

## Resistance Training After Myocardial Infarction in Rats: Its Role on Cardiac and Autonomic Function

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### Abstract

**Background:** Although resistance exercise training is part of cardiovascular rehabilitation programs, little is known about its role on the cardiac and autonomic function after myocardial infarction.

**Objective:** To evaluate the effects of resistance exercise training, started early after myocardial infarction, on cardiac function, hemodynamic profile, and autonomic modulation in rats.

**Methods:** Male Wistar rats were divided into four groups: sedentary control, trained control, sedentary infarcted and trained infarcted rats. Each group with  $n = 9$  rats. The animals underwent maximum load test and echocardiography at the beginning and at the end of the resistance exercise training (in an adapted ladder, 40% to 60% of the maximum load test, 3 months, 5 days/week). At the end, hemodynamic, baroreflex sensitivity and autonomic modulation assessments were made.

**Results:** The maximum load test increased in groups trained control (+32%) and trained infarcted (+46%) in relation to groups sedentary control and sedentary infarcted. Although no change occurred regarding the myocardial infarction size and systolic function, the E/A ratio (-23%), myocardial performance index (-39%) and systolic blood pressure (+6%) improved with resistance exercise training in group trained infarcted. Concomitantly, the training provided additional benefits in the high frequency bands of the pulse interval (+45%), as well as in the low frequency band of systolic blood pressure (-46%) in rats from group trained infarcted in relation to group sedentary infarcted.

**Conclusion:** Resistance exercise training alone may be an important and safe tool in the management of patients after myocardial infarction, considering that it does not lead to significant changes in the ventricular function, reduces the global cardiac stress, and significantly improves the vascular and cardiac autonomic modulation in infarcted rats. (Arq Bras Cardiol. 2014; 103(1):60-68)

**Keywords:** Myocardial Infarction; Rehabilitation; Resistance Training; Exercise; Ventricular Function; Autonomic Nervous System; Rats.

### Introduction

Myocardial infarction (MI) is one of the most prevalent cardiovascular diseases worldwide, leading to high morbidity and mortality rates<sup>1</sup>. MI triggers a ventricular remodeling process characterized by progressive left ventricular (LV) dilatation, rearrangement of the ventricular wall structure, increase in the remaining muscle mass, and decrease in cardiac function<sup>2</sup>. The cardiovascular autonomic imbalance following MI is a key element in the pathophysiology of heart

failure (HF) and is accompanied by abnormalities in the reflex cardiorespiratory control<sup>3,4</sup>.

Since the classical study conducted by Sullivan et al<sup>5</sup> in late 1980, evidences have accumulated regarding the beneficial effects of aerobic exercise training (ET), which is considered a fundamental intervention in preventive cardiology<sup>6-8</sup>. Additionally, the moment to start ET after MI seems to be an important variable as regards the benefits observed<sup>6</sup>. Experimentally, our group has consistently demonstrated that aerobic ET started early after MI is able to reduce the infarct size, improve LV function, increase peripheral blood flow, and promote positive adjustments in the autonomic nervous system of infarcted rats<sup>9-12</sup>.

Not long ago, resistance training (RT) was being traditionally discouraged for patients after MI or with HF, because of concerns about compromising the LV function. However, in recent years, RT has been recommended for patients with HF, based on the logic that this form of training may be more effective in reverting skeletal muscle atrophy and in improving the quality of life of these individuals<sup>13,14</sup>. In fact, RT seems to

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Manuscript received December 03, 2013; revised manuscript February 10, 2014; accepted February 24, 2014.

**DOI:** 10.5935/abc.20140093

attenuate the muscle mass reduction<sup>15</sup> and improve strength<sup>16</sup> and resistance<sup>17</sup>, as well as the maximal oxygen consumption<sup>18</sup> of patients with HF. However, the cardiac and autonomic effects of RT started early after MI are not yet fully understood. Thus, the objective of the present study was to assess the effects of low/moderate-intensity RT started early after MI on ventricular remodeling and function, as well as on the hemodynamic profile and cardiovascular autonomic control of rats undergoing myocardial ischemia.

## Methods

### Animals

Male Wistar rats (250g to 300 g) from the Animal Shelter of Sao Judas Tadeu University were used. The animals were kept in groups, in an environment with temperature between 22°C and 24°C and light controlled in 12-hour cycles (light/dark). Water and food were supplied ad libitum, and the diet had normal protein content. The present study was in accordance with the ethical principles of animal experimentation of the Brazilian College of Animal Experimentation (*Colégio Brasileiro de Experimentação Animal* – COBEA) and the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, National Academy of Sciences, Washington D.C., 1996); it was approved by the Ethics Commission on the Use of Animals of São Judas Tadeu University (CEUA-USJT: 008/2013).

