells, & Sigal, 2001). Currently, it is postulated that the combination of diet, exercise, and changes in activity are most successful for body weight reduction (Boulé et al., 2001; Colberg et al., 2016). In the present study, we only focused on exercise; there was no intervention in diet. This could be why body weight reductions were not observed.

Our CT protocol induced clear increases in muscle strength, as demonstrated by large effect sizes found for the time domain. Furthermore, the IT and NIT groups showed improvements in superior and inferior limb muscle strength during all exercises, except the crunch exercise. These results agree with those of previous studies that involved CT for 8 weeks (Maiorana et al., 2002), 12 weeks (Lambers et al., 2008), 20 weeks (De Feyter et al., 2007), and 1 year (Balducci et al., 2012) and used estimated or absolute 1-RM. Interesting, despite the greater increases in muscle mass observed in IT T2D individuals in the present study, there was no insulin-induced impact on muscle strength. People with TD2 exhibited impairments in muscle strength (Park et al., 2006) that were worse for those who had T2D longer (Mavros et al., 2013), usually because of neuropathy. We speculated that CT optimizes strength levels and reduces losses due to T2D. In addition, increases in strength and muscle mass in elderly individuals may mitigate the effects of sarcopenia, thereby preserving or improving the functional capacity of these subjects (Bales & Ritchie, 2002).

Those with T2D have reduced functional capacity (Milech et al., 2016) and worse cardiovascular conditions (IDF, 2017) than their counterparts without T2D. In this context, increases in aerobic performance expressed by improvements in the distance walked during the 6-MWT observed in the present study could improve the understanding of these deleterious processes. Other authors observed similar results after AT (Geirsdottir et al., 2012) and CT (Lambers et al., 2008; Tan et al., 2012) in the 6-MWT performances. However, IT failed to promote additional effects on aerobic performance of TD2 individuals in the present intervention. Physiological adaptations to endurance training are mainly associated with molecular and morphological alterations in the heart and blood vessels and in the cellular oxidative process, which can explain the absence of insulin-induced improvements in the aerobic performance of our volunteers with T2D.

Interestingly, the IT group showed higher values of glycemia during the pre-session compared with the NIT group. We believe that the baseline difference may be due to the longer time of TD2 observed in the IT group. This could indicate a more advanced stage of diabetes involving difficulty controlling blood glucose levels. Regarding the long-term effects of 12 weeks of CT for capillary glycemia, we did not observe differences when comparing pre-CT and post-CT values. The lack of results regarding glycemic control can be explained by

at least two factors. First, perhaps the most accurate variable for this outcome is glycated hemoglobin rather than capillary glycemia. Second, the literature shows that the weekly volume of training is the variable that most influences glycemic control (Umpierre, Ribeiro, Schaan, & Ribeiro, 2013). Therefore, because the protocol included two to three sessions per week, the observed results may have been limited by this variable. Additionally, during our intervention, we did not promote diet interventions. It is well-established that long-term reductions in blood glucose in TD2 subjects are dependent on a complex interaction between eating behavior, exercise training, and lifestyle. We believe that these points can justify why we have not found long-term changes in blood glucose after CT.

It is important to note the limitations of this study. Because of mortality, less than 55% of the TD2 subjects completed the total training period; therefore, we had a limited sample size. In addition, we did not promote any intervention in diet or medication routines during the CT period, which decreased the experimental control. Finally, we plan on performing future studies using direct measurements of lean and fat body mass (e.g., magnetic resonance imaging or X-ray densitometry) that have more validity and reproducibility compared with inferential skinfold measurements.

Conclusion

The present study showed that CT increased muscle mass and reduced the total fat body mass of T2D IT individuals, and that these results were not observed in NIT individuals. Furthermore, CT for 12 weeks similarly improves cardiometabolic responses, strength, and aerobic exercise performances for both IT and NIT TD2 subjects. Therefore, CT can be used by exercises professionals involved with the treatment of T2D individuals to improve functional capacity and to obtain cardiometabolic benefits.

Conflicts of Interest

There are no conflicts of interest to declare.

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