

# Resistance training does not change glucose and cardiac autonomic function of patients with type 2 diabetes

# Treinamento resistido não altera a glicemia e a função autonômica cardíaca de pacientes com diabetes tipo 2

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#### **RESUMO**

Objetivo: avaliar a influência de um protocolo de TR na função autonômica cardíaca e variáveis cardiovasculares em pacientes com DM-2. Métodos: 9 pacientes com DM-2. Após uma avaliação foi realizada a coleta de dados referentes aos intervalos R-R (iR-R) da frequência cardíaca (FC) e as pressões arteriais sistólica (PAS) e diastólica (PAD) durante a execução de Testes de Função Autonômica Cardíaca (TFAC) de Manobra de Acentuação da Arritmia Sinusal Respiratória (MASR), Manobra Postural Ativa (MPA), Manobra de Valsalva (MVal), Teste de Handgrip e ainda foram analisados os dados da FC, PAS, PAD e duplo produto (DP) nas condições pré e pós TR. Foi aplicado TR com intensidade moderada de 60% de 1RM, exercícios para membros inferiores e superiores, duas vezes por semana durante 12 semanas. Resultados: as variações (dados pós TR menos pré) dos índices calculados para os TFAC não apresentaram diferenças estatísticas significantes (p>0,05). A PAS, PAD e FC também não apresentaram diferença significante no entanto, o DP apresentou diminuição em repouso ( $\Delta$ =-990,55±1154,91) Conclusões: o TR moderado com 12 semanas, em pacientes com DM-2, não promove alteração da função autonômica cardíaca mas, diminui a sobrecarga do miocárdio por atenuar o DP em repouso.

Palavras-chave: Treinamento resistido; Diabetes Mellitus; Função autonômica cardíaca.

#### ABSTRACT

Objective: to evaluate the influence of a RT protocol on the function autonomic heart rate and cardiovascular variables in patients with DM-2. Methods: 9 patients with DM-2 participated in the study. After initial evaluation, data collection was performed regarding the RR intervals (iR-R) of the frequency heart rate (HR) and systolic (SBP) and diastolic (DBP) blood pressures while performing Function Tests Autonomic Cardiac Respiratory Sinus Arrhythmia Accentuating Maneuver (ABR), Active Postural Maneuver (APM), Valsalva Maneuver (ValM), Handgrip Test and the HR, SBP, DBP and double product (DP) data were also analyzed under the pre and post RT. RT was applied with moderate intensity of 60% of 1RM, exercises for lower and upper limbs, twice a week for 12 weeks. Results: the variations of the calculated indices for the TFACs did not show differences significant statistics (p>0.05). PAS, PAD and FC also showed no difference However, the PD showed a decrease at rest ( $\Delta$ = -990.55 ±1154.91) Conclusions: the moderate RT with 12 weeks, in patients with DM-2, does not promote any change in the function autonomic cardiac output but decreases myocardial overload by attenuating PD at rest. **KeyWords:** Resistance training; Diabetes mellitus; Autonomic heart function.

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### **INTRODUCTION**

Diabetes *Mellitus* type 2 (DM-2) can cause degeneration of sympathetic and parasympathetic nerve fibers (EWING; CAMPBELL; CLARKE, 1980; DIMITROPOULOS; TAHRANI; STEVENS, 2014) as well as exercise physical intolerance caused by deficit chronotropic and hyper or hypotension post effort (LOZANO; ENA, 2017). From the stratification of the Maneuver to Accentuate Respiratory Sinus Arrhythmia (MARA), Active Postural Maneuver (APM), Valsalva Maneuver (ValM) and Palmar *Grip Test* – Handgrip (EWING; CAMPBELL; CLARKE, 1980; EWING D.J et al, 1985) it is possible to evaluate the function and classifies it as normal, initial or severe dysfunction.

Various preventive and curative strategies have been the subject of intense investigation, among which is the exercise physical resistance (EPR) that has gained special attention in recent years due to the favorable effects on the levels glycemic levels (ADA, 2015). The EPR is able to increase insulin sensitivity (SBC, 2016; ARORA; SHWETA; SANDHU, 2009), prevent obesity, reduce the expression of local inflammatory markers (COSTA, 2010), increase lean mass and reduce systemic blood pressure, contributing to the functional improvement of activities of daily living (ARORA; SHWETA; SANDHU, 2009).

