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Reversal of Adaptive Left Ventricular Atrophy Following Electrically-stimulated Exercise Training in Human Tetraplegics

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Summary

Left ventricular (LV) myocardial atrophy and diminished cardiac function have been shown to accompany chronic human tetraplegia. These changes are attributable both to physical immobilisation and abnormal autonomic circulatory regulation imposed by a spinal cord injury (SCI). To test whether exercise training increases LV mass following chronic SCI, 8 neurologically complete quadriplegic males at 2 SCI rehabilitation and research centres underwent one month of electrically-stimulated quadriceps strengthening followed by 6 months of electrically-stimulated cycling exercise. Resting M-mode and 2-D echocardiograms were measured before and after exercise training to quantify the interventricular septal and posterior wall thicknesses at end-diastole ($IVST_{ED}$ and PWT_{ED}, respectively), and the LV internal dimension at end-diastole ($LVID_{ED}$). LV mass was computed from these measurements using standard cube function geometry. Results showed a 6·5% increase in $LVID_{ED}$ following exercise training ($p<0·02$), with increases in $IVST_{ED}$ and PWT_{ED} of 17·8 ($p<0·002$) and 20·3% ($p<0·01$), rspectively. Computed LV mass increased by 35% following exercise training ($p=0·002$). These data indicate that myocardial atrophy is reversed in tetraplegics following electrically-stimulated exercise training, and that the changes in cardiac architecture are likely to be the result of both pressure and volume challenge to the heart imposed by exercise.

Key-words: *Tetraplegia; Exercise; Cardiac Atrophy; Echocardiography; Electrical Stimulation.*

The size and architecture of both the developing and the developed human heart are recognised to be influenced by peripheral circulatory volume and systemic pressures.[1–4] It is also known that departure from normal hemodynamic states arising from disease or altered activity levels transform the structure of the heart

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and alter its pumping efficiency. In particular, two pathologically-distinct hemodynamic states are known to promote unique structural alterations of the human heart. The more common of these states occurs when left ventricular pressure or volume are elevated secondary to essential hypertension and peripheral arterial disease,[5] or ventricular outflow obstruction (idiopathic hypertrophy subaortic stenosis or aortic stenosis),[6] disorders which are associated with hypertrophy of the left ventricular (LV) myocardium. In contrast, a less prevalent state resulting in cardiac atrophy has been described in individuals who sustain chronic underloading of ventricular pressure, ventricular volume, or both. The latter changes in hemodynamic state commonly result in undesirable changes in cardiac morphology and function due to diminution of myocardial wall stress.[7] This type of cardiac atrophy is causally and mechanistically distinct from myocardial regression, a process characterised by loss of mass from an already hypertrophied myocardium following pharmacological resolution of chronically-elevated blood pressure.[8]

In contrast to myocardial regression, true cardiac atrophy has been reported in individuals with otherwise normal cardiac structure who sustain extended periods of imposed physical immobilisation,[9] starvation, or abrupt weight loss.[10] More recently, cardiac atrophy has been reported in human tetraplegics, a finding attributable to both physical immobilisation imposed by loss of motor function and diminished cardiac filling following chronic vasomotor paralysis. The cardiac atrophy described in tetraplegics is independent of body surface area and has been documented both by echocardiography and pathological shifting of the electrical axis of the heart toward the right.[11]

Echocardiography is a reliable non-invasive tool which has been used to assess the influences of both cardiac disease and exercise training on cardiac structure and performance in able-bodied persons.[12, 13] Previous cross-sectional and prospective echocardiographic studies have found that LV mass is greater in exercise-trained than in sedentary persons, and have suggested that wall stress imposed by exercise-induced pressure and/or volume challenge is responsible for promoting increased myocardial mass.[14–18] These studies have also suggested that the mechanisms by which LV mass increases following exercise may differ depending on the type of exercise mode and intensity used.

To date, a study examining the effects of exercise on cardiac atrophy in tetraplegic individuals has yet to be performed. Because tetraplegics have limited voluntary use of upper extremity muscle mass and diminished physical work capacity, an exercise intensity sufficient to promote cardiac pressure or volume loading is not easily satisfied by the use of arm ergometry exercise. Therefore, we sought to determine whether electrically-stimulated cycling exercise (ESCE) might provide a training stimulus of adequate intensity and duration to reverse paralysis-related loss of LV mass.

