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SWIMMING TRAINING ATTENUATES REMODELING, CONTRACTILE DYSFUNCTION AND CONGESTIVE HEART FAILURE IN RATS WITH MODERATE AND LARGE MYOCARDIAL INFARCTIONS

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SUMMARY

1. The aim of the present study was to evaluate the effect of swimming on myocardial remodelling after myocardial infarction (MI) in female rats induced by coronary occlusion, which was not performed in sham rats.

2. Rats were divided in six groups, three sedentary (sham (SSh; $n = 14$), moderate infarct (SMI; $n = 8$) and large infarct (SLI; $n = 10$)) and three trained (sham (TSh; $n = 16$), moderate infarct (TMI; $n = 9$) and large infarct (TLI; $n = 8$)) groups. Training (8 weeks, 60 min/day, 5 days/week) was initiated 4 weeks after MI or sham operation. Training did not affect mortality rate, but attenuated the increases in atrial/bodyweight (SSh: 0.07 ± 0.02; TSh: 0.07 ± 0.02; SMI: 0.11 ± 0.03; TMI: 0.09 ± 0.03; SLI: 0.17 ± 0.09; TLI: 0.10 ± 0.05 mg/g) and right ventricular/bodyweight (SSh: 0.15 ± 0.02; TSh: 0.17 ± 0.02; SMI: 0.17 ± 0.07; TMI: 0.20 ± 0.03; SLI: 0.29 ± 0.13; TLI: 0.22 ± 0.08 mg/g) ratios. Myocardial infarction increased pulmonary and myocardial water content in infarcted sedentary animals, whereas no changes were observed in trained infarcted rats. Sedentary infarcted rats showed inotropic and lusitropic depression proportional to the size of the infarct (SSh > SMI > SLI), whereas no differences were noted in trained rats (TLI = TMI = TSh). Indeed, in sedentary rats there was depression of +dT/dt (SSh: 68 ± 25; TSh: 72 ± 21; SMI: 53 ± 20; TMI: 77 ± 30; SLI: 33 ± 15; TLI: 57 ± 22 g/mm^2 per s) and –dT/dt (SSh: 33 ± 13; TSh: 36 ± 11; SMI: 24 ± 5; TMI: 35 ± 11; SLI: 15 ± 4; TLI: 32 ± 11 g/mm^2 per s) compared with trained rats.

3. In conclusion, swimming clearly favoured post-MI cardiac remodelling, attenuated myocardial hypertrophy, contractile and relaxation dysfunction and prevented pulmonary congestion.

Key words: contractile dysfunction, heart failure, myocardial infarction, swimming training.

INTRODUCTION

Data obtained from *in situ* hearts,[1–3] isolated hearts,[4,5] papillary muscles[5–7] and isolated cardiomyocytes[8,9] have documented diastolic and systolic dysfunction following myocardial infarction (MI). In addition, there are indications that the myocardial dysfunction of post-MI remodelling includes impairment of calcium kinetics[9–11] and myofilament responsiveness.[9]

Concurrently, physical exercise is indicated as a procedure that favours myocardial mechanics and ventricular performance.[1,2,9–13] The effect of physical exercise on post-MI myocardial dysfunction has not yet been fully defined. The results reported by authors who have analysed myocardial function in preparations of intact ventricles are controversial, with reports of improvement,[1,2,14] worsening[15] and an absence[16,17] of an effect of exercise on myocardial depression. Studies that have used isolated myocytes to assess myocardial function have consistently reported that exercise improves contraction and relaxation functions.[9–11] These methods for the analysis of myocardial function have inherent limitations when contraction and relaxation properties are being assessed. Changes in chamber shape and dimensions affect cardiac performance in preparations using intact ventricles, leading to poor assessment of myocardial functional performance; isolated cells operate under conditions that are distinct from physiological conditions and, thus, extreme caution is required when interpreting results. A particular limitation is the absence of the interstitium.[9–11]