As for the influence of interventions no pharmacological tests on the responses of the function tests autonomic, no studies were found in the literature on the chronic effects of EPR training on the function. Autonomy assessed by Ewing 's tests.

Thus, the present study proposes to test the hypothesis that resistance training (RT) improves functional autonomic function of patients with DM-2.

# **METHODS**

Ethical Aspects: The study was approved by the Ethics Committee in Research Involving Human Beings in accordance with Resolution 466/2012 and its Complements of the National Health Council (Opinion No. 1,779. 423). The volunteers were informed about the experimental procedures and that they would not affect their health. Furthermore, they were informed about the confidentiality of their identity and the information collected. After reading and agreeing, they signed an informed consent form. Sample Size: considering the variations in the HR values for the MARA between the pre- and post-intervention moments of the Bhagyalakshmi study *et al.* (2010), a type 1 error of 1% and a power of 90%, a sample of 6 sample elements was initially estimated. Considering a sample loss of 30%, 9 volunteers were selected. Subsequently, the study power of 63% was calculated, for a difference between the averages of the HR values of the ASR of 1.14 (bpm). standard deviation of 1.2 (bpm) and 8 sample elements.

Inclusion Criteria: type 2 diabetics, non - insulin dependent (SBC, 2016), of both sexes, age group from 45 to 75 years, not practicing resistance exercise (RE) in the last six months, without limitations physical obstacles that would prevent the practice of PE. Associated comorbid conditions such as dyslipidemia, obesity, and medicated and controlled hypertensives were included.

Criteria of No Inclusion: being smokers and/or active alcoholics, diagnosed with deep vein thrombosis, neoplasms, angina, arrhythmias, insufficiency heart disease, coronary artery disease, lung, kidney and neurological diseases.

The experiments were carried out at the same time of day, to standardize the influences of circadian variations on the organism (NUMATA et al, 2013). The room environment used for data collection was maintained with a temperature between  $22^{\circ}$  C and  $24^{\circ}$  C and a relative humidity between 40% and 60%. The volunteers used appropriate clothing to carry out the experiments; did not ingest alcoholic beverages and/or stimulants 48 hours before; not performing physical activities outside the daily routine; had a regular night's sleep and a light meal at least 2 hours before the experiments. All volunteers underwent data collection familiarization procedures at least 24 hours before the final collection. Before and after the RT, the evaluation procedures (data collection) took place with intervals of 48 to 72 hours between them.

The level of physical activity Exercise score was evaluated Physical and Leisure (EPL) questionnaire *Baecke* (MAZO et al, 2001).

Global obesity was assessed by the Body Mass Index (BMI) (WHO, 2000) and by measuring the percentage of body fat (*Biodynamics, 450 classes I TBW, São Paulo, Brazil*) where men with percentage  $\geq 25\%$  and women  $\geq 35\%$  were considered obese (DEURENBERG, YAP & STAVEREN, 1998; DIJK et al, 2012). Abdominal obesity was assessed by waist circumference (WC), considered increased for men  $\geq$ 94 centimeters (cm) and women  $\geq$ 80 cm (TAYLOR et al, 2000) and the waist/hip ratio (HR/Q) considered increased for men  $\geq$ 0.90 and women  $\geq$ 0.85 (WHO, 2000) and the waist-to-

height ratio (HR/H), where values greater than 0.5 are classified with increased cardiac risk (PITANGA. LESSA, 2006). Finally, the conicity index (ICon) was calculated, with cutoff points of 1.25 for men and 1.22 for women over 50 years of age (PITANGA; LESSA, 2006).

The individual remained at rest, in the supine position, for 20 minutes and heart rate (HR) and systemic blood pressure were recorded (SBC, 2006). The double product (SD) was obtained by calculating the product of HR and systolic blood pressure (SBP) (SD = HR x SBP).

