Experimental Gerontology 113 (2018) 141–149

Contents lists available at ScienceDirect

Experimental Gerontology

journal homepage: www.elsevier.com/locate/expgero

Effects of resistance training on neuromuscular parameters in elderly with type 2 diabetes mellitus: A randomized clinical trial

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ARTICLE INFO

Section Editor: Christiaan Leeuwenburgh

Keywords:
Aging
Muscle strength
Muscle thickness
Glycemic control

ABSTRACT

This study is a randomized controlled clinical trial that verified the resistance training efficacy on neuromuscular parameters, with muscle quality as primary outcome. Forty-four elderly with diabetes type 2 (69.7 ± 6.9 years; 26 men) were randomly allocated to a 12-weeks resistance training group (RTG, 3 times a week), or an active control group with stretching classes (CG, once a week). Primary and secondary outcomes were assessed at baseline and after 12 weeks, as follow: quadriceps muscle thickness and *rectus femoris* muscle quality, maximal knee extension strength, rapid strength, functional performance, visceral adipose tissue, glycemic control, lipid profile and quality of life. Generalized estimating equations were used to analyses based on intention-to-treat and per-protocol approaches, which showed the same results. Among all outcomes measured there were improvements in the knee extension strength ($P < 0.001$) and quadriceps muscle thickness ($P < 0.001$) for RTG. The muscle quality did not improve for both groups ($P = 0.98$). For the secondary outcomes there were no improvements for functional performance, rapid strength, glycemic control, quality of life, visceral adipose tissue and lipid profile in both groups, with exception of triglyceride level reduction for RTG ($P = 0.04$).The resistance training program is an efficacious strategy for improve the neuromuscular health in elderly with T2DM, considering increases in lower limb strength and muscle mass, but the same was not found for muscle quality, rapid strength, functional performance and quality of life. Furthermore, the training program did not induce significant reduction in glycated hemoglobin values of patients who already had suitable glycemic control.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a highly prevalent disease in older people (Guariguata et al., 2014), leading to marked loss of physical function. Compared with non-T2DM counterparts, elderly with T2DM present greater losses of strength (Guerrero et al., 2016; Leenders et al., 2013), muscle mass (Park et al., 2009), and have up to a three-fold increased risk to physical disability in walking speed, balance and lower limb function according to the severity of the disease (Gregg et al., 2000). In this regard, exercise training is an evidence-based recommended intervention (Colberg et al., 2016) not only due to its efficacy for glycemic control but also for potential to partially recover or preserve physical function and avoided comorbidities.

The reductions in strength capacity observed during the aging process are not solely associated with muscle mass decreases, but also with neural impairments (Russ et al., 2012) and increases in intramuscular fat deposition (Goodpaster et al., 2000a). Such alterations are better represented by muscle quality that has been considered a measure with greater functional relevance (Barbat-artigas et al., 2013; Russ et al., 2012), especially in cases of diseases that affect the

Abbreviations: 1-RM, one repetition maximum; CG, control group; MIVC, maximal isometric voluntary contraction; RTD, rate of torque development; RTG, resistance training group; T2DM, type 2 diabetes mellitus

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https://doi.org/10.1016/j.exger.2018.10.001
Received 19 July 2018; Received in revised form 19 September 2018; Accepted 2 October 2018
Available online 05 October 2018
0531-5565/

neuromuscular function (Nomura et al., 2018). The muscle quality may be quantified either by the ratio of strength produced per unit of active muscle mass (specific tension) or by the measures of intramuscular non-contractile tissue. Poor glycemic control in older patients with diabetes was associated with significant risk of decreased muscle quality by specific tension and strength performance status (Yoon et al., 2016). Moreover, the intramuscular fat concentration is greater in the diabetes status of elderly (Delmonico et al., 2009).

Resistance training is an effective exercise strategy for counteracting neuromuscular impairments of age. Especially in non-ill older individuals undergoing resistance training programs, there is abundant evidence showing muscular gains related to strength, power, quality, and mass. Furthermore, such interventions could be the first choice to confer health-related benefits in patients who are unable or unwilling to tolerate aerobic training. Although previous meta-analysis indicated that resistance training intervention is associated with reduction in glycated hemoglobin (HbA1c) levels (Lee et al., 2017; Umpierre et al., 2013), such syntheses also point out that the number of randomized clinical trials in patients with T2DM is small. This scenario is still more scant when considering some neuromuscular outcomes, such as muscle quality, and in exclusive samples of older patients with T2DM.