A more precise assessment of myocardial mechanical properties has been greatly facilitated in the isolated papillary muscle or trabecular preparation, where it is possible to accurately measure and control force and length in a multicellular preparation with relatively simple geometry. The mechanical function of myocardial multicellular samples in post-MI remnant myocardium following physical exercise has been studied by Geenen *et al.*[16] The authors subjected rats with MI to a treadmill protocol and analysed the mechanical function of papillary muscles. They concluded that exercise training did not alter the magnitude of the morphological and physiological adaptations to infarction.[16] The aim of the present study was to evaluate the effect of swimming training on post-MI myocardial remodelling, with the hypothesis that swimming favourably alters myocardial mechanics. In addition, we sought to demonstrate how swimming induces changes in a characteristic associated with heart failure, namely pulmonary water content.

METHODS

Animals, induction of MI and composition of experimental groups

Female Wistar rats, weighing 170–190 g at the start of the study, were housed under a 12 h dark–light cycle, at 22–23°C and under 54–55% humidity. Rats

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were fed a pellet rodent diet *ad libitum* and had free access to water. Myocardial infarction was induced according to the procedure described by Johns and Olson.[18] Rats were anaesthetized with a mixture of ketamine (90 mg/kg, i.p.) and xylazine (10 mg/kg, i.p.), intubated and ventilated (model 683; Harvard Apparatus, Millis, MA, USA; 2.0 mL, 80 strokes/min). A left thoracotomy was performed and a 6.0 silk thread was tied permanently around the left anterior descending coronary artery. In sham rats, the coronary occlusion was not performed. After the heart was returned to the thorax, the chest was closed with a purse string suture and rats remained sedentary for 4 weeks.

Thereafter, transthoracic Doppler echocardiography evaluation was performed in sedated rats (ketamine and xylazine, i.p.) using a 12 MHz transducer (Sonos-5500; Hewlett-Packard, Andover, MA, USA) to determine the presence and size of the MI. The MI was measured according to a well-accepted technique[19,20] and infarcts smaller than 20% were excluded from analysis. The final size of the MI was defined by planimetry at the end of the protocol, as described below. According to the size of the MI obtained by echocardiogram, infarcted rats were divided into the following groups: sedentary moderate infarct (SMI; $n = 8$); trained moderate infarct (TMI; $n = 9$); sedentary large infarct (SLI; $n = 10$); and trained large infarct (TLI; $n = 8$). A moderate infarction was considered as an MI scar occupying 20–39% of the left ventricle; a large MI was defined as an MI scar equal to or larger than 40% of the left ventricle. In addition, two sham groups were studied: sedentary sham (SSh; $n = 14$) and trained sham (TSh; $n = 16$).

Rats were cared for in compliance with the *Principles of Laboratory Animal Care* formulated by the National Institutes of Health (NIH publication no. 96–23, revised, 1996; http://bioethics.od.nih.gov/animals.html) and the study protocol was approved by the Institutional Committee for Animal Care and Use at the Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil.

Exercise training protocol

The exercise protocol conformed to the American Physiological Society's *Resource Book for the Design of Animal Exercise Protocols*.[21] Swimming training was initiated 4 weeks after coronary occlusion and was performed in a container filled with tap water (80 cm deep) kept at 32–34°C by a feedback-controlled electric heating coil. The water was maintained in continuous turbulence to provide continuous exercise. For adaptation, training was limited to 10 min on the first day and increased by 10 min each day until Day 6. Training was then continued for a total period of 8 weeks, 60 min per day and 5 days per week, as described elsewhere.[15,22] Between 10 and 12 rats swam simultaneously. Rats were towelled dry after each swimming session before they were returned to their cages. Rats randomized to the sedentary arm of the study did not swim over the course of the 8 weeks.