The animals were randomly divided into four groups (n = 9, each): sedentary control (SC); trained control (TC); sedentary infarcted (SI); and trained infarcted (TI). After MI or sham surgery, the animals underwent echocardiographic assessment and maximum load test (MLT), and either the RT protocol or follow-up was started. At the end of 3 months, echocardiographic study, MLT, and catheterization of the femoral arteries and veins for direct blood pressure (BP) and heart rate recording were performed.

### Induction of myocardial infarction

Groups SI and TI were anesthetized (ketamine 80 mg/kg, and xylazine 12 mg/kg, i.p.) and underwent MI by surgical occlusion of the left anterior descending coronary artery, as described elsewhere<sup>12,13</sup>. In sum, left thoracotomy was performed, the third intercostal space was dissected, and the heart was exposed. The left descending coronary artery was occluded using nylon 6-0 suture at approximately 1 mm of the left auricle. The thorax was closed using nylon 4-0 suture and the animals were kept under artificial ventilation until recovery. Groups SC and TC underwent the same procedure, except for myocardial ischemia, which was not performed (sham).

### Echocardiographic assessment

Echocardiographic assessment was performed by an observer blind to the groups which the animals had been assigned to, and followed the guidelines of the American Society of Echocardiography. The animals underwent two echocardiographic assessments: the first, 2 days after MI or sham surgery (baseline assessment); and the second, three months after RT or follow-up (final assessment), according to methodology described elsewhere<sup>12,13</sup>.

The rats were anesthetized (ketamine 80 mg/kg, and xylazine 12 mg/kg, i.p.) and the images were obtained using a 10 to 14-MHz linear transducer in a Sequoia 512 device (ACUSON Corporation, Mountain View, CA) for the assessment of the following parameters: (1) morphometric: LV mass, LV diastolic diameter (LVDD) and relative wall thickness (RWT); (2) systolic function: ejection fraction (EF) and velocity of circumferential fiber shortening (VCF); (3) diastolic function: isovolumic relaxation time (IVRT) and E/A wave ratio; and (4) overall function: myocardial performance index (MPI).

### Maximum load test and resistance training

All groups underwent a MLT protocol and RT, performed in a ladder adapted for rats, featuring 54 vertical steps 0.5 cm apart from each other. The animals were gradually adapted to climbing for 5 consecutive days before the MLT. The test consisted of an initial load of 75% of body weight, which was progressively increased with an additional 15% of body weight in subsequent climbings, as previously described by our group<sup>19</sup>. MLT was performed 5 days after MI or sham surgery (baseline assessment), 45 days after training or follow-up for load adjustment (data not presented), and at the end of 3 months of protocol (final assessment).

The RT protocol was performed for 3 months, 5 days a week, 15 climbings per session, with a 1-minute rest between each climbing, at low/moderate intensity (40% to 60% of the maximum load)<sup>19</sup>, as recommended for patients with cardiovascular disease<sup>14</sup>.

### Hemodynamic assessments

One day after the final MLT, two catheters containing 0.06 mL of saline solution were implanted in the femoral artery and vein of the anesthetized animals (ketamine 80 mg/kg, and xylazine 12 mg/kg, i.p.). The next day, the arterial catheter was connected to a pressure transducer (Blood Pressure XDCR; Kent Scientific, Torrington, CT) and the BP and pulse interval (PI) signals were recorded for 30 minutes with the animals awoken, as previously described<sup>12,13,20</sup>.

After the baseline recording, sequential injections (0.1 mL) of up-titrated doses of phenylephrine (0.25 to 32 mg/kg) and sodium nitroprusside (0.05 to 1.6 mg/kg) were administered, inducing responses of increased or decreased mean BP (MBP), ranging from 5 to 40 mmHg. Baroreflex sensitivity was expressed as bradycardic response (BR) and tachycardic response (TR), in beats per minute by millimeter of mercury, as described elsewhere<sup>12,13,20</sup>.

### Cardiovascular autonomic modulation

The overall PI and systolic BP (SBP) variability in the time domain was assessed using standard deviation (SD) of time series. PI and SBP variations were also assessed in the frequency domain, using autoregressive modeling of the spectral analysis. The theoretical and analytical procedures for autoregressive modeling of the oscillatory components are described elsewhere<sup>20,21</sup>. In sum, the PI and SBP series, derived from each recording, were divided into 300-beat segments, with 50% overlapping. The spectra of each segment were

calculated using the Levinson-Durbin algorithm; the order of the model chosen was in agreement with Akaike's criterion, with oscillatory components quantified in low frequency (LF: 0.2 to 0.6 Hz) and high frequency (HF: 0.6 to 3.0 Hz).

