

Patients with chronic high spinal cord injury can be safely treated with neuromuscular electrical stimulation: cardiovascular function is unaffected

Letícia Vargas Almeida¹, Carolina Lins¹, Janaina Tancredo¹, Renato Varoto¹, Wilson Nadruz Junior¹, Alberto Cliquet Junior^{1,II}

^I Universidade de Campinas - UNICAMP, Faculdade de Ciências Médicas, Departamento de Ortopedia e Traumatologia, Laboratório de Biomecânica e Reabilitação do Sistema Locomotor, Campinas, SP, Brazil.

^{II} Universidade de São Paulo – USP, Escola de Engenharia de São Carlos, Departamento de Engenharia Elétrica e de Computação, Laboratório de Biocibernética e Engenharia de Reabilitação, São Carlos, SP, Brazil.

OBJECTIVE: To identify changes in blood pressure and heart rate in individuals with chronic paraplegia undergone neuromuscular electrical stimulation treatment.

METHOD: Design: Observational prospective. Participants: Twenty individuals with chronic paraplegia (neurological level above T6) belonging to two different groups (G1 and G2) were submitted to an upper limb exercise test. G1 patients (n=13) had been treated with neuromuscular electrical stimulation (25Hz, pulses of 300µs, 100V) for 2 years or more, at least once a week; G2 patients (n=7) did not receive neuromuscular electrical stimulation treatment; G3 individuals (n=6) were healthy volunteers. **Procedures:** Arterial blood pressure and heart rate were measured during four phases of the exercise test: at initial rest, during warmup, during the exercise itself, and at rest after the exercise.

RESULTS: Systolic and diastolic blood pressures showed no statistical difference between groups. In the comparison between exercise phases, regardless of the group, systolic pressure was significantly higher and diastolic pressure significantly lower at the end of the exercise itself, when compared to all other phases. Resting heart rate was significantly lower in healthy controls vs. G1 and G2, which were not significantly different between themselves. Exercise increased heart rate in all groups.

CONCLUSION: This study showed that the groups are normotensive and homogeneous in their results; heart rate was higher in both paraplegic groups compared to healthy controls, but no difference was found between treated vs. untreated groups. Thus, neuromuscular electrical stimulation is a safe and effective way to treat individuals with chronic paraplegia.

KEYWORDS: Spinal Cord Injury, Paraplegia, Blood Pressure, Heart Rate, Neuromuscular Electrical Stimulation, Autonomic Dysreflexia.

Almeida LV, Lins C, Tancredo J, Varoto R, Nadruz-Junior W, Cliquet-Junior A. Patients with chronic high spinal cord injury can be safely treated with neuromuscular electrical stimulation: cardiovascular function is unaffected. MedicalExpress (São Paulo, online). 2017 October;4(5):M170503.

Received for Publication on June 23, 2017; First review on July 27, 2017; Accepted for publication on September 10, 2017; Online on September 26, 2017

E-mail: leticia23vargas@yahoo.com.br

INTRODUCTION

Spinal Cord Injury (SCI) is one of the most serious and complex pathologies in the neurological domain and is, in turn, responsible for a series of deleterious complications in the human body. In addition to all the physical, psychic and social damages that affect these individuals,

who, in Brazil, are usually young men, aged 15-35 years, they will still have to deal with Autonomic Dysreflexia, the silent and potentially life-threatening complication.¹

The population of individuals with SCI is increasing in Brazil and in the world, because of car accidents, firearms, cold weapons, diving, falls, among others, or because of natural disasters, such as earthquakes.²⁻⁵

Life expectancy after traumatic SCI improved significantly in Great Britain over a 70-year period, between the decades of 1950-2010.⁶

DOI: 10.5935/MedicalExpress.2017.05.03

Consequently, health complications have become more evident on account of the increase of the SCI population and of their life expectancy. Autonomic Dysreflexia is a complication due to the breakdown of the Autonomic Nervous System function resulting from SCI; 90% of the cases are observed in spinal cord injuries at high neurological levels, i.e. above the sixth thoracic nerves. The clinical signs of autonomic dysreflexia were first observed in 1830 in a patient presenting intense sweating and cutaneous erythema in the head and neck during a vesical catheterization. In 1917, autonomic reflexes were associated to the vesical and cutaneous stimuli below the level of SCI. The relationship between paroxysmal hypertension and the increased number of individuals with SCI was only confirmed in 1947.⁷

It is a well-established fact that negative cardiologic changes are events caused by reduced sympathetic and increased parasympathetic control. The disordered relationships between these two systems results in variations of heart rate and blood pressure and may cause arrhythmias, namely bradycardias with a risk of cardiac arrest in individuals with high cervical and thoracic injuries.⁸

In view of the relationship between harmful skin and vesical stimuli below the lesion level and signs and symptoms generated by the lack of harmony within the autonomic nervous system, the objective of this study was to describe the blood pressure and heart rate changes observed in a group of individuals with high paraplegia who underwent treatment with Neuromuscular Electrical Stimulation (NMES).