Papillary muscle studies

Hearts were removed quickly from anaesthetized rats and placed in oxygenated Krebs'–Henseleit solution (30°C). A papillary muscle was dissected carefully from the left ventricle, mounted between two spring clips and placed vertically in a chamber containing Krebs'–Henseleit solution (28°C), oxygenated with 100% O_2 and a pH of 7.40 ± 0.02. The composition of the Krebs'–Henseleit solution was (in mmol/L): NaCl 132; KCl 4.69; $CaCl_2$ 2.5; $MgSO_4$ 1.16; KH_2PO_4 1.18; $C_6H_{12}O_6$ 5.50; HEPES 20, pH 7.40. The lower spring clip was attached to the bottom of the chamber and the upper spring clip was connected by a thin steel wire to an isometric transducer (model FT03E; Grass Instrument, Quincy, MA, USA) connected to a micrometer for adjustment of muscle length. Preparations were stimulated 12 times/min with 5 msec square-wave pulses through parallel platinum electrodes at voltages that were approximately 10% greater than the minimum stimulus required to produce a maximal mechanical response. After a 60 min equilibration period, during which preparations were permitted to contract isotonically under light loading conditions (0.4 g), papillary muscles were loaded to contract isometrically for 15 min and stretched to the apices of their length–tension curves (L_{max}). The mechanical behaviour of the papillary muscles was evaluated under basal conditions. The following parameters were measured during isometric contractions: peak developed tension (DT; g/mm^2), resting tension (RT; g/mm^2), maximum rate of tension development (+dT/dt; g/mm^2 per s) and decline (–dT/dt; g/mm^2 per s), time to peak tension (TPT; msec) and time from peak tension to 50% relaxation (RT50%; msec). At the end of each experiment, muscle length at L_{max} was measured and the muscle between the two clips was blotted dry and weighed. The muscle cross-sectional area (CSA) was calculated from the muscle weight and length by assuming cylindrical uniformity and a specific gravity of 1.04. All experiments were performed at 28°C.

After papillary muscles had been isolated, the atria and right and left ventricles were dissected carefully and weighed and the infarct size was determined by planimetry. The left ventricle was isolated and unrolled and straight incisions allowed the dome-like shape of the left ventricle to lie flat when placed over a thin glass plate. Using transillumination, the contours of the infarcted area and of the entire left ventricle mass were traced onto a transparent acetate plate and the areas measured with Sigma Scan Pro 5.0 (Systat Software, Richmond, CA, USA). Infarct size is expressed as a percentage of the left ventricular area. Confirming our previous report,[23] MI sizes as measured by echocardiography and planimetry were very similar; thus, it was not necessary to reclassify animals from the moderate to large infarct groups or vice versa after measurement of MI size by planimetry.

Weight and water content

Bodyweight was recorded before and after the experimental protocol. The cardiac mass and the water content of the lungs and liver were determined. The water content of the organs was obtained based on wet and dry weights. After measuring tissue wet weight, tissues were placed in an oven and kept at a temperature of 80°C for 72 h. After recording the dry weight of the lung and liver from each rat, the water content of each organ was determined using the following equation: Water content = Wet weight/Dry weight.

Statistical analysis

Data are given as the mean±SD. Statistical significance was determined using two-way analysis of variance (ANOVA 2 × 3) complemented by Tukey's post hoc test. For ANOVA, training (sedentary *vs* training) and infarction (sham, moderate MI and large MI) effects were considered. $P < 0.05$ was considered significant. Differences in mortality rates were investigated by the Chi-squared test. All statistical procedures were performed using SPSS 12.0 (SPSS, Chicago, IL, USA).

RESULTS

Size of the MI

The size of the MI was similar in sedentary and trained rats for the moderate (31 ± 6 and 31 ± 4%, respectively) and large (47 ± 6 and 49 ± 11%, respectively) infarcts. No differences were found in the mortality rate between sedentary and trained rats over the study period. In the present study, three SLI and two TLI rats died.