### Tissue weighing

After cardiovascular assessments, the animals were euthanized by decapitation, and the soleus and gastrocnemius muscles, as well as the retroperitoneal white adipose tissue were immediately removed and weighed.

### Statistical analysis

The statistical analysis was carried out using the Statistical Package for the Social Sciences (SPSS), version 20.0 for Windows (Chicago, USA). Data are presented as mean  $\pm$  standard error of the mean. After using the Kolmogorov-Smirnov test to confirm that all continuous variables were normally distributed, the statistical differences between the groups were obtained using two-way ANOVA followed by Bonferroni post-test. Statistical differences between data assessed throughout time were obtained using ANOVA for repeated measures, with assessed group factor, followed by Bonferroni test. The significance level was set at  $p < 0.05$ .

## Results

### Physical capacity and body weight

At baseline, the infarcted animals (SI and TI) showed a reduction of MLT in comparison to non-infarcted animals (SC and TC). After the RT or follow-up period, the trained groups (TC and TI) showed increased MLT values in relation to their baseline assessments and in comparison to the respective controls (SC and SI) (Figure 1). However, group TI remained with reduced MLT values in relation to TC at the end of the study. In MLT, there was interaction between the assessment moments and the experimental groups ( $F = 72.402$ ;  $p < 0.001$ ).

At baseline, body weight was similar between the groups studied ( $\sim 277 \pm 7$  g); however, at the end, the experimental groups showed increased body weight in relation to baseline (SC:  $490 \pm 10$ ; TC:  $454 \pm 12$ ; SI:  $478 \pm 13$ ; TI:  $465 \pm 18$  g). As regards the retroperitoneal white adipose tissue weight, groups TC ( $4.5 \pm 0.6$  g) and TI ( $5.9 \pm 0.5$  g) showed reduced values in relation to groups SC ( $8.1 \pm 1.1$  g) and SI ( $7.1 \pm 0.8$  g), respectively. The weight of the soleus and gastrocnemius muscles, which was reduced in group SI ( $0.17 \pm 0.02$  and  $1.00 \pm 0.09$  g) in relation to SC ( $0.28 \pm 0.02$  and  $1.37 \pm 0.05$  g), increased with RT, as observed in groups TC ( $0.41 \pm 0.03$  and  $1.59 \pm 0.04$  g) and TI ( $0.30 \pm 0.02$  and  $1.26 \pm 0.01$  g) in relation to their sedentary peers.

### Morphometry and ventricular function

The echocardiographic variables related to morphometry and ventricular function are presented in Table 1.

The LV infarct size, which was similar among the infarcted groups (ST and TI) in the baseline echocardiographic

assessment, was not modified by the RT period. LV mass and RWT were similar among the groups in the baseline assessment. At the end of the study, the trained groups (TC and TI) showed increased LV mass in relation to the baseline assessments, as well as in comparison to their respective controls (SC and SI). In relation to RWT, group TC showed elevation, and group SI showed reduction of this variable, when compared to SC. However, RT was efficient in preventing this reduction in group TI in relation to group SI. The end-LV diastolic diameter, which was similar among the groups in the beginning of the protocol, was increased at the end of the study in groups SI and TI, in relation to SC (Table 1). In the morphometric variables, there were interactions between the assessment moments and the experimental groups regarding the LV mass assessments ( $F = 19.805$ ;  $p < 0.001$ ) and RWT ( $F = 0.0296$ ;  $p < 0.001$ ).