■ MATERIALS AND METHODS

Twenty individuals with chronic paraplegia (neurological level above T6) selected from of the University Hospital outpatient clinic were included in this study. They divided into two groups. G1: patients (n=13) who had been treated with neuromuscular electrical stimulation (25Hz, pulses of 300µs, 100V) for 2 years or more, at least once a week; G2: patients (n=7) who had not received neuromuscular electrical stimulation treatment; the control group (G3) comprised 6 healthy volunteers. All subjects were volunteer collaborators, and this work was approved by the Institutional Ethics Committee (case # 682.840). The inclusion criteria for G1 and G2 were as follows: (a) male subjects, age over 18 years; (b) a history of at least 2 years of spinal cord injury at a neurological level between T2 and T6; (c) a record of at least 2 years of NMES treatment initiated at least 1 year after injury (only for G1) (d) hemodynamically stable. Exclusion criteria for these groups were: (i) inability to understand the activities; (ii) presence of infection, (iii) functional disability of the upper extremity; (iv) severe medical restrictions. G3 included healthy sedentary male subjects. Individuals with no spinal cord injury or upper extremity musculoskeletal disorders.

The American Spinal Injury Association (ASIA) Impairment Scale (AIS) was applied by a single professional trained and qualified to do so. Briefly, AIS classifies the severity of spinal cord injury, identifying sensory levels (scored for 28 locations, maximum 112 points) and motor levels (scored to a maximum of 100 points).^{9,10}

G1 patients had been treated with NMES for more than 2 years, at least once a week: (treatment initiated at least 1 year after injury). For this, a 4-channel electrical stimulator was used, with a monophasic signal of 25 Hz, rectangular pulses of 300 µs and maximum intensity of 100 V (1 kΩ load). NMES was applied on the quadriceps and on the fibular nerve for 20 and 15 minutes, respectively.

G1 and G2 subjects performed the upper limb exertion test in their daily use wheelchairs during the year 2015; G3 subjects carried out the test in an ordinary chair. A custom-made table with adjustable height was used to accommodate individuals of different stature and various models of wheelchair.

The following materials were used for upper limbs exertion test: static cycle ergometer (*Hand Cycle Endorphin Professional Series, Endorphin Corporation, Pinellas Park, FL, USA*), automatic blood pressure monitor (*Omron Healthcare, Inc., São Paulo, SP, Brazil*), heart rate monitor (*Polar S810-T31 cod, Polar Electro Inc., New York, NY, USA*) and a 1.2x0.8 m table with adjustable height.

During the upper limbs exertion test all subjects were monitored for systolic and diastolic blood pressures, and for heart rate data, which were acquired simultaneously.

The exertion test used was the Conconi model, which was adapted for the wheelchair users.^{11,12} This test was applied three times to all participants on consecutive weeks. The entire activity was divided into four phases: initial rest (5 minutes), warming up, test itself (until fatigue) and final rest (5 minutes). After the initial rest period, the warming up phase consisted of cyclic movements with the upper limbs at a predetermined speed of 5 km/h for 2 minutes. Next came the test itself, which was started with a speed of 7 km/h during the first minute. Verbal commands were given to the subjects to increase speed by 1 km/h at every minute until fatigue set in, at which point the test was concluded. The tests were performed without load, with the test proper lasting in average 11.34 minutes throughout the groups.

Data analysis was done through measures of mean, median, standard deviation, minimum and maximum values. Phases and groups were compared through ANOVA technique for repetitive measures with response variables transformed to segmented factors. The significance level adopted was 5%.

■ RESULTS

Demographics and clinical data on the included subjects are displayed in Table 1. Systolic and diastolic

Table 1 - Demographic and clinical data of subjects (n=26).

	G1	G2	G3
N	13	7	6
Age [years]*	39.15(11.38)	31.43(6.13)	37.83(8.32)
BMI[kg/m2]*	25.68(2.61)	26.27(4.77)	25.88(2.51)
Age of spinal cord injury [years]*	14(7.33)	7(2.67)	-
Neurological level	T2-T6	T3-T5	-
ALS %(A/B)	92.31/7.69	57.15/42.85	-

* Significant difference between G1 vs. G2 (p<0.05)

blood pressures, and heart rate throughout the test, according to phases and the groups are displayed in Figures 1-3, respectively.

