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# HEART ADAPTATIONS TO LONG-TERM AEROBIC TRAINING IN PARAPLEGIC SUBJECTS: AN ECHOCARDIOGRAPHIC STUDY

**Running title:** Paraplegic heart adaptations to endurance training

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**ABSTRACT**

**Study Design**. Case-control.

**Objectives**. To execute an echocardiographic comparison between trained and untrained spinal cord injury (SCI) subjects and to evaluate whether long-term heart adjustments to endurance training are comparable with those observed in able-bodied (ABL) subjects.

**Setting**. Italy.

**Methods**. We enrolled: 1) 17 male SCI patients (lesion level $T_1$-$L_3$, 34±8 years, BMI 23.0±2.8 kg/m$^2$), 10 of whom were aerobically trained for >5 years ($SCI_T$); 2) 18 age, sex and BMI-matched ABL subjects (35±6 years, BMI 23.6±2.8 kg/m$^2$), 10 of whom were aerobically trained for >5 years ($ABL_T$). Training frequency and volume were recorded by a dedicated questionnaire. All subjects underwent a trans-thoracic echocardiography; SCI subjects also performed an exhaustive incremental exercise test. Comparisons were made between ABL and SCI groups; within each group, between trained and untrained subjects (ANOVA).

**Results**. *Effects of SCI.* Compared to ABL subjects, SCI patients showed lower end-diastolic volume (76±21 *vs* 113±23 ml, $P$<0.05) and ejection fraction (61±7 *vs* 65±5%, $P$ <0.05). *Effects of Training*. Compared to untrained status, the intra-ventricular septum thickness (SCI, +18%; ABL +4%), the posterior wall thickness (SCI, +17%; ABL +2%) and the total normalized heart mass (SCI, +48%; ABL +5%) were higher in both $SCI_T$ and in $ABL_T$. $VO_2$peak was higher in $SCI_T$ subgroup compared to $SCI_U$.

**Conclusions**. Heart seems to positively adapt to long-term endurance training in SCI patients. Regular exercise may therefore increase heart size, septum and posterior wall thickness, which likely contributed to improved $VO_2$peak. These morphological and functional changes may reduce cardiovascular risk in SCI individuals.

**Keywords:** spinal cord injury, training, endurance, left ventricle, echocardiography.

## INTRODUCTION

The positive effects of endurance training on heart morphology and function are well acknowledged in able-bodied (ABL) individuals: besides the typical development of bradycardia and the improvement in coronary perfusion, cardiac morphology usually shifts towards a physiologic left ventricular hypertrophy, with increased mass and internal volume of the left ventricle, and improved systolic and diastolic functions (for a review, see Pavlik *et al.*[1]). In ABL endurance trained individuals, the increased stroke volume finally yields an augmented cardiac output during exercise compared to untrained subjects.[2]

A previous study demonstrated a reduction in left ventricular mass and dimension in tetraplegic subjects,[3] and a more recent study showed an altered left ventricular diastolic function and a subclinical decrease in systolic function in spinal cord injury (SCI) individuals.[4] In these patients the reduced venous return due to the loss of sub-lesional vascular sympathetic innervation and of muscular pump may cause a reduced adaptation of stroke volume to exercise,[5] which needs to be compensated by a higher sub-maximal heart rate, compared to that observed in ABL subjects.[6,7] Indeed, Dela et al. demonstrated a stroke volume increase of about +35% in paraplegics compared to a +50% increase in able bodied people during a steady-state moderate exercise.[5] This may limit cardiac output during physical workout which would directly relate to a lower $VO_2$peak.

While the known heart adaptations to endurance training have been confirmed by some proponents of exercise in SCI people,[8] such adaptations have been questioned by other opponents of exercise.[9] Gates and coworkers found no differences in left ventricular structure and function between endurance- and power-trained SCI athletes compared with sedentary SCI subjects.[9] Moreover, it is still uncertain whether in SCI subjects the exercise-induced modifications of myocardial structure and function can be preserved in the long term by maintaining an adequate level of aerobic physical fitness.

Aims of this study were to compare baseline echocardiographic parameters between SCI and ABL subjects, and to assess whether heart adjustments to long-term training are comparable in SCI and ABL subjects. In addition, we aimed at evaluating the differences in maximal aerobic capacity and the relationship between echocardiographic parameters and maximal oxygen uptake between sedentary and trained SCI individuals.