Accordingly, we conducted a randomized clinical trial, with an active control group, and 1:1 allocation ratio, to assess the effects of resistance training on neuromuscular outcomes in elderly patients with T2DM. The primary outcome was the muscle quality measured by specific tension and echo intensity of muscle image. The secondary outcomes were muscle strength and muscle thickness, functional performance, lipid markers, glycemic control, visceral adipose tissue and quality of life. The conceptual hypothesis was that RTG could lead to superior neuromuscular gains compared with an active CG.

2. Material and methods

2.1. Study design

The present study is a 3-month randomized controlled clinical trial named Diabetes Resistance Training Adaptations in Elderly (NCT02548000) with two groups: RTG and active CG. The resistance training program was performed three times a week, while the CG performed a stretching workout once a week. Patients attended the laboratory five times for evaluations, at least48 hours apart. On the first day, participants underwent ultrasonography assessment for quantification of visceral adipose tissue, muscle thickness and echo intensity. On the second, third and fourth days strength and functional tests were carried out. These three repeated assessments at pre-intervention were realized to avoid measurement biases led by familiarization effects. On the last day the blood collection was performed. All outcomes were evaluated at baseline and post 12 weeks. The study was carried out for three semesters since July 2015 until December 2016 at Hospital de Clínicas de Porto Alegre and at School of Physical Education, Physiotherapy and Dance of Universidade Federal do Rio Grande do Sul. The patient's recruitment occurred in three waves. We considered the CONSORT recommendations for reporting the present clinical trial.

2.2. Sample size

Initially, a sample size of 18 patients was calculated for primary outcome considering a difference between groups of 0.2 N/cm^3 (specific tension) and an expected standard deviation of 0.1 N/cm^3 (Tracy et al., 1999). However, to consider a hypothesized benefit on glycemic control, we further calculated the sample size for HbA1c changes. Using as reference a study with comparable population and intervention modality, we found that 36 subjects would be required to find a difference of 1% on HbA1c between groups with an expected standard deviation of 1.6% (Castaneda et al., 2002). We exceeded this sample size in 8 subjects due to the expected dropout. The power considered was 90%, with a two-tailed alpha of 0.05.

2.3. Recruitment and eligibility criteria

Participants were recruited by oral invitation or by media, such as newspaper, social networks, posters and pamphlets. Participants who expressed interest in the study were screened either via telephone or face to face using a scripted screening considering the inclusion and exclusion criteria. Inclusion criteria were: a) age ≥ 60 years old; b) previous clinical diagnostic of T2DM; c) body mass index between 18.5 kg/m^2 and 34.9 kg/m^2; d) and to be a non-smoker (within past six months). Exclusion criteria were patients under use of insulin, major cardiovascular events (i.e., myocardial infarction) in the past six months, uncontrolled hypertension, diabetic neuropathy or retinopathy, uncompensated heart failure, unstable angina, peripheral amputations, chronic kidney disease, major depression, musculoskeletal impairment that makes patients unable to enroll a physical exercise program, and the current participation in resistance training within past six months.

Study's exclusion criteria were verified by questionnaire in a face-to-face interview, and the cardiovascular status was accessed through ergometry conducted by a cardiologist. T2DM status was defined by the HbA1c levels measured between the previous six months and study enrollment, using the threshold of 6.5% (American Diabetes Association, 2013). All participants were under pharmacological treatment by oral anti-hyperglycemic medication. The study was approved by the ethical board, conducted according to the Declaration of Helsinki and all the participants signed the informed consent before evaluations.

2.4. Randomization

After completion of baseline evaluations, participants were randomly allocated in equal number to two groups, according to block design sizes of 8 subjects, stratified by sex, with a 1:1 ratio, and allocation concealment. The randomization sequence was computer-generated in a website (www.random.org) by a researcher without contact with the patients. The allocation was blinded also with a response e-mail containing a respective group that patient was allocated.

2.5. Interventions

2.5.1. Resistance training program

The resistance training program was performed three times a week, using a linear periodization model (Table 1). Strength exercises were performed on traditional machines, free weights and functional exercises (i.e. squat and steps up and down). In all sessions, participants' blood pressure and capillary blood glucose were assessed and recorded before and after the resistance training program. A digital sphygmomanometer (OMROM-HEM7113, São Paulo, Brazil) and a glucometer

Table 1
Resistance training program

Weeks	Repetitions	Intensity	Series	Rest between series
Functional exercises (squat and steps up and down)				
1–4	10	Additional load or step	2	60 s
5–8	10	if < 6 on OMNI scale	3	60 s
9–12	15		3	90 s
Traditional exercises (leg press, leg extension, leg curl, hip abduction, inclined bench press, low row, biceps curl, triceps, crunch)				
1–4	12	15 RMs	2	60 s
5–8	12	15 RMs	3	60 s
9–12	10	12 RMs	3	90 s

RMs: repetitions maximum; OMNI scale from 0 to 10.