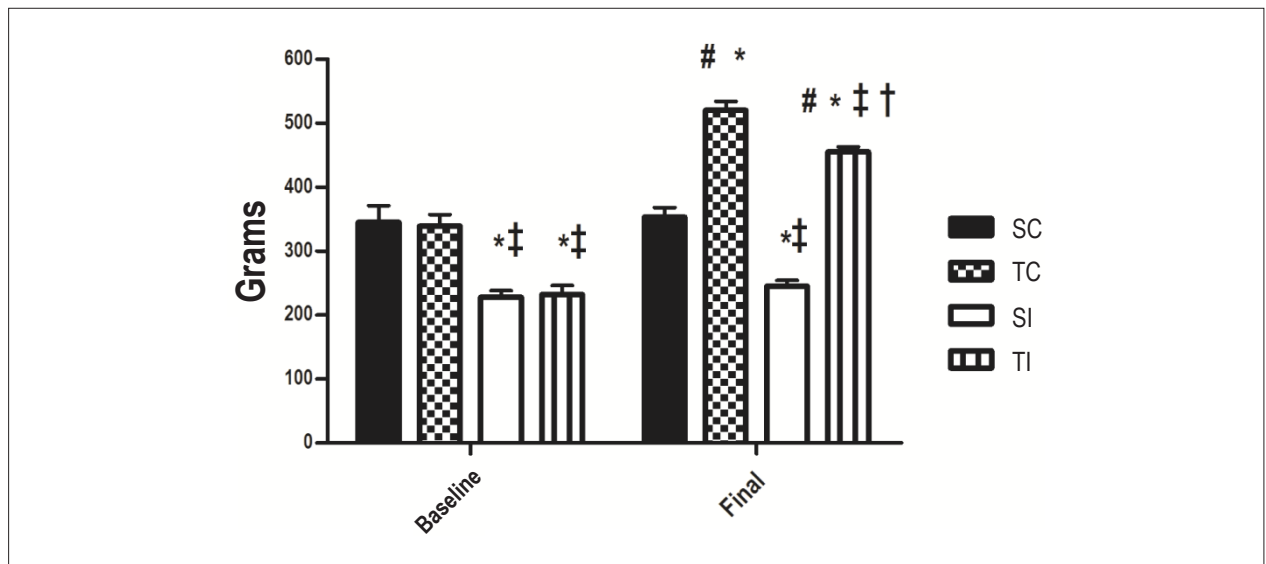
As regards the LV systolic function variables, groups SI and TI showed reduction in EF and shortening velocity in the baseline and final echocardiographic assessments in relation to groups SC and TC. The E/A ratio, initially increased in animals of groups SI and TI, improved with RT in IT animals when compared to SI animals as well as in relation to their baseline assessment. In the final assessment, this diastolic function parameter was increased in groups TC and SI in relation to SC, as well as in group SI in relation to TC. On the other hand, IVRT did not change with MI or RT (Table 1).

The global LV function assessment, performed by MPI, was similar among the groups in the beginning of the study. However, at the end of the study, this variable increased in group SI in comparison to SC. We should point out that the RT period improved MPI in groups TC and TI in relation to their respective controls (SC and SI). However, group TI remained with increased MPI in relation to TC. Interactions between the assessment moments and the experimental groups were observed in the cardiac function variables: E/A ratio ( $F = 2248.060$ ;  $p < 0.001$ ) and MPI ( $F = 23.293$ ;  $p < 0.001$ ).

### Hemodynamic assessments

Group SI showed reduction in SBP in relation to group SC. Although differences between TI and SC were not observed, group TI showed decreased SBP in relation to SC. As regards SBP, there was interaction between RT and MI ( $F = 13.068$ ;  $P = 0.001$ ). Additionally, no differences were observed in the parameters related to diastolic BP (DBP), MBP and HR among the groups assessed, as shown in Table 2.

TR to blood pressure drops after injection of sodium nitroprusside was reduced in animals of groups SI and TI in relation to those of groups SC and TC. BR to blood pressure increases after up-titrated doses of phenylephrine was reduced in animals of group SI in relation to those of group SC. RT induced BR increase in group TC rats in comparison to group SC. We should point out that no differences were observed in BR between groups TI and SC; however, group TI showed reduced BR in relation to TC (Table 2). Interaction between RT and MI was observed in BR ( $F = 12.087$ ;  $p = 0.001$ ).



**Figure 1** – Values of the maximum load test in groups sedentary control (SC), trained control (TC), sedentary infarcted (SI), and trained infarcted (TI). #  $p < 0.05$  vs. baseline assessment; \*  $p < 0.05$  vs. SC; ‡  $p < 0.05$  vs. TC; †  $p < 0.05$  vs. SI.