## MATERIALS AND METHODS

*Subjects*

We enrolled 17 male SCI patients (lesion level $T_1$-$L_1$, ASIA Scale A, age 34±8 years, Body Mass Index (BMI) 23.6±2.8 kg/m$^2$), 10 of whom were aerobically trained ($SCI_T$) for at least 5 years. In addition, 18 age- and BMI-matched ABL male subjects (35±6 yrs, BMI 23.0±2.8 kg/m$^2$), 10 of whom were aerobically trained ($ABL_T$) for at least 5 years were recruited. None of the subjects was a current smoker and no one had arterial hypertension or diabetes. Other exclusion criteria were the presence of severe cardiac diseases (cardiomyopathies, cardiac failure, moderate to severe cardiac valvulopathies, recent myocardial infarction, ventricular aneurysms) which could limit the cardiac function and/or cause a left ventricular remodelling. The demographic data of the enrolled subjects, stratified according to pathology and training status (T, trained; U, untrained), is shown in Table 1. After receiving a full explanation of the purpose of the study and of the experimental procedures, all subjects signed a written informed consent. The study was approved by the ethical committee of the Don C. Gnocchi Foundation and performed according to the principles of the Declaration of Helsinki.

*Statement of Ethics***.** We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research.

*Experimental procedures*

*Echocardiography*. All subject underwent a trans-thoracic echocardiography (mod. Sequoia Acuson 512, Siemens, Germany, equipped with a 3.5 MHz phased-array transducer). According to the statements of the American Society of Echocardiography Standards[10] the following parameters were measured: 1) Left Ventricular (LV) End-Diastolic Diameter (EDD) and Volume (EDV); 2) Intra-Ventricular Septum Thickness (IVST, end-diastole); 3) Posterior Wall Thickness (PWT, end-diastole); 4) Ejection Fraction (EF), calculated from the apical four-chamber view as:

$$[(EDV-ESV)/EDV)*100],$$

where EDV is End Diastolic Volume and ESV is End Systolic Volume;

5) LV mass (LVM), calculated according to the Devereux and Reicheck formula,[11] and normalized per body surface area:

$$LVM = 1.04 \cdot [(LVID + PWT + IVST)^3-(LVID)^3]-13.6 \text{ g},$$

where LVID is diastolic LV internal diameter, PWT is Posterior Wall Thickness and IVST is Intra-Ventricular Setptum Thickness; 6) Peak early inflow velocity (E), peak atrial inflow velocity (A) and peak early/atrial velocity ratio (E/A); 7) Iso-Volumic Relaxation Time (IVRT), defined as the time interval between aortic valve closure and mitral valve opening, which reflects the rate of left ventricular relaxation.[12]

*Incremental exercise test*. An incremental exercise test up to exhaustion was executed on a separate day on SCI subjects only. The testing procedure was performed by an adapted wheelchair ergometer (Ergotronic 4000, Sopur, Germany). The exercise protocol began at an initial velocity of 2 $km \cdot h^{-1}$ and continued with 3-min steps, with a speed increment of 2 $km \cdot h^{-1}$ per step; the test was stopped at the volitional exhaustion. This protocol is similar to that reported in Hartung et al.[13], which measured maximal oxygen uptake by steps of 2 min and increments of 3 $km*h^{-1}$. In our protocol we chose to increase the step time and reduce the velocity increment: in this way, oxygen consumption for each step is likely to reach a sufficiently long steady-state in the last phase of each step. Three-minute steps on manual ergometers were used by other Authors[14].

Respiratory gases were collected at rest for about 3 min and during the last minute of each exercise step. The following parameters were measured: heart rate (HR, bpm) by continuous electrocardiographic recording in $V_5$ lead (Cardioline Delta 1 Plus, Italy); volumes and $O_2$ and $CO_2$ concentrations in expired air (% vol)(Oxygen Analyser, Servomex, UK, and Binos C, Fisher Rosemouth, Germany), collected in 150 l Douglas bags. Gas analyzers were calibrated before each experiment.