The purpose of this study was to examine whether electrically-stimulated cycle ergometry exercise training reverses cardiac atrophy in human tetraplegics.

Methods

Subjects

Eight SCI volunteers from two SCI centres served as study subjects. The

participants were healthy neurologically-stable quadriplegic males between the ages of 22 and 39 years (28·4±5·3, mean±S.D.) with chronic spinal cord injuries (SCI) of 3–11 (6·1±2·6) years duration at the C5–C7 levels. All subjects had either clinically complete upper motor neuron lesions without preserved motor or sensory function (Frankel Classification A), or motor complete lesions with absence of volitional motor function below the level of lesion, but some preserved sensation (Frankel Classification B). None of the subjects had volitional bowel or bladder function and in all cases their physical immobilisation was attributable to quadriplegia alone. Medical physician examination revealed that all participants were in good health, defined operationally as being asymptomatic for treatable illness. Blood chemistries performed before the initiation of treatment showed all subjects to have normal blood counts, proteinaemia, and albuminaemia. Twelve lead electrocardiograms were recorded to rule out pathology characterised by disturbances in cardiac rate and rhythm showed no electrocardiographic evidence of ischaemia or previous myocardial infarction. Range of motion of the lower extremities was within functional limits for each subject, and none had evidence of bone or joint pathology. Radiographic examination confirmed the absence of lower extremity fractures and implanted metal instruments. At the time of study none of the participants was actively engaged in a programme of strength or cardiorespiratory exercise conditioning or recreational sports. They did not change their method of wheelchair propulsion or levels of physical activity throughout the course of study. Subjects gave informed consent for treatment in accordance with the Institutional Review Board regulations at their respective institutions. Descriptive data on the study subjects are shown in Table 1.

Exercise training

Study subjects underwent one month of quadriceps muscle training using transcutaneous electrical current (compensated monophasic rectangular wave, 40 Hz, 375 microseconds pulse duration, constant current, Therapeutic Technologies, Inc.) applied to the anterior thigh using three carbon silastic electrodes. Subjects were trained three times weekly on non-consecutive days using a progressive resistance exercise algorithm. During each training session the seated

Table I Demographic characteristics of the study subjects

Subject	Level of injury	Age (years)	Duration of injury (years)	Wheelchair type
1	C6	26	9	Manual
2	C5	24	5	Electric
3	C6	32	11	Manual
4	C7	22	6	Manual
5	C5,6	26	5	Manual
6	C6	39	5	Manual
7	C5	30	5	Electric
8	C6	28	3	Electric
Mean		28·4	6·1	
S.D.		5·3	2·6	

subjects performed 45 repetitions of electrically-stimulated knee extension through 45° range from the 90° gravity-dependent position. All subjects began training with a one pound weight attached to their ankle. When the subjects were able to complete the targeted 45 repetitions, the weight was increased by two pounds for the next training session. If the subject was unable to complete this designated number of contractions the weight was reduced by one pound. Each quadriceps contraction lasted 6 seconds (3 seconds concentric, 3 seconds eccentric) with a 14 second rest period between lifts.

Following the quadriceps muscle training phase, subjects underwent cycle ergometry training three times weekly on non-consecutive days for 6 months. Subjects were prepared for electrically-stimulated cycling using three carbon silastic electrodes placed over the bilateral quadriceps, hamstring and gluteus muscle groups. Cycling was performed in the seated position using computer sequenced electrical current (compensated monophasic rectangular wave, 40 Hz, 375 microsecond pulse duration, constant current, Therapeutic Technologies, Inc.) for 30 minutes each training session. If the subject fatigued before the completion of 30 minutes of treatment, multiple ergometry runs up to a maximum of five were allowed. Subjects began training without external resistance applied to the ergometer. When they could sustain 30 minutes of continuous steady-state cycling without the onset of fatigue, the resistance was increased by 1/8 kilopound. Fatigue was determined operationally by the inability of the subject to maintain a pedal rate greater than 35 revolutions per minute (RPM) during peak current stimulation at 130 milliamperes.

