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Conflicts of interest: None

Abstract

Purpose: Subjects with spinal cord injury (SCI) have been reported to present impaired left ventricular (LV) diastolic function in comparison with able-bodied ones. The present study investigated the effect of regular physical activity on the cardiac structure and function of SCI subjects.

Methods: Fifty-eight SCI men [29 sedentary (SCI-S) and 29 athletes (SCI-A)] and 29 able-bodied men (AB) were cross-sectionally evaluated by clinical, laboratory, hemodynamic and echocardiographic analysis. All enrolled subjects were normotensive, non-diabetic, non-smoker and normolipemic and the studied groups presented similar age and body mass index.

Results: SCI-S presented similar LV structural and systolic parameters, but higher E/Em (8.0±0.5) and lower Em/Am (1.18±0.09) ratios than SCI-A and AB (E/Em=6.4±0.3 and 5.9±0.3, respectively; Em/Am=1.57±0.12 and 1.63±0.08, respectively; all $p<0.05$ compared to SCI-S). Analysis of SCI individuals according to injury level revealed that tetraplegic athletes had similar features compared to sedentary tetraplegics subjects, except for higher Em (10.9±0.6 vs. 8.6±0.7 cm/s; $p<0.05$) and lower E/Em ratio (6.3±0.4 vs. 8.8±0.8; $p<0.05$), while paraplegic athletes had similar features compared to sedentary paraplegic individuals, except for higher LV end-diastolic diameter (49.4±1.4 vs. 45.0±1.0 mm; $p<0.05$) and Em/Am ratio (1.69±0.20 vs. 1.19±0.08; $p<0.05$), and lower LV relative wall thickness (0.330±0.012 vs. 0.369±0.010; $p<0.05$) and heart rate (67.1±4.2 vs. 81.9±2.8 b.p.m.; $p<0.05$).

Conclusion: Regular physical activity is associated with improved LV diastolic function in SCI subjects and might exert distinct cardiac structural effects in tetraplegic and paraplegic subjects.

Keywords: paraplegia; tetraplegia; echocardiography; tissue Doppler; exercise.

Introduction

Subjects with spinal cord injury (SCI) have been reported to exhibit increased cardiovascular risk in comparison with able-bodied individuals independent of variation in traditional risk factors (12, 17, 24, 23). In addition, for long-term SCI, morbidity and mortality from cardiovascular causes now exceed those caused by renal and pulmonary conditions, the primary causes of mortality in previous decades (4).

Left ventricular (LV) diastolic dysfunction is consistently associated with increased risk for cardiovascular events (18). Previous reports have shown that individuals subjected to prolonged bed rest and spaceflight are known to develop LV diastolic dysfunction (19, 20), thus supporting the notion that physical inactivity might play a role in LV diastolic alterations. Likewise, data from tissue Doppler analysis demonstrated that subjects with SCI, who are subjected to remarkable physical inactivity, present worse LV diastolic function in comparison with able-bodied individuals (13).

Several studies have evaluated the impact of physical activity on cardiovascular phenotypes in SCI subjects. In this regard, SCI athletes were reported to exhibit reduced subclinical atherosclerosis in comparison with sedentary SCI ones independent of variation in traditional cardiovascular risk factors (14), indicating that physical inactivity *per se* might directly influence atherogenesis in injured subjects. Alternatively, the analysis of the influence of regular physical activity on cardiac structure of SCI subjects has yielded conflicting results (6, 22, 11, 25). Furthermore, studies using conventional echocardiography have failed to demonstrate differences in LV diastolic function between trained and untrained SCI individuals (6, 22, 11). In this report, we hypothetized that SCI-induced reductions in LV diastolic function, assessed by

tissue Doppler analysis, might be attenuated by performance of regular physical activity. Thus, the purposes of this study were to evaluate cardiac function and structure by conventional echocardiography and tissue Doppler analysis in trained SCI athletes (SCI-A) and to compare the data with those from sedentary SCI individuals (SCI-S) and able-bodied subjects (AB). In addition, we assessed whether possible differences in cardiac features between SCI-A and SCI-S were influenced by injury level (tetraplegia or paraplegia).