Pulmonary and hepatic water content

The ANOVA identified an effect of MI ($P = 0.020$) in sedentary rats (Fig. 1) with respect to lung wet/dry weight: this ratio was higher in SLI than SMI or SSh (5.39 ± 0.35, 4.91 ± 0.17 and 4.74 ± 0.33, respectively). This difference was not observed in trained rats (4.90 ± 0.35, 5.03 ± 0.44 and 4.86 ± 0.48 in TSh, TMI and TLI, respectively). The ANOVA detected an interaction effect, with pulmonary congestion in SLI indicating left heart failure that was prevented by physical exercise (SLI > TLI; $P = 0.003$, Tukey's test). In addition, no difference was observed with respect to the liver wet/dry weight

ratio in sedentary (3.27 ± 0.20, 3.24 ± 0.07 and 3.26 ± 0.15 in SSh, SMI and SLI, respectively) or trained (3.24 ± 0.11, 3.27 ± 0.11 and 3.18 ± 0.10, TSh, TMI and TLI, respectively) rats, thus indicating the absence of right heart failure.

Heart mass

Taking into account the fact that infarcted rats presented with congestive heart failure, the dry weight (Table 1) and wet/dry weight ratio (Fig. 2) were analysed when the myocardial mass was evaluated in order to determine the contribution of protein and water to the increase in myocardial mass.

When related to bodyweight, the dry mass of the atria, right ventricle and heart increased in sedentary rats as a function of size of the MI, whereas in trained rats no differences were observed in these indices (Table 1). Indeed, the atria of sedentary rats exhibited a significant

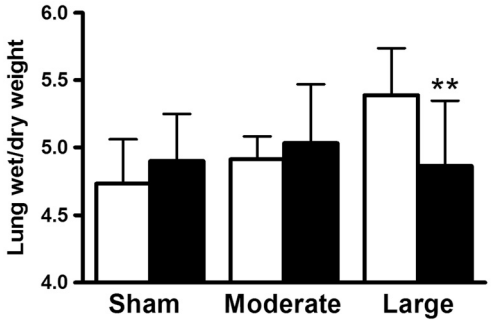

Fig. 1 Mean (±SD) ratio of lung wet/dry weight in sedentary (□) and trained (■) rats. The results of two-way ANOVA indicated a significant effect of infarction ($P = 0.02$) and interaction ($P = 0.006$), but not of training itself. $^{**}P < 0.01$ compared with sedentary rats (Tukey's test).