*Physical activity questionnaire*. All the trained ABL and SCI individual were athletes referring to the Sports Medicine Centre of the Don C. Gnocchi Foundation (Milan, Italy) for pre-participation screening in agonistic activities during the last 5 years. The training duration was therefore retrieved by their individual clinical records: one subject was classified as "long-trained endurance athlete" if he had a history (>5 years) of endurance training (e.g. long distances in track and field, wheelchair marathon, hand-bike, swimming, Nordic skiing, etc.) at least 3 times weekly (1.5 hours at least for each training session). The actual training status of the subjects was assessed by the localized Italian version of the validated IPAQ (International Physical Activity Questionnaire) questionnaire.[15] The study participants were classified as "sedentary" if they were categorized in the "lowest activity level" of the Questionnaire. The duration of the sedentary status, if any, was finally assessed by a non-validated recall questionnaire on previous recreational/sport activities in ABL subjects.

Based on the questionnaires results, we divided each of the SCI and the ABL groups in 2 further sub-groups: $SCI_T$ (trained)(n=10), $SCI_U$ (untrained)(n=7), $ABL_T$ (n=10) and $ABL_U$ (n=8).

*Statistical analysis.* If not otherwise stated, results are shown as mean±standard deviation (SD). All parameters were normally distributed (Shapiro-Wilk test) and there were no missing data. The one-way analysis of variance (ANOVA) was preliminary applied to verify the data matching between the 4 trained and untrained sub-groups. A 2 x 2 factorial ANOVA was then used to evaluate the differences in echocardiographic parameters between the 4 sub-groups, and the *post hoc* LSD Fisher test was applied where appropriate. The statistical regression was computed by the least squared method, and the *r* coefficient was then calculated.

The level of statistical significance was set at $P<0.05$. Statistical analyses were performed using the Statistical software package Statistica 7.0 (StatSoft, USA).

## RESULTS

The demographic and anthropometric data of the enrolled subjects, stratified according to pathology and training status (T, trained; U, untrained), were matched between groups (Table 1).

*Echocardiography*

*SCI vs ABL subjects*. To assess the statistical differences in cardiac parameters due to SCI, we pooled $SCI_T$ and $SCI_U$ data and $ABL_U$ and $ABL_T$ data. SCI patients showed significantly lower EDD (44.3±5.6 *vs* 47.5±5.4 mm, $P$=0.04) and EDV (76.2±20.8 *vs* 112.9±22.9 ml, $P$=0.001) than ABL subjects, respectively. Similarly, the ejection fraction (60.7±7.0 *vs* 65.3±5.3 %, $P$=0.03) was significantly lower in SCI compared to ABL individuals. Surprisingly, the IVST was slightly but significantly higher in SCI subjects (9.5±1.3 *vs* 8.7±0.7 mm, $P$=0.02), whereas the PWT (9.2±1.3 *vs* 8.6±0.7 mm) did not significantly differ, although a trend towards a higher value in SCI group was perceived. The LVM normalized per body surface area was not significantly different between SCI (71.6±21.0 $g \cdot m^{-2}$) and ABL (76.2±14.8 $g \cdot m^{-2}$) subjects. The peak early inflow velocity (E: 0.66±0.14 $m \cdot s^{-1}$ in SCI and 0.71±0.14 $m \cdot s^{-1}$ in ABL), peak atrial inflow velocity (A: 0.48±0.10 $m \cdot s^{-1}$ in SCI and 0.44±0.07 $m \cdot s^{-1}$ in ABL) and peak early/atrial velocity ratio (E/A: 1.56±0.56 in SCI and 1.66±0.39 in ABL) did not differ between SCI and ABL groups. Finally, the IVRT was significantly higher in SCI subjects (103±8 ms) compared to ABL individuals (56±9 ms)($p<0.001$).

*Sub-group analysis in trained vs untrained subjects*. The main echocardiographic parameters, stratified according to the training status, are shown in Table 2. In particular, The $SCI_T$ subgroup showed higher IVST values and a trend towards an increased PWT compared to the $SCI_U$ subgroup. Furthermore, LVM normalized per surface area was significantly higher (+48%) in $SCI_T$ *vs* $SCI_U$ subgroup ($P$=0.01 in the pairwise comparison at the *post-hoc* test). Such positive trend (+5%) was observed also between the $ABL_T$ and the $ABL_U$ subgroups although it did not reach the statistical significance (pairwise comparison at the *post-hoc* test).