Methods

Subjects

A total of 58 men (29 SCI-A and 29 SCI-S) with at least one year of SCI and 29 AB men were cross-sectionally evaluated. SCI-S were enrolled from the hospital of the State University of Campinas, while AB were recruited from employees and students of the same university. Subjects labeled as AB and SCI-S did not perform sports, recreational physical activity or labor that required physical effort. SCI-A comprised competing tetraplegic athletes that were regularly performing wheelchair rugby (n=15) and competing paraplegic ones that were regularly performing basketball (n=12), handball (n=1) and tennis (n=1) for at least one year. All athletes were enrolled from the School of Physical Education of the State University of Campinas and had been training in average 10.8±1.2 hours per week for 4.2±0.5 years. Exclusion criteria for all groups included diabetes mellitus, systemic hypertension, hyperlipidemia (4), current or past smoking, known coronary artery, cardiac or pulmonary disease, cancer, regular medical therapy and clinical evidence of active infection. SCI subjects presented no preserved motor function below the injury level. In this regard, 50 SCI subjects were ASIA A and 8 individuals were

ASIA B (4 SCI-S and 4 SCI-A). Among tetraplegic SCI-S, 11 and 4 subjects had injury at C4-C5 and C6-C7, respectively, while among paraplegic SCI-S, 9 and 5 individuals had injury at <T6 and ≥T6, respectively. Among tetraplegic SCI-A, 7 and 8 subjects had injury at C4-C5 and C6-C7, respectively, while among paraplegic SCI-A, 5 and 9 individuals had injury at <T6 and ≥T6, respectively. Written informed consent was obtained from each patient and the study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a *priori* approval by the institution's human research committee. The study was approved by the University of Campinas Research Ethics Committee, and all participants provided written informed consent.

Clinical, laboratory and hemodynamic data

Clinical data included information on the participants' age and injury duration. Among SCI-A, cumulative training time was calculated as years of training X hours/week of training. Body mass index was calculated as body weight divided by height squared. Blood samples were obtained on the morning after 12h of fasting for analysis of glucose, lipid fractions and C-reactive protein.

Office blood pressure was measured using validated digital oscillometric device with the subjects in the sitting position (Omron HEM-705CP, Omron Corp, Kyoto, Japan). Two readings were averaged and if they differed by more than 5mmHg, one additional measurement was performed and then averaged.

Echocardiography studies

Echocardiography studies were performed by a skilled physician on each subject in the sitting position with a Vivid 3 Pro apparatus (General Electric, Milwaukee, WI, USA) equipped with a 2.5-MHz transducer, as previously described (13, 9). Aortic root, LV and left atrial dimensions were assessed from 2D guided M-mode tracings, according to the recommendations of the American Society of Echocardiography (10). LV mass was calculated according to the formula: 1.04*(LV end-diastolic diameter + septal thickness + posterior wall thickness)^3-(LV end-diastolic diameter)^3-13.6g (3). Relative wall thickness was computed as twice the posterior wall thickness divided by LV end-diastolic diameter. Mitral inflow velocity was examined with pulsed Doppler from the 4-chamber apical view and the following indices were evaluated: peak early inflow velocity (E), peak atrial inflow velocity (A), and peak early/atrial velocity ratio (E/A). Tissue Doppler imaging evaluated the septal and lateral ventricular walls, as previously described (13). Peak spectral longitudinal contraction (Sm), initial (Em), and final (Am) diastolic velocities for 3 consecutive beats were analyzed. Stroke volume was generated from Doppler interrogation of transaortic flow at the aortic annular level and aortic cross-sectional area (2). Cardiac output was calculated as stroke volume X cardiac frequency, while peripheral vascular resistance was obtained by the formula: mean blood pressure/cardiac output. Intraobserver LV mass, Sm and Em variabilities were <6%, <7% and <7%, respectively.