To evaluate the function the following tests were applied: Valsalva maneuver, whose reference value for normality is  $\geq 1.21$  (EWING et al, 1985); Respiratory Sinus Arrhythmia Accentuation Maneuver (EWING et al, 1985), whose difference between the expected HR values in expiration and inspiration must be  $\geq 15$  and the ratio between the iR-R (ms)  $\geq 1.04$  for the age group between 60 and 64 years (LOZANO; ENA, 2017); Palmar Grip Test - Handgrip (North Coast *Hydraulic Hand Dynamometer*), whose methodology followed the recommendations of the *American Society of Hand Therapists* (FESS, 1992). RR intervals were recorded continuously (*Polar* <sup>®</sup> *model RS800-CX*) one minute before palm grip with 30% of maximum strength, previously measured, during one minute of grip and three minutes of recovery. SBP and DBP were measured before and at the end of the test and the difference between DBP at initial rest and exercise was considered to assess the MARA response. peripheral and this delta should be > 16 to be considered normal (EWING et al, 1985).

Intervention Protocol: a training protocol with EPR was developed involving exercises for large muscle groups of the upper limbs and trunk and for the lower limbs (LL) based on the recommendations of the *American Heart Association* (ACMS, 2009).

To define the training load, the test of 1 repetition maximum (1RM) was used and 60% of 1RM was calculated with rest intervals of 90s between sets and 2 minutes between exercises. For the upper limbs, 3 sets of 15 repetitions were applied and for the lower limbs, 2 sets of 15 repetitions. The adjustments of the loads took place weekly and for this, a method proposed by Santos (2009) was used, which consists of performing the last series of each exercise until the concentric failure, where the exceeded repetitions, in relation to the number of pre-determined repetitions, were used. as an indication for the load increment for the next training session. 0.5 kg was added for each repetition exceeded for the upper limbs and 1 kg for the lower limbs. In addition to this proposal,

the submaximal HR of each volunteer as well as any sign of discomfort were also criteria for interruption of the sequence of repetitions.

Vital signs (BP and HR) were monitored daily before the session, at the 1st and 5th minute after the exercises. The HR was also measured during the execution of the series of exercises. For this purpose, a Polar model Ft1 heart monitor was used.

The intervention had a total duration of 12 weeks, totaling 24 interventions. Volunteers who participated at least 85%, that is, 20 sessions were categorized as volunteers who fulfilled the intervention proposal.

Analysis statistics - the variables were measured in the phases before and after intervention. Considering that the study intended to analyze the effect of the intervention period on the group, the focus of the analysis consisted of the variation of values between the phases, a variation that represents the effect. Thus, the effect was analyzed by delta ( $\Delta$ ) variation (post-pre). The variables biochemistry, measures and indices anthropometrics, body composition and the indices obtained with the function tests Resumen autonomic parameters were analyzed for their quantitative values. Data are described by the mean and standard deviations for the quantitative variables. Qualitative variables are described by the relative (%) and absolute (*f*) frequency distribution. The normality distribution was verified by the *Shapiro-Wilk test*. For the conditions in which the effect is intended to be analyzed, the delta variation ( $\Delta$ ) was calculated in the phases before and after at rest, and for the comparison of two means within the group, the *Student t* test was used. for paired sample or the *Wilcoxon test when the data violated the* normality distribution assumption.

### RESULTS

Between June 2015 and January 2017, volunteers were selected to participate in the study. Figure 1, shows the flow of participants from recruitment to the final outcome after intervention.

Figure 1 - Study flowchart.



Source: Author's own collection.

Table 1 shows the data referring to the characteristics anthropometrics, body composition, variables biochemical and hemodynamic changes in the resting condition. Only the DP showed a significant difference between the phases (p<0.05).