Conversely, EDD and EDV were unchanged in $SCI_T$ *vs* $SCI_U$ , subjects whereas in $ABL_T$ subjects EDV was higher than in $ABL_U$ subjects ($P$=0.006 in the pairwise comparison at the *post-hoc* test).

*Exercise test.* The maximal velocity achieved on the wheelchair ergometer, the peak $O_2$ consumption ($pVO_2$) and the resting and peak heart rate (HR) in the paraplegic group, stratified according to training status, are shown in Table 3. Significantly higher maximal velocity (+52%) and peak $VO_2$ (+63%) were observed in the $SCI_T$ compared to the $SCI_U$ subgroup. Resting HR was significantly lower in $SCI_T$ subgroup (-13%), whereas peak HR was not different between subgroups.

None of the echocardiographic parameters significantly correlated with peak oxygen uptake, except for the Aortic Flow Velocity, which showed a significant positive relationship with peak $VO_2$ (Figure 1) in SCI subjects, independently from the training status. Finally, although not reaching the statistical significance (p=0.07), a positive trend was observed between peak oxygen consumption and normalized LVM (Figure 2) in the pooled data of paraplegic subjects.

## DISCUSSION

The main finding of this study is that, despite some differences in left ventricular dimensions and function, SCI individual have similar training response as ABL subjects. A regimen of regular aerobic physical activity may therefore positively change heart morphology and function in paraplegics, thus limiting their cardiovascular risk.

In healthy subjects the end-diastolic dimensions are closely related to preload and venous compliance, and their increase with aerobic training is related to an increased stroke volume. We observed lower end-diastolic dimensions of the left ventricle in paraplegics compared to ABL subjects, which suggests a compromise that may result in a lower stroke volume and therefore a higher HR when exercising or working: this is similar to what was observed after prolonged bed rest.[16] In SCI patients, the chronic cardiovascular deconditioning due to prolonged wheelchair permanence and the reduced venous return due to the sub-lesional (i.e. splanchnic and lower limbs vasculature) blood pooling may be among the leading causes for this left ventricular atrophy.[6] However, in this study the IVST was surprisingly higher in paraplegic subjects (both trained and untrained) compared to healthy individuals, and there was also a trend toward an increased PWT ($P$=0.13). IVST and PWT are usually increased in endurance athletes, as a response of symmetrical cardiac hypertrophy; therefore, their higher values in both trained and untrained paraplegics were unexpected. However, as recently proposed by Matos-Souza *et al.*,[4] this may suggest that the chronically reduced venous return may have been compensated by a subsequent activation of the hormonal regulatory system, such as the renin-angiotensin-aldosterone system, in order to maintain blood pressure. This, in turn, may have stimulated LV remodeling, increasing left ventricular wall thickness. Interestingly, such effect seems not to occur during the ABL individual long-term adaptation to training, as suggested by the significance of the interaction term of factorial ANOVA (Table 2): IVST and PWT increased in SCI subjects only. In addition, EDV tended to decrease in SCI and to increase in ABL subjects (with significant interaction), suggesting probable different mechanisms of adaptation to the training stimulus, which deserves further research. Other previous findings suggest a higher neuro-hormonal influence on the cardiovascular control of SCI subjects.[15] It is possible that these neuro-hormonal changes (as an increased norepinephrine level or an activation of the renin-angiotensin-aldosterone system), coupled with the typical blood pressure instability,[18] contribute to the increased cardiovascular risk which characterize paraplegic people.

The diastolic function, as assessed by E, A and E/A ratio, was not significantly impaired in our SCI individuals. This data is consistent with what was obtained by Eysmann *et al.*[19] by conventional echocardiography, whereas more recently Matos-Sousa *et al*.[4] demonstrated a lower early diastolic filling in a group of paraplegics compared to ABL subjects. Interestingly, we reported a higher IVRT in our SCI individuals, which may suggest some difficulties in the very early diastolic filling. Maybe, the possible reduction of LV compliance in paraplegics may have been compensated by an increased isovolumic relaxation time in order to fill the LV adequately, without compromising the subsequent diastolic filling.