Statistical Analysis

Results were analyzed using SPSS 15.0™. Continuous normal and non-normal variables are presented as mean ± standard error and median (25–75th percentile), respectively. Based on

previous studies (13, 14), a sample size of at least 14 individuals in each group was considered suitable for detecting significant differences in LV diastolic function regarding values of alpha error = 0.05 and beta error = 0.80. The Kolmogorov–Smirnov test was used to test for normal distribution of the variables. Differences in clinical, laboratory, hemodynamic and echocardiographic continuous variables were evaluated by unpaired t-test or one-way ANOVA followed by Tukey test for pairwise comparisons, while differences in triglycerides levels were evaluated by Mann–Whitney test or Kruskal–Wallis test followed by Wilcoxon signed rank test for pairwise comparisons. χ^2 was used to compare categorical variables. Assessment of bivariate correlations between variables was examined using Pearson's correlation coefficient for normally distributed data and Spearman's rank correlation coefficient for non-normal data. Two-way ANCOVA was used to assess intergroup differences in selected variables after adjustment for relevant covariates. A p-value <0.05 was considered significant.

Results

Clinical, laboratory and hemodynamic features of enrolled subjects are presented in Table 1. The studied groups exhibited similar features, except for lower systolic blood pressure values in SCI-A and SCI-S compared to AB. In addition, SCI-S exhibited higher C-reactive protein levels than AB and higher heart rate than SCI-A.

Echocardiographic features of the studied individuals are shown in Table 2. Structural cardiac variables were similar among the studied groups, except for lower left atrial diameter in both SCI groups in comparison with AB, and lower LV chamber diameter and stroke volume in SCI-S compared to SCI-A. The analysis of LV diastolic function revealed that SCI-S and SCI-A

presented lower Em levels than AB. However, SCI-A and AB exhibited similar E/Em and Em/Am ratios, which were respectively lower and higher than those detected in SCI-S. The differences in E/Em and Em/Am ratios between SCI-A and SCI-S and between SCI-S and AB remained statistically significant after adjustment for heart rate, systolic blood pressure and C-reactive protein levels. Furthermore, no differences in markers of LV systolic function, namely ejection fraction and Sm, were detected among the studied groups.

The next step was to evaluate whether differences between SCI-S and SCI-A were influenced by injury level (paraplegia or tetraplegia). Tetraplegic athletes presented similar, clinical, laboratory, hemodynamic and echocardiographic features compared to sedentary tetraplegic individuals, except for higher E/Em ratio and lower Em values (Table 3). Paraplegic athletes exhibited higher Em/Am ratio, LV chamber diameter and stroke volume and lower heart rate and relative wall thickness in comparison with sedentary paraplegic individuals (Table 4). There was also a trend toward higher LV mass index ($p=0.07$) in paraplegic athletes. No further difference was detected between the paraplegic subgroups. In addition AB presented E/Em (5.9±0.3) and Em/Am (1.63±0.08) values that were statistically similar to those exhibited by tetraplegic athletes (E/Em=6.3±0.4; $p=0.398$ compared to AB; Em/Am=1.46±0.14; $p=0.181$ compared to AB) and paraplegic athletes (E/Em=6.6±0.5; $p=0.192$ compared to AB; Em/Am= 1.69±0.20; $p=0.728$ compared to AB).

We then assessed whether cumulative training time, estimated as the product of years of training X hours/week of training, correlated with echocardiographic features of tetraplegic and paraplegic athletes. In tetraplegic athletes no correlation was detected between training time and cardiac features. In paraplegic athletes, however, cumulative training time correlated with stroke volume ($r=0.91$; $p<0.001$), LV end-diastolic diameter ($r=0.84$; $p<0.001$), relative wall thickness

(r=0.77; p=0.001), LV mass index (r=0.73; p=0.003) and LV end-systolic diameter (r=0.67; p=0.009), but with no further echocardiographic parameter.