Chronotropic and pressor responses to acute exercise

Average chrontropic and pressor responses were quantified during two successive bouts of 30 minutes of steady state cycling on non-consecutive days, each at the highest resistance level attained by the individual subjects. The heart rate (HR) was taken before and after electrically-stimulated exercise by palpation of the radial artery for 10 seconds. Systolic and diastolic blood presures ($BP_{SYSTOLIC}$ and $BP_{DIASTOLIC}$, respectively) were obtained by auscultation of the left brachial artery, with mean blood pressure (BP_{MEAN}) calculated as twice the diastolic BP plus once the systolic BP divided by three. Heart rate and BP measurements were also taken liberally throughout exercise training at other times.

Echocardiography

Echocardiograms were performed before and after exercise training with subjects placed in the left lateral decubitus position. Standard M-mode sweeps and 2-dimensional [2-D] views [long axis, short axis, and four chamber] were recorded on a Hewlett Packard Sonos 1000 (or earlier Revision K) Echocardiographic system. M-mode studies were measured by conventional criteria[19] for left ventricular internal dimension at end-diastole ($LVID_{ED}$), posterior wall thickness at end-diastole (PWT_{ED}), and interventricular septal thickness at end-diastole ($IVST_{ED}$) (Figure). Left ventricular mass was determined using combined cube function geometry with a modified convention for determination of left ventricular internal dimension (LVID), posterior wall thickness (PWT), and interventricular septal

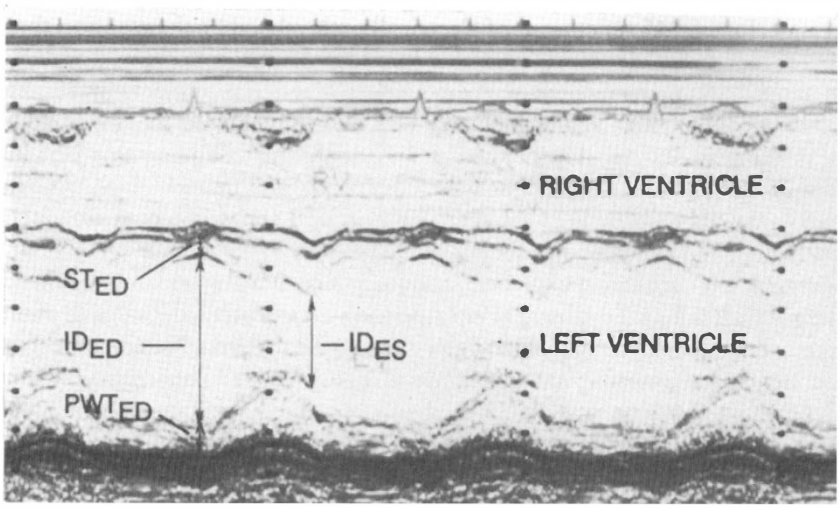

Figure M-mode echocardiogram of the left ventricle (LV) showing the method used for measurement of the septal thickness (ST_{ED}), posterior wall thickness (P_{WTED}), and internal dimension (ID_{ED}), all at end-diastole, and the internal dimension at end-systole (ID_{ES}).

thickness (IVST) which excluded the thickness of the endocardial echo lines from wall thicknesses and included the thicknesses of the left septal and posterior wall echo lines in the LVID.[20] Anatomic left ventricular mass was computed as follows:

$$LVM = 1{\cdot}04([LVID_{ED}+PWT_{ED}+IVST_{ED}]^3-[LVID_{ED}]^3)-14g.$$

where $LVID_{ED}$ is the left ventricular internal dimension at end-diastole, PWT_{ED} is the posterior wall thickness at end-diastole, and $IVST_{ED}$ is the interventricular septal thickness at end-diastole.

Data analysis

Differences between pre- and post-training mean values for the dependent measures were tested for significance using one-way multivariate analysis of variance (MANOVA). A difference between the two means was considered statistically significant if a probability equal to, or less than 0·05 was obtained.

Results

Analysis of the pre-training electrocardiograms showed that none of the subjects began treatment with brady- or tachyrhythmia, evidence of resting myocardial ischaemia or a history of myocardial infarction. Two-dimensional echocardiograms performed on all subjects confirmed the presence of normal shaped ventricles without evidence of wall motion irregularity, ventricular aneurysm, mitral valve prolapse, or hypertrophic cardiomyopathy.