Variables	Results	Δ	$\Delta\%$	р
Age years)	63.55±9.69			
BM (kg)	71.30±13.54	$-0.63 \pm 1.78$	-0.88	0.31
BMI (kg/m²)	28.25±5.21	-0.36±0.78	-1.27	0.20
FM (%)	34.35±5.81	0.13±3.99	0.37	0.92
LM (Kg)	46.27±6.86	$-0.63 \pm 2.79$	-1.36	0.51
WC (cm)	96.52±14.83	$-2.34 \pm 3.81$	-2.42	0.10
WR/Q	0.96±0.11	$-0.01\pm0.02$	-1.04	0.41
HR/H	$0.60 \pm 0.08$	$-0.01\pm0.02$	-1.67	0.11
ICon	1.31±0.10	$-0.02\pm0.05$	-1.53	0.29
Blood glucose	119.89±23.09	$10.00 \pm 15.28$	8.34	0.08
(mg/dl)				
TC (mg/dl)	192.22±39.05	-3.11±28.87	-1.62	0.75
LDL (mg/dl)	109.31±46.73	-8.62±48.81	-7.89	0.61
HDL (mg/dl)	47.55±15.53	$-0.44 \pm 13.45$	-0.93	0.92
TG (mg/dl)	194.66±82.83	11.88±64.33	6.10	0.59
SBP (mmHg)	130.44±17.22	-4.66±18.89	-3.57	0.50
DBP (mmHg)	$79.00 \pm 10.88$	$-0.88 \pm 11.62$	-1.11	0.62
HR (bpm)	70.00±7.71	-5.00±9.09	-7.14	0.13
PD (mmHg.bpm)	9094.22±1266.58	-990.55±1154.91	-10.89	0.02

**Table 1** - Demographic, anthropometric, body composition, variables biochemical and physiological variables (at rest) in the pre - intervention phase in absolute values the variations calculated with the data from the post training phase of the studied volunteers (n=9).

Note:  $\Delta$ : variation FM: fat mass; BM: body mass; LM: lean mass Kg: kilograms; m: meters; BMI: body mass index; Kg/m2: kilograms per square meter; cm: centimeters; WC: waist circumference; cm: centimeters; WR/Q: waist-hip ratio; HR/H: waist-to-height ratio; ICon: conicity index; mg/dl: milligrams per deciliter; TC: total cholesterol; LDL: low density lipoprotein; HDL: high density lipoprotein; TG: triglycerides; mmHg: millimeters of mercury; SBP: systolic blood pressure; DBP: diastolic blood pressure; bpm: beats per minute; HR: frequency heart; DP: double product.

Table 2 shows the data from the function tests autonomic in the pre and post phases intervention, variation and analysis results statistic.

**Table 2** - Mean data, standard deviations and variations between the phases before and after the intervention of the variables and indices obtained with the function tests autonomic (n=9).

VariablesPre $\Delta$ $\Delta\%$ p					
	Variables	Pre	$\Delta$	$\Delta\%$	р

Parasympathetic Indices				
ValM	1.36±0.24	0.42±0.10	30.88	0.25
APM (RR)	1.13±0.19	-0.01±0.18	-0.88	0.86
MARA (RR)	9.95±7.30	-1.13±3.11	-11.36	0.30
MARA (FC)	1.15±0.13	$-0.01 \pm 0.04$	-0.87	0.47
Sympathetic Indices				
Handgrip (PAD)	4.44±6.04	$2.11 \pm 10.44$	47.52	0.56
APM (PAS)	2.33±8.21	0.88±13.34	37.77	0.84

Note: Δ: variation; %: percentage; ValM: Valsalva Maneuver; MARA: Respiratory Sinus Arrhythmia Maneuver; RR: RR intervals; FC: frequency heart; SBP: systolic blood pressure; DBP: diastolic blood pressure; APM: active postural maneuver.

The classification function testing clinic autonomic response before and after RT is shown in Table 3.

	Classification					
	Pre			Post		
Tests	Normal	borderline	Not normal	Normal	borderline	Not normal
Parasympathetic						
- ValM	6	3	0	6	3	0
-MPA (RR)	6	2	1	4	3	2
- MARA (RR)	3	0	6	3	0	6
- MARA (FC)	9	-	0	8	-	1
Sympathetic						
Handgrip (PAD)	0	2	7	0	3	6
APM (PAS)	8	1	0	8	1	0

**Table 3** - Classification function testing clinic autonomic status of the volunteers studied (n=9).

Note: ValM: Valsalva Maneuver; MARA: Respiratory Sinus Arrhythmia Maneuver; RR: RR intervals; FC: frequency heart; SBP: systolic blood pressure; DBP: diastolic blood pressure; APM: Active Postural Maneuver.

## DISCUSSION

After three months of RT the variables anthropometric, body composition, biochemical and function autonomic have not been modified. Among the variables hemodynamics, only the PD significantly decreased.