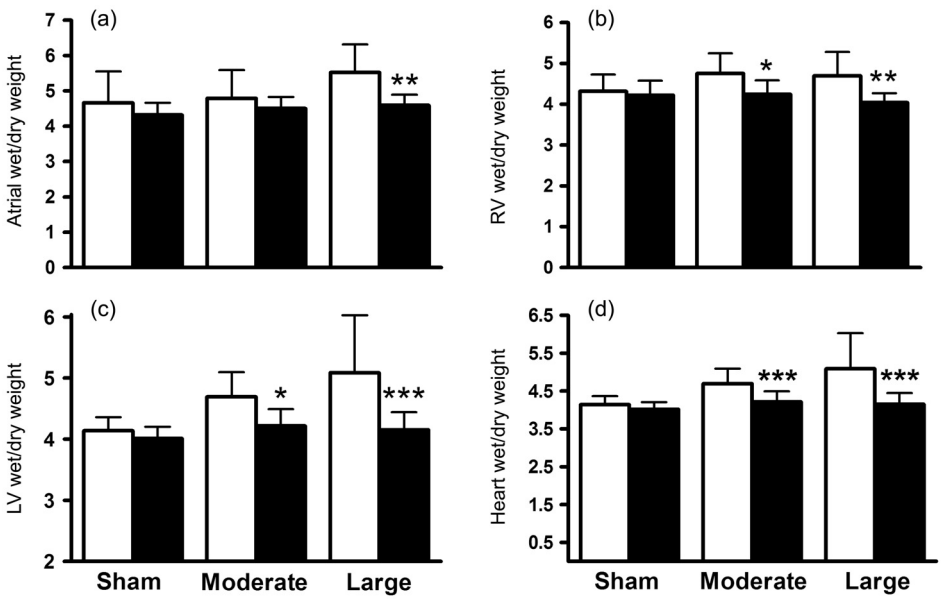

Fig. 2 Mean (±SD) ratio of (a) atrial, (b) right ventricular (RV), (c) left ventricular (LV) and (d) heart wet/dry weight in sedentary (□) and trained (■) rats. Results of two-way ANOVA indicated a significant effect of infarction ($P = 0.015$) and training ($P = 0.002$) on atrial weight; training only ($P = 0.001$) on RV weight; infarction ($P < 0.001$), training ($P < 0.001$) and the interaction ($P = 0.012$) on LV weight; and infarction ($P < 0.001$), training ($P < 0.001$) and the interaction ($P = 0.001$) on heart weight. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ compared with sedentary rats (Tukey's test).

Table 1 Mean±SD bodyweight and myocardial dry weight : bodyweight ratios in sedentary and trained rats with moderate and large myocardial infarctions

	BW (g)	Atria/BW (mg/g)	RV/BW (mg/g)	LV/BW (mg/g)	Dry heart/BW (mg/g)
Sham					
Sedentary ($n = 14$)	224 ± 29	0.07 ± 0.02	0.15 ± 0.02	0.52 ± 0.05	0.73 ± 0.07
Trained ($n = 16$)	245 ± 14	0.07 ± 0.02	0.17 ± 0.02	0.54 ± 0.04	0.78 ± 0.05
Moderate MI					
Sedentary ($n = 8$)	223 ± 21	0.11 ± 0.03	0.17 ± 0.07	0.52 ± 0.03	0.80 ± 0.12
Trained ($n = 9$)	239 ± 26	0.09 ± 0.03	0.20 ± 0.03	0.54 ± 0.04	0.83 ± 0.05
Large MI					
Sedentary ($n = 10$)	223 ± 21	0.17 ± 0.09	0.29 ± 0.13	0.52 ± 0.07	0.98 ± 0.17
Trained ($n = 8$)	244 ± 20	0.10 ± 0.05***	0.22 ± 0.08*	0.55 ± 0.04	0.87 ± 0.10*
Effects (ANOVA)					
Infarction	$P > 0.100$	$P < 0.001$	$P < 0.001$	$P > 0.100$	$P < 0.001$
Training	$P = 0.002$	$P = 0.011$	$P > 0.100$	$P = 0.027$	$P > 0.100$
Interaction	$P > 0.100$	$P = 0.007$	$P > 0.050$	$P > 0.100$	$P = 0.023$

The results of two-way ANOVA are also shown. $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$ compared with sedentary rats (Tukey's test).
BW, bodyweight; RV, right ventricle; LV, left ventricle; MI, myocardial infarction.

Table 2 Effects of training on postinfarction myocardial function

	DT (g/mm^2)	RT (g/mm^2)	+dT/dt (g/mm^2 per s)	–dT/dt (g/mm^2 per s)	TPT (msec)	50%RT (msec)
Sham						
Sedentary ($n = 14$)	6.93 ± 1.70	0.56 ± 0.26	68 ± 25	33 ± 13	171 ± 18	157 ± 38
Trained ($n = 16$)	6.67 ± 1.65	0.56 ± 0.35	72 ± 21	36 ± 11	153 ± 11**	130 ± 22*
Moderate MI						
Sedentary ($n = 8$)	5.72 ± 1.79	0.52 ± 0.24	53 ± 20	24 ± 5	174 ± 12	151 ± 18
Trained ($n = 9$)	6.82 ± 1.96	0.71 ± 0.29	77 ± 30*	35 ± 11*	150 ± 11**	127 ± 33*
Large MI						
Sedentary ($n = 10$)	4.02 ± 1.53	0.68 ± 0.48	33 ± 15	15 ± 4	175 ± 20	154 ± 38
Trained ($n = 8$)	4.92 ± 1.35	0.85 ± 0.27	57 ± 22*	32 ± 11**	144 ± 13***	100 ± 19***
Effects (ANOVA)						
Infarction	$P < 0.001$	$P > 0.100$	$P = 0.002$	$P = 0.006$	$P > 0.100$	$P > 0.100$
Training	$P > 0.100$	$P > 0.100$	$P = 0.004$	$P < 0.001$	$P < 0.001$	$P < 0.001$
Interaction	$P > 0.100$	$P > 0.100$	$P > 0.100$	$P > 0.100$	$P > 0.100$	$P > 0.100$