All subjects completed both leg training and cycle ergometry phases of exercise without medical complication. No episodes of brady- or tachycardia, autonomic hyperreflexia, or vasovagal syncope were sustained during or following any of the

Table II Acute chronotropic and pressor responses (mean±S.D.) to steady-state electrically-stimulated cycle exercise (n=8)

	Pre-exercise	Post exercise	Significance
HR (bpm)	70·0±8·6	95·8±12·5	p<0·001
$BP_{SYSTOLIC}$ (mmHg)	90·2±6·8	129·0±10·6	p<0·001
$BP_{DIASTOLIC}$ (mmHg)	65·0±4·7	50·2±5·5	p<0·001
BP_{MEAN} (mmHg)	73·1±3·4	76·2±5·9	n.s.

Abbreviations: HR: heart rate; bpm: beats per minute; $BP_{SYSTOLIC}$: Systolic blood pressure; mmHg: millimeters mercury; $BP_{DIASTOLIC}$: diastolic blood pressure; MAP: mean arterial pressure.

Table III Echocardiographic dimensions and computed cardiac mass (mean±S.D.) before and after electrically-stimulated exercise training (N=8)

	Pre-training	Post training	Significance
$LVID_{ED}$ (mm)	48·9±3·4	52·1±4·1	p<0·02
$IVST_{ED}$ (mm)	7·5±1·3	9·1±1·1	p<0·002
PWT_{ED} (mm)	7·4±1·2	8·9±1·1	p<0·01
LV mass (g)	139·9±51·8	188·9±42·1	p=0·002

Abbreviations: $LVID_{ED}$: left ventricular internal dimension at end-diastole; $IVST_{ED}$: interventricular septal thickness at end-diastole; PWT_{ED}: posterior wall thickness at end-diastole; LV mass: left ventricular mass; mm: millimeters; g: grams.

exercise treatment sessions. Heart rate and blood pressure responses to steady state exercise at the highest attained cycling resistance are shown in Table II. Significant increases in exercise HR (p<0·001) and $BP_{SYSTOLIC}$ (p<0·001) were sustained by the subjects, accompanied by significant reduction of $BP_{DIASTOLIC}$ (p<0·001). No significant effect of exercise on BP_{MEAN} was observed.

Comparison of pre- and post-training echocardiograms showed significant changes for all LV dimensions studied (Table III). $LVID_{ED}$ increased 6·5% from 48·9±3·4 to 52·1±4·1 millimeters (p<0·02). Thicknesses of the septum and posterior wall at end-diastole increased by 17·8 (p<0·002) and 20·3% (p<0·01), respectively. Computed LV mass increased by 35% from 139·9±51·8 to 188·9±42·1 grams following completion of the exercise training programme (p=0·002).

Discussion

It is commonly recognised that cervical spinal cord trauma and disease lead to cardiodynamic states differing profoundly from those observed in the neurologically intact system.[21, 22] When compared to healthy able-bodied persons, tetraplegics show cardiovascular and hemodynamic adjustments including reduction of resting cardiac output and stroke volume[11, 23] secondary to diminished venous return. Peripheral venous insufficiency and pooling have also been noted in chronic tetraplegics, findings which are explained by loss of vascular smooth muscle tone accompanying sympathectomy,[24, 25] absence of active lower extremity muscle pump, extravasation of fluids in the lower extremities,[26] and altered breathing

mechanics favoring diminished efficiency of the abdominal-thoracic vascular pump.[27] It would reasonably be expected that these hemodynamic conditions coupled with diminished resting sympathetic division outflow of the autonomic nervous system (ANS)[22] would lead to reduced cardiac wall stress and diminished myocardial work, with subsequent compensatory changes in cardiac structure and performance.