Regarding anthropometric measurements and body composition, our study corroborates other studies that did not find changes in total body mass, global obesity (SIGAL et al, 2007; CAUZA et al, 2005) and abdominal obesity (SIGAL et al, 2007) and body mass lean (DUNSTAN et al, 2002) after RT. However, it differs from others who found an increase in lean mass, a decrease in global and abdominal obesity (HUNTER et al, 2000).

One of the factors that can explain these differences is related to the intensity of the training. In our study, the intensity remained at 60% of the maxima, while Hunter et al (2000), who found a decrease in global obesity and an increase in lean mass, used 65 to 85% of the MR of the elderly. In addition, training and diet time can also influence. Elderly patients with DM2 submitted to six months of high intensity RT and food control for weight loss maintained lean mass and decreased % total body fat and WC (DUNSTAN et al, 2002).

In relation to the variables hemodynamic parameters, as in other studies, the decrease in HR (SIGAL et al, 2007; VINCENT et al, 2003), 5 bpm, and SBP, 4.66 mmHg, were not statistically significant, but these variations are of great importance. because, according to Kelley (1997), a reduction of 5 mmHg in BP at rest reduces the risk of stroke and acute myocardial infarction by 40% and 15%, respectively.

However, it differs from other studies that found a decrease in HR (WOOD et al, 2001; LOIMAALA et al, 2003; ARORA; SHWETA; SANDHU, 2009) and systemic blood pressure (VINCENT et al, 2003; LOIMAALA et al, 2003; CAUZA et al, 2005; ARORA; SHWETA; SANDHU, 2009). However, these studies used different training protocols Wood *et al.* (2001) used 75% of the force maxima, Vincent *et al.* (2003) applied trained two groups, one with 50% and the other with 80% of the RM for six months, 3 weekly sessions and verified that the SBP presented greater attenuation in the group that trained with greater intensity. Similar results were reported by Cauza *et al.* (2005), with 22 DM-2, presented lower values of SBP and DBP at rest after the four-month intervention, and Loimaala *et al.* (2003) who observed a decrease in SBP and HR after 6 months of RT. On the other hand, a randomized, controlled and randomized study with 64 patients with DM-2 underwent 6 months of progressive RT weekly and in the reassessment the SBP and DBP showed slight attenuation with no significant difference (SIGAL et al, 2007).

The decrease in PD is directly related to the reduction in cardiac work, which is correlated with myocardial oxygen consumption (GOBEL et al, 1978), therefore, it represents better heart efficiency.

In a recent review Giacon *et al.* (2017) studied the influence of EF in patients with diabetes and described 10 studies found where only one of them used RT as a form of intervention and this one used frequency variability heart rate (HRV) as a tool to assess the ANS on the heart. In our proposal, the function tests autonomic function were used as ANS assessment methods, which can be used separately as tests of parasympathetic from HR variations obtained with APM, MARA and MVa, and function sympathetic by variations in SBP, in APM, and DBP in contraction isometric (*handgrip*) (WEIMER, 2010) or together to classify NAC as absent, dysfunction initial or borderline, definite or severe (EWING; CAMPBELL; CLARKE, 1980; EWING D.J et al, 1985). Zoppini *et al.* (2015) considered it important to apply a battery of tests to assess the possibility of dysfunction autonomic soon after diagnosis.

Jyotsna *et al.* (2009) found dysfunction parasympathetic and sympathetic in 44% and 51.9%, respectively, of the 145 DM-2 they investigated. Sucharita *et al.* (2011) reported changes in all tests in patients with DM-2 when compared to the control group. In our study, taking into account the criteria adopted by Jyostna *et al.* (2009), 77.7% of the volunteers had dysfunction sympathetic, by alteration in the DBP of the *Handgrip test*, and 66.6% dysfunction parasympathetic, being higher than those found by Jyostna *et al.* (2013).

The mean values, at baseline, presented in our study of the ValM index was 1.36, close to that evaluated by Pagkalos *et al.* (2008) who showed 1.40 in the DM-2 group without NAC and with NAC of 1.22. The index obtained with ValM shows variations in its values considered as a physiological response, being equal to or greater than 1.21 (LOZANO; ENA, 2017) or 1.12 (EWING et al, 2985) as normal responses, and it is important to emphasize that it tends to decrease with advancing age (FREEMAN; CHAPLEAU, 2013; LOZANO; ENA, 2017).