Another possible consequence of the impaired venous return in SCI individuals is that stroke volume cannot be adequately increased during incremental exercise. Indeed, as previously demonstrated by Hopman *et al.*[6], stroke volume is significantly reduced in paraplegics either at maximal and submaximal working level (about -20% and -25% at 40 and 60% of the maximal power output) during an incremental arm-cranking test, compared to ABL subjects. This finally limits the maximal cardiac output and therefore the maximal $VO_2$ measured in SCI people. Our data confirm this hypothesis as, on average, the maximal oxygen uptake of the trained paraplegic subgroup only halved the average value commonly found in aerobically trained able-bodied people. However, the maximal oxygen uptake was significantly higher and the resting HR was significantly lower in $SCI_T$ vs $SCI_U$ subgroup, demonstrating the positive effects of long-term endurance training on the whole cardiovascular function and a shift towards the parasympathetic predominance of HR control, which can be typically observed in aerobically trained athletes.

Besides training status, we noticed a positive and significant relationship between aortic flow velocity, which can be considered a surrogate marker of stroke volume, and peak oxygen uptake in the SCI groups. This suggests that even though in paraplegics the aerobic performance may be influenced by the reduction of stroke volume induced by the sub-lesional blood pooling, such inability appears to be partially compensated by physical training (Figure 1). In addition, the LVM normalized per body surface area was significantly increased in $SCI_T$ compared to $SCI_U$ subgroup, and there was a clear trend, although the statistical regression was just below the significance limits, between LVM and peak $VO_2$ (Figure 2). It is acknowledged the LVM is increased by long term endurance training, and that it represents an independent predictor of maximal work capacity.[20] Therefore, our findings suggest that aerobic training is able to induce a physiologic ventricular hypertrophy even in SCI people. This last data is in agreement with other previous results on the effect of endurance training on oxygen uptake in paraplegics[21] and of high intensity interval training on peak stroke volume in SCI subjects.[8] In addition, these results parallel those of Dorfman *et al*.[16] who showed that the cardiac atrophy which follows the prolonged bed rest can be reversed by training. Finally, although Gates *et al.*[9] described only small adaptations of left ventricle to aerobic training, they however reported a trend towards an increase in left ventricular mass in SCI athletes, which is in line with the present findings.

In conclusion, this study showed a reduced diastolic filling capacity, an altered heart morphology similar to that of the deconditioned heart in SCI patients with respect to ABL subject. However, in trained paraplegics heart seemed to positively adapt to training, as normalized heart mass and left ventricular wall thickness were both increased: these changes persisted after 5-year training, and parallels those observed in able-bodied individuals. Therefore, despite some possible limitations in venous return, aerobic training in SCI individuals seems to promote a physiologic cardiac hypertrophy, which may reverse the pathologic left ventricular atrophy typically occurring after SCI. Such heart adaptations are similar to what was found in ABL subjects. This may be relevant from a clinical point of view, as aerobic training may contribute to significantly reduce cardiovascular risk, which is known to be higher in SCI people.[22]

## STUDY LIMITATIONS

This is a case-control study: longitudinal designs would have been preferable in determining the effects of training on heart structure. In addition, we cannot exclude that the small sample size of our study groups could have affected data generalizability.

The heart dimensional and functional measures were obtained from conventional trans-thoracic echocardiography: maybe, the more recent spectral techniques in tissue Doppler imaging may have added further results, especially on diastolic function.

We did not perform the incremental test in ABL subjects, because they were not used to the wheelchair propulsion on the wheelchair rolling ergometer.

Thus the results of such tests could not be easily compared between ABL and SCI group. Finally, all the able-bodied athletes enrolled in this study had a prevalent use of lower limbs during their training, whereas the trained paraplegic used upper limbs during training. Although we consider this aspect of minor relevance for heart adaptation to training, we cannot exclude that this may have produced unpredictable results.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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**TABLES AND FIGURES**

**Table 1.** Demographic and anthropometric features of the enrolled subjects, divided for pathology and training status. Data are mean±SD. *P* value (one-way ANOVA).

| | $SCI_U$ | $SCI_T$ | $ABL_U$ | $ABL_T$ | *P* |
|---|---|---|---|---|---|
| **n** | 7 | 10 | 8 | 10 | |
| **Lesion level** | $T_1$-$L_3$ | $T_1$-$L_1$ | - | - | |
| **Age (yrs)** | 36±10 | 33±7 | 33±6 | 33±8 | 0.55 |
| **Weight (kg)** | 73±10 | 70±8 | 73±14 | 72±6 | 0.87 |
| **Height (cm)** | 173±8 | 178±3 | 174±7 | 177±6 | 0.28 |
| **BMI (kg/m$^2$)** | 24.1±3.1 | 22.1±2.3 | 24.3±3.7 | 23.0±1.9 | 0.29 |

*P*, significance value from one-way ANOVA.