The adaptive responses of cardiac muscle to naturally occurring pathological and experimentally-imposed conditions have been described both in humans and in laboratory animals.[7, 10, 28] The effects of altered systemic pressure and volume on cardiac wall stress and architecture have been investigated in able-bodied persons,[9] and more recently, studied in individuals with SCI.[11] In a study comparing echocardiographically-derived cardiovascular findings in tetraplegic, paraplegic and normal subjects, tetraplegics had 26% less LV mass, a finding characterised by reduction of LV cavity size with unremarkable wall thicknesses. The same subjects also showed decreased resting cardiac output, stroke volume, and mean arterial pressure in the sitting position, and elevated peripheral vascular resistance. The computed systolic wall stress index was significantly reduced in these subjects, a finding thought to be responsible for the underlying LV atrophy. The major factor contributing to the diminished calculated wall stress was a decreased LV chamber dimension, a function of chronically depressed venous return. While cardiac end-systolic volume (afterload) was observed to be normal in tetraplegics, cardiac end-diastolic volume (pre-load) was observed to be significantly diminished when compared to paraplegic and able-bodied subjects.

Numerous adaptations to the cardiac system have been associated with exercise training in healthy able-bodied individuals including increased resting cardiac output and stroke volume,[29] and a resting bradycardia attributable to decreased sympathic and increased vagal tone.[30, 31] That exercise also imposes circulatory and hemodynamic conditions of sufficient magnitude to increase left ventricular mass in subjects with normal myocardia has been shown in a number of cross-sectional and prospective studies. While it has long been recognised that the heart volume of athletes is greater than non-athletes,[32] more recent studies have used echocardiographically-derived measurements to determine wall thickness and chamber size of the left ventricle and accurately compute its mass. Cross-sectional comparison of 20 endurance runners and 26 young sedentary subjects using M-mode echocardiography has shown nominal LV chamber enlargement with demonstrable left ventricular hypertrophy in athletes when cardiac measurements were indexed to the subject's body surface area.[33] In a prospective conditioning and deconditioning study, 8 competitive swimmers increased 6·7% in $LVID_{ED}$, and from 9·4 to 10·1 mm in the PWT_{ED} following 9 weeks of swim training.[34] The same authors studied 6 competitive runners who discontinued their training for 3 weeks and sustained a 2·7 mm decrease of $LVID_{ED}$ and a reduction of PWT_{ED} from 10·7 to 8·0 mm, respectively. These studies suggest that exercise training-induced adaptive changes in LV dimension occur rapidly, mimic a pattern of chronic cardiac volume overload, and that modest degrees of LV enlargement are reversible after cessation of training.

Previous research performed on tetra- and paraplegic subjects has shown that ESCE training promotes increased physical work capacity as assessed by arm ergometry testing.[35] The present study reports that tetraplegics undergoing a

similar ESCE exercise training protocol also sustain significant changes in cardiac morphology characterised by increases in wall thickness, chamber size, and the mass of the left ventricle. The LV mass changes observed in this study exceed those evoked by cardiorespiratory exercise training in able-bodied persons on a percentage basis, but do not approach levels considered predictive of a pathological state.[36] While the increases in LV mass by the study subjects may be large, to date, no studies have been performed examining the effect of exercise conditioning on individuals with either documented cardiac atrophy or systemically altered hemodynamic patterns. In one representative prospective study on able-bodied subjects, arm and leg exercise training was shown to promote increased LV mass in able-bodied persons by 9·5%, but the study subjects started the training programme with a mean LV mass of 190±28 grams, and normal thicknesses of the posterior wall and interventricular septum.[37] These initial levels of cardiac mass contrast with our study subjects who had a dramatically lessened pre-training mean LV mass (139·9±51·8 grams) with significantly thinned walls and small LV chamber dimension. Thus, the extent of their physical deconditioning may have contributed to the large increase in LV mass found following exercise training. This finding is consistent with other cardiorespiratory conditioning studies in which the greatest changes cardiac dimensions are sustained by those subjects who are most deconditioned at the time of entry into the study.[38, 39]

It is interesting to note that the increase in cardiac mass found following ESCE training is attributable both to increased LV wall thickness and chamber size. The exercise literature suggests that LV hypertrophy following exercise training may result from one or both of two distinct hypertrophic mechanisms depending upon the mode and intensity of exercise or cardiac overload. In one study of 56 athletes aged 18 to 24 years, mean ventricular end-diastolic volume and mass were reported to increase in aerobic athletes (runners and swimmers), whereas isometric athletes (wrestlers) had increased wall thickness and mass.[40] Thus, changes in LV mass for the endurance athlete may result from hemodynamic mechanisms favouring chronic volume overload, whereas hypertrophy associated with resistance exercise is more likely attributable to chronic pressure overload.[41] That LV hypertrophy in the present study is attributable both to increased LV chamber size and wall thickness suggests that both pressure and volume overload imposed by the ESCE exercise were responsible for the observed changes in cardiac structure.