Regarding MARA, the same application related to age is also observed in the literature where the variation of HR between the moments of inspiration and expiration tends to decrease with age (FREEMAN; CHAPLEAU, 2013). Novak (2011) presents different values for age groups from 10 years old. In our study, the mean age was 63.55 years and, according to Novak's study, the MARA index must be greater than or equal to 7. The MARA index obtained in the present study was 9.95, which presented similarity with DM-2 classified as NAC in the Pagkalos *et al.* (2008) study which was 10.32. Lozano and Ena (2017) report that the index obtained by the ratio between the averages of the highest and lowest RR of the MARA must be greater than or equal to 1.04 for people between 60 and 64 years old. In our study, the mean age was 63.55 years and the index was 1.13 before the intervention, and there was no change after.

As for the performance of the *handgrip*, it is well established that cardiovascular and hemodynamic adjustments are mediated mainly by changes in parasympathetic and sympathetic neural activity (MITCHELL, 1990). In the *handgrip test*, where 30% of the MVC is imposed to perform it, the literature still differs as to how long contraction should be kept static. Lozano and Ena (2017) describe the maneuver time as 5 minutes, while other studies point to 3 to 5 minutes (EWING et al, 1985) and a proposal of 3 minutes (FREEMAN; CHAPLEAU, 2013). However, in both, DBP must vary above 16 mmHg between rest and exercise. In our study, the mean value of this variation was lower, 4.44 mmHg. In this case, the time factor may have been responsible for the small increase in DBP during exercise since we perform 30% of CVM for 1 minute only and this time does not seem to be enough to promote sympathetic adjustments needed to increase DBP in the exercise (ROWLAND; FERNHALL, 2007).

In the qualitative assessment presented in the present study, no positive changes occurred with the performance of the tests. There were 36 parasympathetics in all volunteers (4 index calculations in 9 participants) and 24 of these presented normal results, 5 borderline and 7 abnormal in the evaluation pre RT. In the post-intervention period, there was a decrease in normal tests, with 21 normal, 6 borderline and 9 abnormal, demonstrating a negative oscillation. As for the sympathetic tests, the variation of SBP in APM did not show any change (8 normal and 1 borderline) with the RT, but the DBP of the *handgrip* presented in the period pre 2 borderline and 7 abnormal and post RT 3 borderline and 6 abnormal. Bhagyalakshmi *et al* (2010)<sup>9</sup>applied aerobic training in DM-2 and the MARA technique, analyzing the difference in iR-R (ms) to assess whether the training was able to promote improvement in function autonomic function in this patient profile. After nine months of intervention, the index showed a significant increase from 13.03 to 16.50.

No studies were found in the scientific literature relating RT and function tests as pre- and post-intervention evaluative parameters. The studies with DM-2 found investigated the effect of nine months of aerobic training (BHAGYALAKSHMI et al, 2010) and six months of walking alone and another group associated with Yoga (JYOTSNA et al, 2010). Both studies found improvement in function autonomic.

### **Study limitations**

In the present study, the number of participants and the power of the study are not able to bring evidence solid evidence that the proposed protocol can promote changes in the function of the studied sample. With regard to the adaptations of the function autonomy to resistance training, it is desirable that the number of participants is greater to give greater power to the study.

# Final Considerations

Function tests used in the present study did not undergo changes with training, demonstrating the non- efficiency of the proposed protocol to influence these ANS reflex stimuli. However, the tests showed good clinical applicability because they are inexpensive and easy to use realization.

The absence of studies that applied the same methodology of evaluation of the function before and after intervention hindered a more consistent discussion of the effectiveness of these tests, thus, the proposal of implementing the battery of tests as a routine of evaluation before and after intervention in patients with DM-2.

# CONCLUSION

The RT protocol proposed in the present study was not effective in promoting changes in autonomic heart rate, lipid profile, blood glucose and body composition in patients with DM-2. But the data suggest that it promoted an important clinical improvement in HR and SBP and also, significant attenuation of the double product.

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