Discussion

In the present report we showed that: 1) worse LV diastolic function was detected in SCI-S compared to SCI-A and AB, independent of variation in clinical, hemodynamic, metabolic and inflammatory variables; 2) analysis split by injury level revealed that both tetraplegic and paraplegic athletes exhibited markers of improved diastolic function in comparison with respective sedentary individuals; and 3) paraplegic athletes presented a pattern of eccentric LV remodeling in comparison with sedentary paraplegic individuals. In general, these findings suggest that regular physical activity is associated with improved LV diastolic function in SCI individuals and further indicate that injury level may influence the effects of regular exercise on cardiac structure.

Sedentary SCI subjects have been reported to present worse diastolic function than able-bodied individuals (13). Likewise, individuals subjected to prolonged bed rest and spaceflight are known to develop LV diastolic dysfunction (19, 20). These data suggest that physical inactivity might play an important role in the setting of LV diastolic alterations in these aforementioned populations. In the present report we found that SCI-S exhibited echocardiographic evidence of worse diastolic function, namely higher E/Em ration and lower Em/Am, compared to the SCI-A and AB. In addition, separated analysis of paraplegic and tetraplegic individuals confirmed that trained subjects from both groups presented markers of better diastolic function compared to untrained ones. Previous studies have evaluated the cardiac function and structure in trained and

untrained SCI individuals (6, 22, 11), but they did not report any difference in echocardiographic markers of diastolic function. The reason for these discrepancies can be explained by differences in the echocardiographic protocol. None of those aforementioned studies performed tissue Doppler analysis, which is a more sensitive approach in order to assess LV diastolic function (10, 18). Indeed, differences in diastolic function between trained and untrained SCI individuals in our study were only detected by tissue Doppler analysis and not by conventional echocardiography. Therefore, our findings provide novel evidence that regular training is coupled with better diastolic function in SCI individuals and further support the notion that tissue Doppler analysis is a more adequate procedure in order to assess LV function in these populations.

The reasons by which physical activity might influence LV function in SCI individuals are not apparent in our study. Noticeably, better diastolic function in SCI-A was independent of variation in time and level of injury as well as in hemodynamic (blood pressure and cardiac output), metabolic (body mass index, glucose and lipid profile) and inflammatory (C-reactive protein) variables when compared to SCI-S. These findings suggest that alternative mechanisms could explain the impact of physical activity on LV diastolic function. In this context, previous studies showed that regular exercise stimulates increases in myocardial sarcoplasmic reticulum calcium uptake, thus improving LV relaxation (7, 8, 1). Nevertheless, further studies are necessary to unveil the precise mechanisms underlying the association between physical activity and LV diastolic function in injured subjects.

Our analysis of tetraplegic subjects revealed similar characteristics between trained (wheelchair rugby players) and untrained subjects, except for higher Em and lower E/Em ratio in athletes, which are echocardiographic markers of better diastolic function (10, 18). To our knowledge,

this is the first report to compare the cardiac features between trained and untrained tetraplegic individuals. In addition, similar E/Em ratio and Em/Am ratio were detected in trained tetraplegics and AB subjects. These latter findings are in agreement with those reported by West et al (25), who found comparable LV diastolic function assessed by tissue Doppler analysis in 12 tetraplegic wheelchair rugby players and 12 able-bodied subjects. This aforementioned report also showed lower LV mass and LV end-diastolic diameter in SCI athletes, which was assumed to be consequent to lower cardiac output levels observed in these individuals. In our report, however, cardiac output did not statistically differ between tetraplegic athletes and AB individuals, which could explain the similar LV mass and LV end-diastolic diameter values observed in these groups.