Conclusions

We conclude that ESCE exercise training reverses the adaptive LV atrophy which accompanies chronic human tetraplegia, and that augmented LV mass following training is attributable both to increased ventricular wall thicknesses and chamber size. This suggests that the observed chronic change in cardiac architecture results from both increased circulatory volume and pressure accompanying this form of exercise. The physiological and anatomical effects of this treatment on other body systems of the tetraplegic individual require additional investigation.

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References

1. Grossman W, Jones D, McLaurin LP. Wall stress and patterns of hypertrophy in the human left ventricle. J Clin Invest 1975: 56:56–64.
2. Grossman W, Braunwald E, Mann T, McLaurin LP, Green LH. Contractile state of the left ventricle in man as evaluated from end-systolic pressure-volume relations. Circ 1977: 56:845–852.
3. Grossman W. Cardiac hypertrophy: useful adaptation or pathologic process? Am J Med 1980: 69:576–584.
4. Gunther S, Grossman W. Determinations of ventricular function in pressure overload hypertrophy in man. Circ 1979: 59:679–688.
5. Koren MJ, Devereaux RB, Casale PN, Savage DD, Laragh JH. Relation of left ventricular mass and geometry to morbidity and mortality in uncomplicated essential hypertension. Ann Int Med 1991: 114:345–352.
6. Bennet DH, Evans DW, Raj MVJ. Echocardiographic left ventricular dimensions in pressure and volume overload. Their use in assessing aortic stenosis. Br Heart J 1975: 37:971–977.
7. Cooper G, Tomanek RJ. Load regulation of the structure, composition, and function of the mammalian myocardium. Circ Res 1982: 50:788–798.
8. Reichek N, Franklin BB, Chandler T, Muhammad A, Plappert T, St John Sutton MG. Reversal of left ventricular hypertrophy by antihypertensive therapy. Eur Heart J 1982: 3 (Suppl A):165–169.
9. Hellerstein HK, Santiago-Stevenson D. Atrophy of the heart: A correlative study of eighty-five proved cases. Circ 1950: 1:93–126.
10. St John Sutton MG, Plappert T, Crosby L, Douglas P, Mullen J, Reichek N. Effects of reduced left ventricular mass on chamber architecture, load, and function: A study of anorexia nervosa. Circ 1985: 72 (5):991–1000.
11. Kessler KM, Pina I, Green BA, Burnett B, Laighold M, Bilsker M, Palomo AR, Myerburg RJ. Cardiovascular findings in quadriplegic and paraplegic patients and in normal subjects. Am J Cardiol 1986: 58:525–530.
12. Feigenbaum H. Assessment of echocardiography in clinical practice. Prog Cardiovasc Dis 1978: 57:237–243.
13. Popp RL. Echocardiographic assessment of cardiac disease. Circulation 1976: 54:538–552.
14. Parker BM, Londeree BR, Cupp GV, Dubiel JP. The noninvasive cardiac evaluation of long-distance runners. Chest 1978: 73:376–381.
15. Ikaheimo MJ, Palasti IJ, Takkunen JT. Noninvasive evaluation of the athletic heart: sprinters versus endurance runners. Am J Cardiol 1979: 44:24–30.
16. Blair NL, Youker IE, McDonald IG, Jelinek VM. Echocardiographic assessment of cardiac chamber size and left ventricular function in aerobically trained athletes. Aust NZ J Med 1980: 10:540–547.
17. Rost R. The athlete's heart. Eur Heart J 1982: 3(suppl A):193–198.
18. Fagard R. Aubert A, Staessen J, VanDen Eynde E, Vanhees L, Amery A. Cardiac structure and function in cyclists and runners. Comparative echocardiographic study. Br Heart J 1984: 52:124–129.
19. O'Rourke RA, Hanrath P, Henry WN, Hugenholtz PG, Piza Z, Roelandt J, Tanaka M. Report of the Joint International Society and Federation of Cardiology/World Health Organization Task Force on Recommendations for Standardization of Measurements from M-Mode Echocardiograms. Circ 1984: 69:854A–857A.
20. Devereaux RB, Reichek N. Echocardiographic Determination of Left Ventricular Mass in Man. Circ 1977: 55(4):613–618.
21. Figoni SF. Cardiovascular and haemodynamic responses to tilting and to standing in tetraplegic patients. A review. Paraplegia 1984: 22:99–109.
22. Freyschuss U, Knutson E. Cardiovascular control in man with transverse cervical cord lesions. Life Sci 1969: 8:421–424.
23. Corbett JL, Debarge O, Frankel HL, Mathias C. Cardiovascular responses in tetraplegic man to muscle spasm, bladder percussion, and head-up tilt. Clin Exp Pharmacol Physiol 1975: (Suppl 2):189–193.
24. Nash MS, Montefusco CM, Rhodes BA. Peripheral vascular response to exercise-induced and post-occlusive reactive hyperemia (PORH) in quadriplegics. Surg Forum 1990: 41:498–99.
25. Vallbona C, Lipscomb HS, Carter RE. Endocrine responses to orthostatic hypotension in quadriplegia. Arch Phys Med Rehabil 1966: 44:7–18.
26. Claus-Walker J, Halstead LS. Metabolic and endocrine changes in spinal cord injury. II. Partial decentralization of the autonomic nervous system. Arch Phys Med Rehabil 1981: 63:576–601.
27. Fremont-Smith F. The role of elongation and contraction of the inferior vena cava, coincident with respiration, in the return of blood to the heart: report of an observation on men. J Mt Sinai Hosp 1942: 9:432–434.