**Table 2.** Echocardiographic parameters divided for pathology and training status. Data are mean±SD. The last 3 columns show the *P* values estimated by the factorial ANOVA for the effects of lesion, training and for their interaction. Abbreviations: LVEDD, Left Ventricular End Diastolic Diameter; IVST: Intra-Ventricular Septum Thickness; PWT: Posterior Wall Thickness; EDV: End Diastolic Volume; EF: Ejection fraction; E: peak early inflow velocity; A: peak atrial inflow velocity; IVRT: Iso-Volumic Relaxation time. ns: not significant.

| **Parameter** | **$SCI_U$** | **$SCI_T$** | **$ABL_U$** | **$ABL_T$** | ***Effect of SCI*** | ***Effect of training*** | ***Inter-action*** |
|---|---|---|---|---|---|---|---|
| **EDD, mm** | 41.4 ± 5.3 | 46.6 ± 5.1 | 46.0 ± 5.8 | 48.7 ± 5.1 | 0.040 | ns | ns |
| **IVST, mm** | 8.6 ± 0.8 | 10.2 ± 1.1 | 8.3 ± 1.9 | 8.6 ± 0.7 | 0.020 | 0.014 | 0.001 |
| **PWT, mm** | 8.4 ± 1.1 | 9.8 ± 1.2 | 8.2 ± 1.9 | 8.4 ± 0.7 | ns | ns | 0.050 |
| **EDV, ml** | 80.4 ± 18.7 | 72.6 ± 21.7 | 108.9 ± 30.2 | 125.0 ± 20.5 | 0.001 | ns | 0.009 |
| **EF, %** | 61.4±4.6 | 60.1±8.8 | 67.4±5.4 | 63.6±4.8 | 0.030 | ns | ns |
| **LVM, $gr^{\cdot}m^{-2}$** | 56.3±17.5 | 83.1±15.7 | 74.0±16.2 | 78.0±14.1 | ns | 0.014 | ns |
| **E, $m^{\cdot}s^{-1}$** | 0.66±0.17 | 0.66±0.11 | 0.70±0.17 | 0.71±0.12 | ns | ns | ns |
| **A, $m^{\cdot}s^{-1}$** | 0.50±0.11 | 0.46±0.10 | 0.44±0.71 | 0.43±0.08 | ns | ns | ns |
| **E/A** | 1.64±0.80 | 1.49±0.30 | 1.59±0.47 | 1.70±0.34 | ns | ns | ns |
| **IVRT, ms** | 107.9±17.7 | 100.6±15.7 | 54.6±13.8 | 57.7±9.9 | 0.001 | ns | ns |

**Table 3.** Maximal velocity achieved on the wheelchair ergometer, peak $O_2$ consumption ($VO_2$), resting and peak heart rate in the paraplegic group divided for training status. Data are mean±SD.

| | $SCI_U$ | $SCI_T$ | ***P*** |
|---|---|---|---|
| **Maximal Velocity, km·h$^{-1}$** | 4.73 ± 0.98 | 7.20 ± 1.30 | 0.001 |
| **Peak $VO_2$, l·min$^{-1}$·kg$^{-1}$** | 13.3 ± 3.3 | 21.8 ± 4.8 | 0.001 |
| **Resting Heart Rate, bpm** | 77 ± 10 | 67 ± 7 | 0.05 |
| **Peak Heart Rate, bpm** | 140 ± 19 | 150 ± 16 | ns |