Conflicting data have been reported regarding the impact of regular exercise on cardiac parameters in paraplegic individuals. Gates et al evaluated 21 trained and 5 sedentary paraplegic subjects and found no differences in LV structure and function (6). Likewise, Schumacher et al investigated 25 endurance-trained SCI athletes and 10 untrained SCI subjects (both groups were mostly composed by paraplegic individuals) and observed no differences in echocardiographic features between the samples (22). Conversely, Maggioni et al. investigated 10 aerobically-trained and 7 untrained paraplegic individuals and found higher LV mass and septal thickness in trained subjects (11). In the present report, paraplegic athletes (mostly wheelchair basketball players) exhibited significantly higher LV chamber diameter and stroke volume and lower relative wall thickness and a trend toward higher LV mass index than sedentary ones. The explanations for the differences among the studies are not clear, but may be related to variation in exercise protocols, sample sizes and background features of studied subjects. Nevertheless it was noticeable that the LV eccentric remodeling pattern coupled with lower heart rate seen in

our paraplegic athletes resembled a pattern of volume overload, commonly seen in aerobically trained able-bodied subjects who exhibit preserved autonomic function (21). Since paraplegic subjects present lower SCI levels, and therefore, more preserved autonomic function and volemic regulation (16), it seems intuitive that paraplegic athletes developed cardiovascular adaptations closer to AB than to tetraplegic ones. In addition, cumulative training time (the product of years of training X hours of training/week) directly correlated with LV chamber volume, stroke volume and LV mass in paraplegic athletes, supporting the notion that LV structural remodeling was related to the time of training experienced by these individuals. Finally, tissue Doppler analysis revealed higher Em/Am ratio in physically active paraplegic individuals than in sedentary ones. Given that Em/Am ratio exhibits a direct relationship with better LV diastolic function (15), it can be argued that regular activity was also coupled with improved LV diastolic function in subjects with lower injury level.

One aspect of our protocol that deserves further comments was the strict criteria of subject selection and therefore the homogeneity of our sample. We excluded individuals with obesity, hyperlipidemias, diabetes mellitus, hypertension and smoking, which are commonly seen after chronic SCI (16) and could be potential confounders in the analysis. In addition, we only included SCI subjects without any preserved motor function below the injury level, a feature that is associated with increased physical inactivity. However, two potential limitations should be acknowledged. First, the cross-sectional design limits our ability to infer a causal relationship between physical inactivity and variation in cardiac parameters in SCI individuals. Second, the inclusion of only male patients means that the results cannot yet be applied to female patients.

In summary, this report showed that regular physical activity was associated with improved LV diastolic function in SCI subjects, independent of variation in hemodynamic, metabolic and inflammatory parameters. In addition, paraplegic, but not tetraplegic athletes, exhibited a pattern of LV eccentric remodeling. Further longitudinal studies are necessary to confirm the current evidence and to unveil the precise mechanisms by which physical inactivity is associated with impaired LV diastolic function.

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Table 1. Clinical and hemodynamic features of all enrolled subjects.

Variable	AB (n=29)	SCI-S (n=29)	SCI-A (n=29)
Clinical features			
Age, years	30.8±0.9	31.9±1.3	29.4±1.2
Time of injury, years	—	7.5±0.9	9.2±1.1
Tetraplegic, n (%)	—	15 (52)	15 (52)
Body mass index, kg/m^2	23.7±0.6	23.3±0.6	22.4±0.6
Glucose, mg/dL	81.0±1.6	82.8±1.6	80.2±1.0
LDL-cholesterol, mg/dL	100.2±8.5	104.9±5.5	98.8±5.1
HDL-cholesterol, mg/dL	44.5±2.4	39.7±1.2	39.4±1.5
Triglycerides, mg/dL	89 (42)	89 (59)	82 (33)
Log C-reactive protein, mg/dL$^{\#}$	1.11±0.15	1.68±0.12*	1.40±0.18
Systemic hemodynamic features			
Systolic BP, mmHg	119.4±2.5	106.7±2.8*	109.9±3.3*
Diastolic BP, mmHg	72.1±2.4	65.9±2.1	68.5±2.4
Heart rate, b.p.m.	72.0±1.7	76.5±2.1	68.8±2.4†
Cardiac output (L/min)	5.0±0.2	4.7±0.2	4.8±0.2
PVR (dynes x s x cm^{-5})	1471±79	1386±52	1456±68