The results of two-way ANOVA are also shown. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ compared with sedentary rats (Tukey's test).

DT, developed tension; RT, resting tension; +dT/dt, –dT/dt, maximum rate of increase and decrease of tension, respectively; TPT, time to peak tension; 50%RT, time to 50% relaxation.

($P < 0.001$) MI effect (SSh < SMI < SLI), whereas in the trained groups there was no effect of MI. In the groups with a large MI, a training effect ($P = 0.011$) was noted, with the SLI group having heavier atria than the TLI group ($P < 0.001$, Tukey's test).

The dry mass of the right ventricle in the SLI group was higher than that of the other sedentary rats (infarct effect: SSh = SMI < SLI; $P < 0.001$), as well as TLI rats ($P = 0.041$, Tukey's test). No differences were noticed between trained rats (TSh = TMI = TLI) in terms of right ventricular dry mass.

With respect to the ratio of dry weight of the left ventricle/bodyweight (Table 1), ANOVA did not indicate significant infarction or interaction effects. A training effect was detected ($P = 0.027$) when comparing all sedentary animals with all trained rats; however, Tukey's test did not identify which of the comparisons attained significance.

In addition, with respect to the dry heart weight/bodyweight ratio (Table 1), ANOVA identified significant infarction ($P < 0.001$) and interaction ($P = 0.023$) effects. In the sedentary groups, SSh = SMI < SLI, but in the trained groups TSh = TMI = TLI. An interaction effect was found ($P = 0.023$) for comparisons of trained and sedentary rats with a large MI, with the dry weight of the heart in the SLI group being greater than that in the TLI group ($P = 0.026$, Tukey's test).

To summarize, MI induced an increase in the dry mass of the atria, right ventricle and heart dry in sedentary rats, whereas swimming training prevented cardiac growth.

The wet/dry weight ratio (Fig. 2) allowed us to determine that myocardial congestion was present in sedentary rats, but not in trained rats. Indeed, an infarction effect ($P = 0.015$) was observed in the atrial wet/dry weight ratio of the sedentary rats (SSh = SMI < SLI: 4.66 ± 0.89, 4.79 ± 0.79 and 5.52 ± 0.79, respectively), but not in trained groups (4.32 ± 0.34, 4.51 ± 0.32 and 4.60 ± 0.60 for TSh, TMI and TLI, respectively). A significant training effect ($P = 0.002$) was observed indicating atrial congestion in SLI compared with TLI ($P = 0.003$, Tukey's test). No effect of MI was found on the right ventricle between the sedentary (4.32 ± 0.41, 4.75 ± 0.49 and 4.70 ± 0.58 for SSh, SMI and SLI, respectively) and trained (4.22 ± 0.35, 4.25 ± 0.34 and 4.04 ± 0.23 for TSh, TMI and TLI, respectively) groups. However, SMI > TMI ($P = 0.015$) and SLI > TLI ($P = 0.002$) indicated a training effect (ANOVA, $P < 0.001$).

With respect to the left ventricle, ANOVA identified an infarction effect ($P < 0.001$) in the sedentary groups (SSh < SMI = SLI: 4.14 ± 0.22, 4.69 ± 0.60 and 5.09 ± 0.94, respectively) that was not present in the trained groups (4.01 ± 0.19, 4.22 ± 0.28 and 4.15 ± 0.28 for TSh, TMI and TLI, respectively). In addition, a significant training effect ($P < 0.001$) was observed, with SMI > TMI ($P = 0.029$) and SLI > TLI ($P < 0.001$).