**Table 1** – Baseline and final echocardiographic assessments of morphometry and cardiac function in groups sedentary control (SC), trained control (TC), sedentary infarcted (SI), and trained infarcted (TI)

Variables/groups		SC	TC	SI	TI
LV mass (g)	Baseline	1.07 ± 0.02	1.10 ± 0.04	1.15 ± 0.04	1.11 ± 0.05
	Final	1.10 ± 0.05	1.77 ± 0.09#*	1.29 ± 0.05#*	1.71 ± 0.08#*†
RWT	Baseline	0.39 ± 0.04	0.43 ± 0.02	0.37 ± 0.02	0.44 ± 0.05
	Final	0.40 ± 0.01	0.52 ± 0.03*	0.28 ± 0.02*	0.48 ± 0.04†
LVDD (cm)	Baseline	0.65 ± 0.01	0.63 ± 0.01	0.80 ± 0.01	0.82 ± 0.02
	Final	0.73 ± 0.01	0.74 ± 0.02	0.92 ± 0.04*	0.87 ± 0.05*
<b>Systolic function</b>					
EF (%)	Baseline	74 ± 3	72 ± 6	46 ± 4*‡	44 ± 3*‡
	Final	71 ± 1	68 ± 2	43 ± 4*‡	40 ± 2*‡
VCF (circ/seg 10-4)	Baseline	51 ± 4	49 ± 3	30 ± 5*‡	35 ± 2*‡
	Final	46 ± 1	45 ± 5	32 ± 2*‡	33 ± 3*‡
<b>Diastolic function</b>					
IVRT (ms)	Baseline	30 ± 2	31 ± 1	28 ± 1	30 ± 2
	Final	31 ± 3	32 ± 1	30 ± 1	32 ± 3
E/A	Baseline	1.57 ± 0.11	1.61 ± 0.22	2.74 ± 0.12*	2.77 ± 0.21*
	Final	1.61 ± 0.12	1.87 ± 0.04*	2.69 ± 0.05*‡	2.07 ± 0.10#*†
<b>Overall function</b>					
MPI	Baseline	0.44 ± 0.03	0.46 ± 0.03	0.45 ± 0.04	0.46 ± 0.02
	Final	0.37 ± 0.03	0.19 ± 0.01*	0.54 ± 0.04*	0.33 ± 0.02#*†

Values express mean ± standard error of the mean. #  $p < 0.05$  vs. baseline assessment; \*  $p < 0.05$  vs. SC; †  $p < 0.05$  vs. SI; ‡  $p < 0.05$  vs. TC.  
LV: left ventricle; RWT: relative wall thickness; LVDD: left ventricular diastolic diameter; EF: ejection fraction; VCF: velocity of circumferential fiber shortening; IVRT: isovolumic relaxation time; E/A: E and A waves ratio; MPI: myocardial performance index.

**Table 2 – Hemodynamic assessments in groups sedentary control (SC), trained control (TC), sedentary infarcted (SI), and trained infarcted (TI)**

Variables/groups	SC	TC	SI	TI
<b>Hemodynamics</b>				
SBP (mmHg)	125 ± 4	130 ± 3	113 ± 2*	121 ± 4†
DBP (mmHg)	85 ± 2	87 ± 3	85 ± 4	88 ± 5
MBP (mmHg)	98 ± 5	101 ± 4	94 ± 4	99 ± 3
HR (bpm)	327 ± 8	334 ± 10	351 ± 12	355 ± 14
<b>Baroreflex sensitivity</b>				
TR (bpm/mmHg)	3.5 ± 0.1	4.4 ± 0.6	1.8 ± 0.1*†	2.2 ± 0.3*†
BR (bpm/mmHg)	-2.4 ± 0.09	-4.3 ± 0.31*	-1.3 ± 0.05*†	-2.1 ± 0.21†

Values express mean ± standard error of the mean. \*  $p < 0.05$  vs. SC; †  $p < 0.05$  vs. TC.

SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; HR: heart rate; TR: tachycardic response; BR: bradycardic response.

### Cardiovascular autonomic modulation

Data regarding PI and SBP variability in the time and frequency domains are shown in Table 3. Group SI animals showed a reduction of the standard deviation of PI (SD-PI), of PI variance (PI-var), and of the root mean square of successive RR-interval differences (RMSSD) in relation to SC animals. There was additional PI-var reduction in groups SI and TI also in relation to group TC. After the RT period, further reduction of PI-var was prevented in group TI in relation to group SI; also, RMSSD became normal in group TI, since it showed values similar to those of group SC. There was interaction between RT and MI in the PI-var variable ( $F = 12.106$ ;  $p = 0.001$ ). As regards PI-var, no changes were observed in the experimental groups.

MI induced changes in the cardiac autonomic modulation of the animals studied, namely a reduction in LF (Figure 2A) and HF (Figure 2B) bands of PI, as well as in the autonomic balance (LF/HF) in group SI in relation to SC. We should point out that 3 months of RT were efficient in preventing these changes, as observed in group TI. However, both the LF range and the HF band remained reduced in group TI in relation to TC. On the other hand, the LF band of SBP, which was increased in group SI, became normal in group TI (Figure 2C). There was interaction between RT and MI in the absolute values of LF band of PI ( $F = 11.041$ ;  $p = 0.02$ ).