Legend. AB – able-bodied; SCI-S – sedentary SCI; SCI-A – SCI athletes; SCI – spinal cord injury; LDL – low density lipoprotein; HDL – high density lipoprotein; BP – blood pressure; PVR - peripheral vascular resistance; *p at least<0.05 compared to AB. $^{\dagger}p$ at least<0.05 compared to SCI-S. $^{\#}$ A constant (2.00) was added to each value of log C-reactive protein.

Table 2. Echocardiographic features of all enrolled subjects.

Variable	AB (n=29)	SCI-S (n=29)	SCI-A (n=29)
Aortic root diameter, mm	31.4±0.6	30.0±0.6	31.0±0.6
Left atrium diameter, mm	32.4±0.9	29.5±0.8*	28.8±0.8*
LV end-diastolic diameter, mm	46.8±0.8	44.6±0.7†	47.6±0.9
LV end-systolic diameter, mm	29.0±0.7	28.0±0.6†	30.2±0.7
Stroke volume, mL	69.4±2.8	61.2±2.3†	70.2±3.0
Interventricular septum, mm	8.5±0.2	8.4±0.2	8.2±0.1
Posterior wall thickness, mm	8.3±0.2	8.0±0.1	8.0±0.1
Relative wall thickness, mm	0.359±0.008	0.360±0.008	0.338±0.008
LV mass index, g/m^2	86.8±4.0	78.1±2.6	85.4±2.9
LV Ejection fraction, %	68.2±1.1	67.1±0.9	66.3±0.8
E/A Ratio	1.60±0.04	1.53±0.09	1.63±0.08
Em, cm/s	13.2±0.7	9.2±0.4*	11.0±0.5*
Am, cm/s	8.1±0.3	8.6±0.5	7.9±0.6
Em/Am Ratio	1.63±0.08	1.18±0.09*†#	1.57±0.12
E/Em Ratio	5.9±0.3	8.0±0.5*†#	6.4±0.3
Sm, cm/s	10.3±0.4	10.1±0.5	10.3±0.5

Legend. AB – able-bodied; SCI-S – sedentary SCI; SCI-A – SCI athletes; SCI – spinal cord injury; LV – left ventricular. *p at least<0.05 compared to AB. †p at least<0.05 compared to SCI-A. #p at least<0.05 compared to AB or SCI-A adjusted for heart rate, systolic blood pressure and C-reactive protein.

Table 3. Clinical, hemodynamic and echocardiographic features of tetraplegic subjects.

Variable	Sedentary (n=15)	Athletes (n=15)
Clinical features		
Age, years	31.6±1.9	29.0±1.6
Time of injury, years	7.7±1.1	7.6±1.1
Body mass index, kg/m^2	21.8±0.9	21.3±0.6
Glucose, mg/dL	82.7±2.0	80.0±1.6
LDL-cholesterol, mg/dL	93.0±8.1	100.3±8.3
HDL-cholesterol, mg/dL	36.6±1.3	36.2±1.4
Triglycerides, mg/dL	95 (96)	73 (51)
Log C-reactive protein, mg/dL$^{\#}$	1.70±0.14	1.27±0.18
Systemic hemodynamic features		
Systolic BP, mmHg	98.7±2.9	102.0±4.9
Diastolic BP, mmHg	61.4±2.4	64.5±2.9
Heart rate, b.p.m.	70.4±2.3	70.4±2.6
Cardiac output (L/min)	4.2±0.2	4.5±0.4
PVR (dynes x s x cm^{-5})	1414±66	1441±88
Echocardiographic features		
Aortic root diameter, mm	29.6±0.9	30.3±0.7
Left atrium diameter, mm	28.8±0.9	27.6±1.0
LV end-diastolic diameter, mm	44.2±1.0	45.8±0.9
LV end-systolic diameter, mm	27.9±0.8	29.3±0.6
Stroke volume, mL	59.6±3.4	63.9±3.2
Interventricular septum, mm	8.3±0.3	8.2±0.2
Posterior wall thickness, mm	7.7±0.2	7.9±0.2
Relative wall thickness, mm	0.351±0.011	0.344±0.009
LV mass index, g/m^2	76.7±4.3	81.5±3.6
LV Ejection fraction, %	66.7±1.3	65.7±0.9
E/A Ratio	1.58±0.12	1.72±0.12
Em, cm/s	8.6±0.7	10.9±0.6*
Am, cm/s	8.6±0.9	8.4±0.8
Em/Am Ratio	1.17±0.16	1.46±0.14
E/Em Ratio	8.8±0.8	6.3±0.4*
Sm, cm/s	9.5±0.6	10.6±0.8