28. Borow KM, Neumann A, Arensman FW, Yacou MH. Left ventricular contractility and contractile reserve in humans after cardiac transplantations. Circ 1985: 71(5):866–872.
29. Scheuer J, Tipton CM. Cardiorespiratory adaptations to physical training. Ann Rev Physiol 1977: 39:221–251.
30. Frick M, Elovainio R, Somer T. The mechanism of bradycardia evoked by physical training. Cardiologia 1967: 51:46–54.
31. Sigvardsson K, Svanfeldt E, Kilblom A. Role of the adrenergic nervous system in development of training-induced bradycardia. Acta Physiol Scand 1977: 101:481–488.
32. Kjellberg S, Rudhe U, Sjostrand T. The amount of hemoglobin and the blood volume in relation to the pulse rate and cardiac volume during test. Acta Physiol Scand 1949: 19:136–145.
33. Gilbert CA, Nutter DO, Felner JM, Perkins JV, Heymsfield SB, Scjlant RC. Echocardiographic study of cardiac dimensions and function in the endurance-trained athlete. Am J Cardiol 1977: 40:528–33.
34. Ehsani AA, Hagberg JM, Hickson RC. Rapid changes in left ventricular dimensions and mass in response to physical conditioning and deconditioning. Am J Cardiol 1978: 42:52–56.
35. Ragnarsson KT, Pollock S, Petrofsky J, O'Daniel W, Edgar R, Nash MS. Clinical evaluation of computerized functional stimulation after spinal cord injury: a multicenter pilot study. Arch Phys Med Rehabil 1988: 69:672–677.
36. Pelliccia A, Maron BJ, Spataro A, Proschan MA, Spirito. The upper limit of physiologic cardiac hypertrophy in highly trained elite athletes. N Engl J Med 1991: 324(5):295–301.
37. Thompson PD, Lewis S, Varady A et al. Cardiac dimension and performance after either arm or leg endurance training. Med Sci Sports Exerc 1981: 13(5):303–309.
38. Landry F, Bouchard C, Dumesnil J. Cardiac dimension changes with endurance training: indications of a genotype dependency. JAMA 1985: 254(1):77–80.
39. Maron BJ. Structural features of the athlete heart as defined by echocardiography. J Am Col Cardiol 1986: 7(1):190–203.
40. Demaria AN, Newman A, Lee G, Fowler W, Mason DT. Alterations in ventricular mass and performance induced by exercise training in man evaluated by echocardiography. Circ 1978: 57:237–244.
41. Morganroth J, Maron BJ, Henry WL, Epstein SE. Comparative left ventricular dimensions in trained athletes. Ann Intern Med 1975: 82:521–524.