Corroborating the data regarding baroreflex sensitivity, as assessed by responses to vasoactive drugs, the alpha index of the LF band of SBP, which was reduced in group SI, did not change with RT.

### Discussion

The present study was conducted to test the hypothesis that low/moderate intensity dynamic RT could bring benefits to the cardiac function and improve the autonomic control of circulation in infarcted rats. The main findings of this study point to the fact that RT promoted ventricular morphometric changes in infarcted animals, which are not associated with changes in cardiac function. However, although the baroreflex sensitivity and the alpha index had not improved, RT was efficient in preventing further impairment of the cardiovascular autonomic modulation in animals undergoing MI.

RT has been accepted as the main component of an encompassing exercise program both for apparently healthy individuals and for those with cardiovascular disease. In this sense, the guidelines stress the importance of incorporating RT for an optimal exercise prescription for patients with heart diseases, with the purpose of improving muscular strength, physical capacity and the quality of life<sup>14-18</sup>.

Corroborating clinical data, in the present study, RT increased MLT values in infarcted animals in relation to sedentary animals, thus suggesting improvement of muscular strength in these animals. In addition, the reduction in the retroperitoneal adipose tissue and the weight increase of the soleus and gastrocnemius muscles in trained infarcted rates suggest a positive body composition change in these animals. Our findings in previous studies had already demonstrated positive adaptations to RT in body composition and in the increase in muscular strength in diabetic ovariectomized rats<sup>19</sup> and healthy rats<sup>22</sup>.

Despite its known benefits on the quality of life, muscular strength, and body composition, RT had been traditionally discouraged for patients with HF<sup>23</sup> due to concerns that it could lead to impairment of the LV function and have a potential adverse effect on cardiac remodeling, especially resulting from increased afterload. However, when RT was performed at a low/moderate intensity by patients with HF, the hemodynamic responses did not exceed the levels reached during a standard exercise test<sup>24</sup>, and adverse cardiac remodeling was not observed in patients after a RT period<sup>15</sup>.

In the present study, although the MI size and LVDD had not changed with RT in infarcted animals, the LV mass increased and RWT became normal in these animals, and these changes could suggest a positive cardiac remodeling. However, when variables related to the ventricular function were assessed, positive adaptation in EF, VCF, and IVRT were not observed in trained infarcted animals. Unlike these findings, our group has previously demonstrated that aerobic RT was able to reduce the MI size, LVDD, and improve the systolic and diastolic function of infarcted rats<sup>10,13</sup>. It is possible that a greater training volume, as well as the hemodynamic overload triggered by the aerobic training, had been responsible for these adaptations.

**Table 3 – Pulse interval and systolic blood pressure variability, in the time and frequency domains, in groups sedentary control (SC), trained control (TC), sedentary infarcted (SI), and trained infarcted (TI)**

Variables/groups	CS	CT	IS	IT
<b>PI variance</b>				
SD-PI (bpm)	11.5 ± 0.7	9.4 ± 1.3	5.3 ± 0.4*	8.1 ± 0.4*†
PI-var (ms <sup>2</sup> )	136.4 ± 16.1	140.0 ± 15.3	35.7 ± 7.0*‡	64.4 ± 4.0*†‡
RMSSD (ms)	6.3 ± 0.4	8.4 ± 0.8*	4.6 ± 0.2*‡	6.0 ± 0.2
HF/LF	0.41 ± 0.02	0.43 ± 0.05	0.19 ± 0.03*	0.28 ± 0.07
<b>SBP variance</b>				
SBP-var (mmHg <sup>2</sup> )	27.5 ± 6.0	23.2 ± 3.9	19.7 ± 2.2	26.9 ± 4.4
HF (mmHg <sup>2</sup> )	1.9 ± 0.2	1.7 ± 0.2	1.3 ± 0.2	1.8 ± 0.3
α index (LF, ms/mmHg)	1.13 ± 0.09	1.33 ± 0.32	0.62 ± 0.24*	0.76 ± 0.06*

Values express mean ± standard error of the mean. \*  $p < 0.05$  vs. SC; †  $p < 0.05$  vs. SI; ‡  $p < 0.05$  vs. TC.