To summarize: myocardial congestion was present only in sedentary rats, suggesting that swimming training precludes heart failure.

Papillary muscle data

In sedentary rats with a moderate and large infarct, CSA increased compared with that obtained for sham rats in infarcted sedentary rats (1.3 ± 0.3, 1.5 ± 0.5 and 0.9 ± 0.3 mm^2, respectively; $P = 0.016$). There was no difference in CSA in the TSh, TMI and TLI groups (0.9 ± 0.2, 1.0 ± 0.4 and 1.2 ± 0.3 mm^2, respectively; $P = 0.083$).

Data regarding myocardial mechanics (Table 2) identified a depression of contraction in infarcted sedentary animals, which was attenuated in trained rats. In analysing DT values, ANOVA identified a significant infarction effect ($P < 0.001$) between the sedentary rats (SSh > SLI), not demonstrated in trained rats (TSh = TMI = TLI). No effect was observed for training. When the +dT/dt values were compared, differences in contractile function between sedentary and trained rats were disclosed. Indeed, MI decreased the rate of tension rise ($P = 0.002$) in sedentary rats (SSh > SLI), although no significant differences in +dT/dt were found in trained rats. The attenuation of myocardial depression made possible by swimming is shown clearly when sedentary and trained rats are compared (ANOVA, $P = 0.004$). The differences identified were: SMI < TMI ($P = 0.036$, Tukey's test) and SLI < TLI ($P = 0.029$, Tukey's test). In addition, ANOVA did not identify a significant infarction effect on the duration of the contraction period (TPT; msec) of sedentary or trained rats. However, all TPT values in all trained groups were significantly lower than those in corresponding sedentary groups ($P \leq 0.002$).

Differences between sedentary and trained rats were found for relaxation (Table 2), as detected by the –dT/dt and RT50% values.

Indeed, the –dT/dt indicated depression of relaxation ($P = 0.006$) in sedentary infarcted rats (SSh > SLI), which was not present in trained rats. Comparisons between sedentary and trained rats identified conspicuous differences between the respective infarcted groups: SMI < TMI ($P = 0.039$) and SLI < TLI ($P = 0.002$). The RT50% values were not affected by MI in sedentary or trained rats. A clear prolongation of RT50% was observed in the sedentary groups compared with trained groups: SSh > TSh ($P = 0.021$), SMI > TMI ($P = 0.049$) and SLI > TLI ($P < 0.001$). However, no significant effects of infarction, training or interaction were shown for resting tension in the different groups (SSh = SMI = SLI and TSh = TMI = TLI).

DISCUSSION

In the literature, some restrictions regarding the regular practice of physical exercise by patients with ventricular dysfunction are proposed[24–27] owing to concerns that physical exercise creates haemodynamic overload, intensifies sympathetic activity and may worsen myocardial hypertrophy and heart failure. In addition, there is also the fear that physical exercise may increase the mortality rate of cardiopathies.[15,24,28] The results obtained in the present study in rats contradict the concept that exercise may worsen cardiac remodelling and increase mortality. Even though the very low mortality rate in the present study made it difficult to analyse survival statistically, the data indicate that physical exercise does not increase the mortality rate of MI animals. Similar results have been reported by others in humans[29] and animals.[30,31] In fact, exercise reduces the indicators of myocardial hypertrophy, attenuates myocardial dysfunction and prevents pulmonary congestion.[30]

When analysing MI animals subjected to swimming training, Gaudron *et al.*[15] reported that the mortality rate increased among rats with large infarctions that swam 90 min/day, 6 days/week for 8 weeks. The result of the present study add weight to the arguments that physical exercise does not necessarily compromise survival after MI. Indeed, Konhilas *et al.*,[30] McMullen *et al.*[31] and Orenstein *et al.*[32] have reported reduced mortality after regular exercise in animals.