Legend. LDL – low density lipoprotein; HDL – high density lipoprotein; BP – blood pressure; PVR - peripheral vascular resistance; LV – left ventricular. *$p<0.05$ compared to sedentary subjects. $^{\#}$ A constant (2.00) was added to each value of log C-reactive protein.

Table 4. Clinical, hemodynamic and echocardiographic features of paraplegic subjects.

Variable	Sedentary (n=14)	Athletes (n=14)
Clinical features		
Age, years	32.3±1.8	29.8±1.9
Time of injury, years	7.3±1.5	10.8±1.8
Body mass index, kg/m^2	24.9±0.7	23.5±0.9
Glucose, mg/dL	83.1±2.7	80.3±1.3
LDL-cholesterol, mg/dL	117.6±5.8	97.4±6.4
HDL-cholesterol, mg/dL	43.1±1.7	42.6±2.5
Triglycerides, mg/dL	89 (97)	84 (40)
Log C-reactive protein, mg/dL$^{\#}$	1.67±0.20	1.40±0.18
Systemic hemodynamic features		
Systolic BP, mmHg	115.3±3.7	119.9±3.4
Diastolic BP, mmHg	70.6±2.8	73.5±3.6
Heart rate, b.p.m.	81.9±2.8	67.1±4.2*
Cardiac output (l/min)	5.2±0.3	5.1±0.3
PVR (dynes x s x cm^{-5})	1358±82	1474±110
Echocardiographic features		
Aortic root diameter, mm	30.4±0.9	31.8±0.9
Left atrium diameter, mm	30.2±1.4	30.0±1.2
LV end-diastolic diameter, mm	45.0±1.0	49.4±1.4*
LV end-systolic diameter, mm	28.1±0.9	31.3±1.1*
Stroke volume, mL	62.8±3.2	77.0±4.5*
Interventricular septum, mm	8.5±0.2	8.2±0.2
Posterior wall thickness, mm	8.3±0.1	8.1±0.2
Relative wall thickness, mm	0.369±0.010	0.330±0.012*
LV mass index, g/m^2	79.4±3.2	89.6±4.4
LV Ejection fraction, %	67.6±1.2	66.4±1.2
E/A Ratio	1.48±0.13	1.54±0.09
Em, cm/s	9.8±0.5	11.0±0.9
Am, cm/s	8.6±0.6	7.4±0.8
Em/Am Ratio	1.19±0.08	1.69±0.20*
E/Em Ratio	7.2±0.5	6.6±0.5
Sm, cm/s	10.8±0.7	10.0±0.6

Legend. LDL – low density lipoprotein; HDL – high density lipoprotein; BP – blood pressure; PVR - peripheral vascular resistance; LV – left ventricular. *p at least<0.05 compared to sedentary subjects. $^{\#}$A constant (2.00) was added to each value of log C-reactive protein.