PI: pulse interval; SD-PI: standard deviation of the pulse interval; PI-var: pulse interval variance; RMSSD: root mean square of successive RR interval differences; LF: low frequency band; HF: high frequency range; SBP: systolic blood pressure; SBP-var: systolic blood pressure variance; HF: high frequency.

On the other hand, the E/A ratio and MPI, an index that represents the overall cardiac stress, improved with RT in infarcted animals, thus suggesting some favorable cardiac adaptation to dynamic RT in these animals. Corroborating this hypothesis, group SI animals showed a SBP reduction in comparison to those of group SC. However, after the RT period, this variable became normal in trained animals. Recognizing that SBP reflects the cardiac work capacity, as suggested by Yu and McNeill<sup>25</sup>, we can hypothesize that the SBP reduction observed in the present study may be related to a reduction in ventricular performance in the sedentary group, thus becoming normal after the RT period.

Using a RT equipment different from the one used in the present study, Pinter et al<sup>26</sup> demonstrated that a 8-week RT promoted reduction in BP and HR, improvement in papillary muscle contractility and increase in cardiac myosin ATPase activity in healthy rats. On the other hand, Barauna et al<sup>22</sup> suggest that RT leads to the development of concentric cardiac hypertrophy without changing the ventricular function or cavity in healthy rats. Thus, the disagreement between the findings related to the cardiac function may have resulted from the choice of the RT model, as well as from the presence of ventricular dysfunction triggered by MI in the animals.

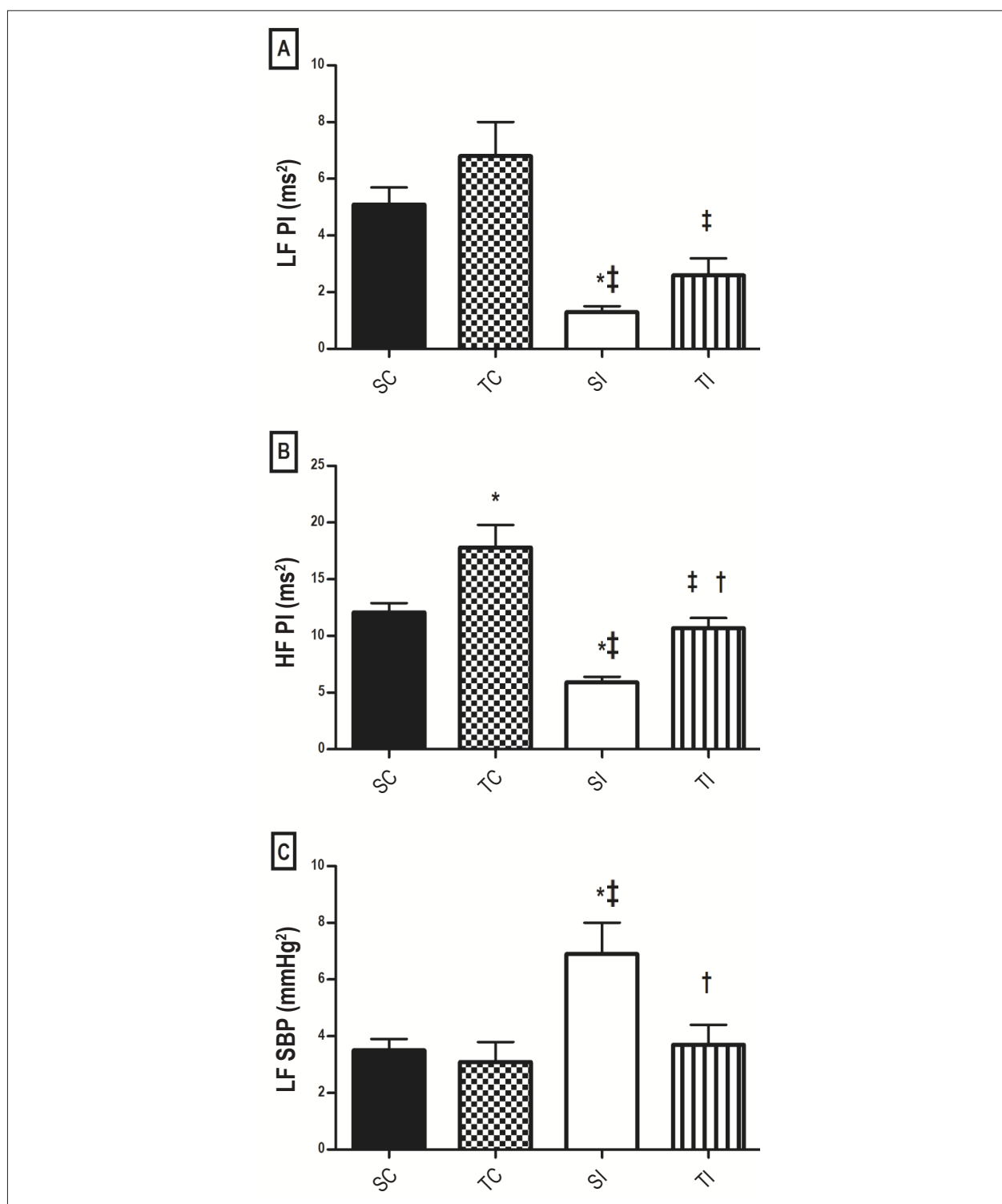
Evidences from the literature suggest that aerobic RT performed during MI recovery provided increased HR variability, which is an important index of the autonomic function and predictive of mortality<sup>27</sup>. In addition, La Rovere et al<sup>8</sup> showed that aerobic RT after MI may favorably modify the long-term survival and that this benefit is probably related to improvement of the baroreflex sensitivity and, consequently, of the autonomic imbalance after training in these infarcted individuals. In agreement with findings in humans, our group recently demonstrated that a 3-month aerobic training was able to improve HR variability, autonomic modulation, and baroreflex sensitivity in rats after MI<sup>10,13</sup>, thus increasing the survival of trained animals.