Based on the information provided by others,[33,34] it is reasonable to assume that the oxygen consumption of rats in the present study does not exceed 75% of maximum oxygen consumption, which indicates moderate intensity exercise. It seems reasonable to assume that regular swimming training at this intensity is acceptable in terms of safety after MI, even in the case of large MI with manifestations of marked myocardial dysfunction.

Regular physical exercise may generate an increase in cardiac mass. Therefore, it is intuitive that physical exercise may intensify cardiac hypertrophy in infarcted animals. In the present study, it was clear that swimming training did not intensify myocardial growth. In contrast, the data indicate that the increase in myocardial mass was attenuated in MI rats that underwent exercise training compared with sedentary rats. Other authors have also reported that hypertrophy is attenuated by physical training.[9,10,32,35]

The reported functional effect of physical exercise on post-MI remodelling seems to depend on the method used to evaluate myocardial function. The results reported by others analyisng the intact ventricle[1,2,9,14,15,32,35] or isolated cell preparations[9–11] are controversial. The intact ventricle includes chamber dimensions and shape as relevant determinants of cardiac function, whereas results obtained in isolated cardiomyocytes may not indicate properly the mechanical action of the entire myocardium owing to the absence of the interstitium. The mechanical function of multicellular samples following physical exercise in MI remnant myocardium has been assessed previously by only one paper. Geenen *et al.*[16] subjected infarcted rats to a treadmill protocol. While analysing papillary muscles, they concluded that treadmill exercise training did not alter the magnitude of the pathophysiological adaptations to infarction. Gaudron *et al.*,[15] Alhaddad *et al.*[17] and Orestein *et al.*[32] evaluated the effect of swimming training on the cardiac function of infarcted rats. However, because these authors used isolated isovolumetric left ventricle, they studied chamber performance and did not focus on myocardial function, as we have done. The results of the present study showed a marked benefit of swimming training on inotropic and lusitropic functions in moderate and large MI in association with advantageous effects on myocardial mass.

The results of the present study verify that pulmonary and myocardial water content demand close attention. It is of note that previous studies[35,36] describing the effect of a treadmill protocol on the pulmonary water content of infarcted rats reported lung congestion in trained animals compared with normal lung water content of sedentary rats. The present data, obtained with swimming training, yielded the opposite results: sedentary animals exhibited a significant increase in pulmonary and myocardial water content, whereas trained rats maintained water content at normal levels. It is conceivable that the present results, indicating that swimming exercise improves contraction and relaxation, may allow the heart to fill at a lower end-diastolic pressure per end-diastolic volume. In addition, the increased myocardial water content in sedentary rats and the normal myocardial water content in trained rats confirms the beneficial effect of exercise for heart failure in infarcted rats. Otherwise, it remains to be determined whether the myocardial oedema of sedentary infarcted rats contributed to the inotropic and lusitropic depression.

It seems advisable to state that the rat model for MI does not fully reproduce the coronary occlusion in humans. Coronary occlusion in the rat occurs in a scenario of normality of the remaining coronary, whereas in humans coronary artery disease is not commonly restricted to the culprit vessel. It seems necessary to take into account that coronary plaques that are distant from the culprit vessel can trigger myocardial ischaemia and/or cardiac arrhythmias in some patients. Such possibilities should be always considered when recommending a training protocol to coronary patients.

In summary, despite the possible risks that may be posed by acute exercise, it seems that long-term swimming training results in functional benefit to the remnant myocardium after moderate and large MI. Physical exercise (swimming) did not induce a higher mortality rate or intensify the indicators of myocardial remodelling and heart failure in rats. The impaired contraction and relaxation observed in sedentary infarcted rats were significantly attenuated in trained rats. Moreover, pulmonary congestion was prevented in trained rats with a large MI.

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