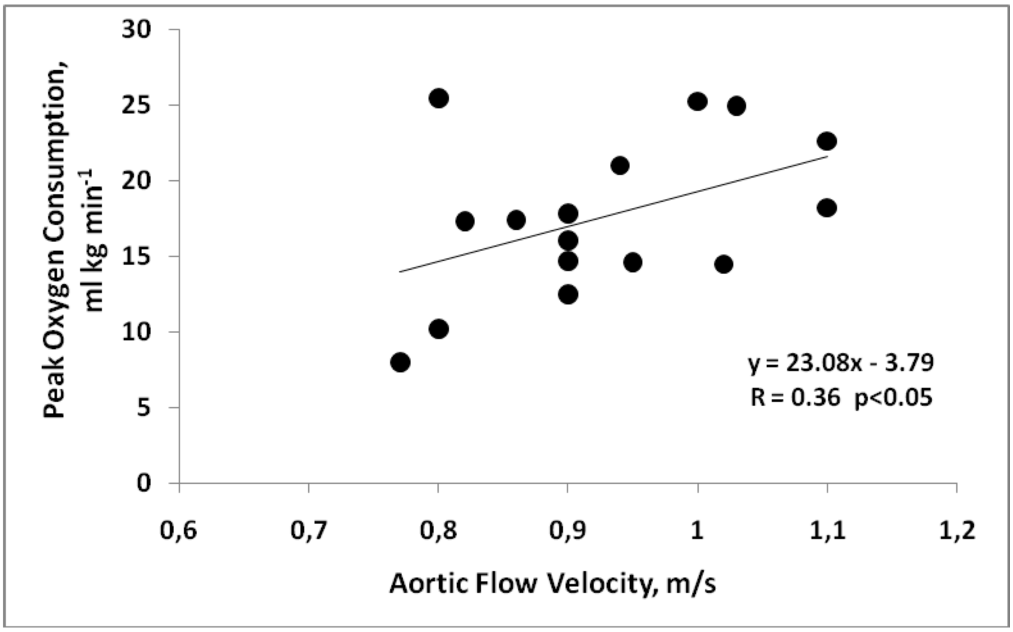
P, significance value from unpaired Student's *t* test.

**TITLES AND LEGENDS TO FIGURES**

**Figure 1.** Relationship between aortic flow velocity and maximal oxygen uptake in the groups of paraplegic subjects.

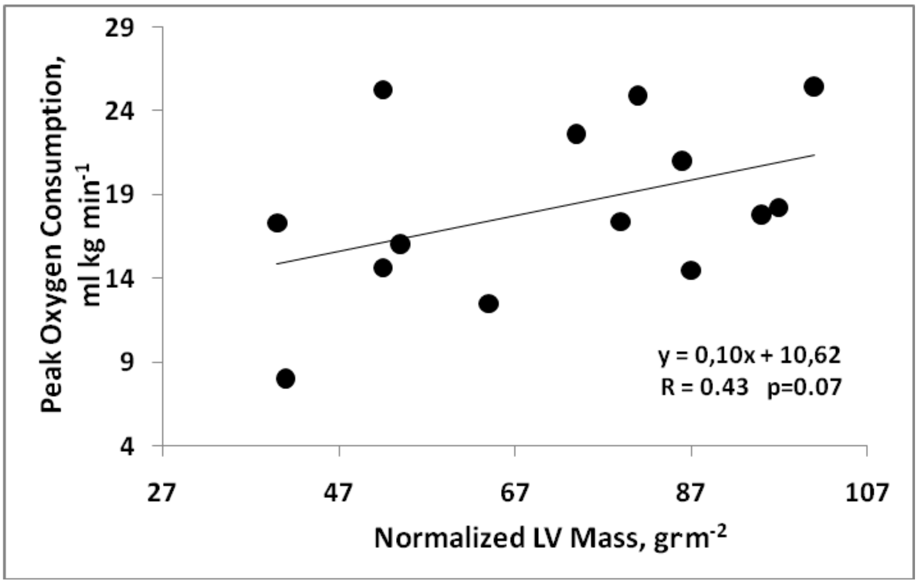
**Figure 2.** Relationship between normalized LV mass and maximal oxygen uptake in the groups of paraplegic subjects.

**Figure 1.**



Peak Oxygen Consumption, ml kg min-1
30
25
20
15
10
5
0
0,6
0,7
0,8
0,9
1
1,1
1,2
Aortic Flow Velocity, m/s
y = 23.08x - 3.79
R = 0.36 p<0.05

**Figure 2.**



Peak Oxygen Consumption, ml kg min-1
29
24
19
14
9
4
27
47
67
87
107
Normalized LV Mass, grm-2
y = 0,10x + 10,62
R = 0.43 p=0.07