In fact, most of the studies point to aerobic RT as an important tool for the management of autonomic dysfunction in patients after MI; however, the effects of RT on the cardiac autonomic variables remain poorly examined. In clinical and experimental studies with CI, increases in the LF band of HR variability have been shown to be linked to the degree of sympathoexcitation, as assessed by direct measures of the sympathetic nervous activity or of plasma norepinephrine<sup>28,29</sup>. However, in advanced stages of the disease, the opposite is also true, i.e., the LF band of HRV almost disappears because of increased sympathetic activity<sup>30,31</sup>. Reduction of this component has been associated with a poor prognosis in patients with heart failure, since La Rovere et al<sup>32</sup> showed that decreased LF band is an independent predictor of cardiovascular mortality in these individuals.

In the present study, although the baroreflex sensitivity and alpha index did not change, RT promoted positive adaptations in SD-PI and RMSSD, increased the LF and HF bands of PI, and normalized the LF/HF balance. In addition, group TI showed a reduction in the LF range of SBP in relation to group SI. Therefore, we can suggest that RT triggered a reduction in the cardiac and vascular sympathetic modulation, and promoted an increase in the parasympathetic modulation, thus improving, in turn, the cardiac autonomic balance of infarcted rats undergoing 3-month RT. The failure to change the baroreflex sensitivity and the alpha index of SBP suggests that RT may have led to important adaptations in the cardiovascular control centers, which could explain a better cardiac and vascular autonomic control in trained animals. However, further studies investigating the effects of RT on the central control of circulation are necessary to better explain these evidences.

## Conclusions

In conclusion, the findings of the present study suggest that low/moderate intensity resistance exercise training may be an important and safe therapeutic tool after myocardial infarction, considering



**Figure 2** – Absolute values of low (A) and high frequency (B) bands of pulse interval variability, and of low frequency band (C) of systolic blood pressure in the experimental groups. \*  $p < 0.05$  vs. group sedentary control (SC); ‡  $p < 0.05$  vs. group trained control (TC); †  $p < 0.05$  vs. Group sedentary infarcted (SI), Trained infarcted (TI).

that it does not lead to considerable changes in ventricular function, reduces the overall cardiac stress, and significantly improves the cardiac and vascular autonomic modulation.

## Acknowledgements

To Professor Dr. Claudia Borim, for her technical support in the statistical analyses.

This study was financially supported by *Fundação de Amparo à Pesquisa do Estado de São Paulo* (FAPESP), protocol 2013/14788-9. CFG had a Masters scholarship from *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior* (CAPES). MCI, KDA, and BR had financial support from *Conselho Nacional de Pesquisa e Desenvolvimento* (CNPq-BPQ).

## Author contributions

Conception and design of the research: Irigoyen MC, Rodrigues B; Acquisition of data: Grans CF, Feriani DJ, Abssamra MEV, Rocha LY, Carrozzi NM, Mostarda C, Figueroa

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## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

## Sources of Funding

This study was funded by CAPES and FAPESP.

## Study Association

This article is part of the thesis of master submitted by Camila F. Grans, from Universidade São Judas Tadeu (USJT).

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