Figure 1 shows that systolic blood pressure exhibited no significant differences between groups (p = 0.147), regardless of phase. However, at the end of the fatigue phase systolic pressure was significantly higher (p < 0.001), compared to the values of the other three phases.

Diastolic blood pressure (Figure 2) shows that similarly to systolic pressure, no significant differences occurred between groups (p = 0.311). However, and independently of groups, diastolic pressure was significantly lower (p < 0.001) at the end of the fatigue phase, compared to the other three phases.

Figure 3 shows that significant differences (p < 0.001) were observed between the groups for heart rate. Regardless of the phase, G3 presented significantly lower values than the G2 (p = 0.037) and G1 (p-value = 0.009). There were no significant differences between G1 and G2 (p = 0.9538). Significant differences were also observed between phases independently of the group: the initial rest phase presented the lowest, whereas the fatigue phase presented the highest values of the series.

DISCUSSION

In this work, the aim was to analyze heart rate and blood pressure during the physical exertion test of upper limbs and NMES, identifying possible changes caused by the treatment in individuals with chronic paraplegia. It is known that NMES provides benefits to individuals with SCI such as recruitment of muscle fibers, improvement of muscle tissue oxygenation and venous return, orthostatism, gait and adequacy of upper limb tasks, as well as increased cardiac blood flow.¹³ Faced with so many benefits and considering its important role in the rehabilitation of these individuals, it was necessary to investigate the cardiologic aspects and its possible changes in this treatment strategy.

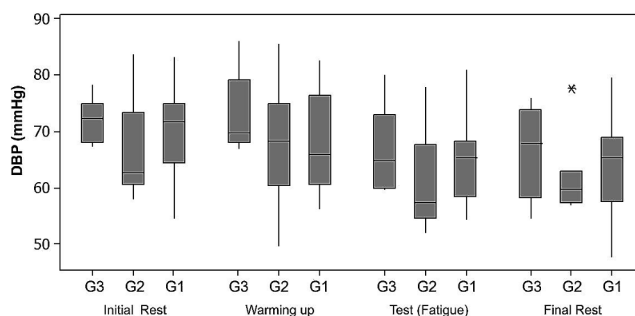


Figure 1. Systolic arterial pressure for G3 (controls), G2 (no previous NMES) and G1 (previous NMES). * indicates that systolic pressure was significantly higher for all groups at the end of the fatigue phase, for all groups.

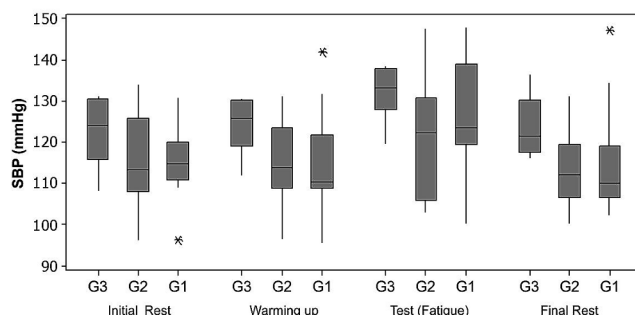


Figure 2. Diastolic arterial pressure for G3 (controls), G2 (no previous NMES) and G1 (previous NMES). * indicates that diastolic pressure was significantly lower for all groups at the final rest period.

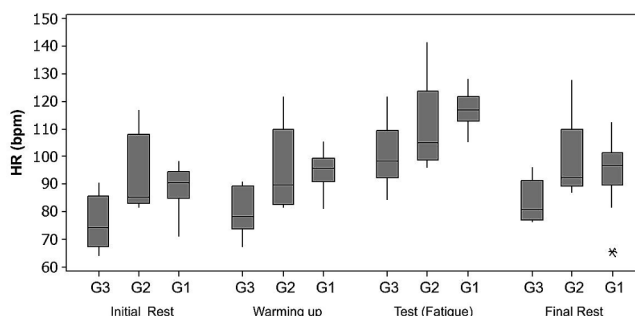


Figure 3. Heart rate for G3 (controls), G2 (no previous NMES) and G1 (previous NMES). * indicates that diastolic pressure was significantly lower for controls vs test groups.

Gallo et al¹⁴ have shown that physical activity generates important metabolic alterations and autonomic modifications that influence in the cardiovascular system.

The hypothesis regarding the lack of active musculature and the accumulation of adipose tissue is a significant indicator in which the increase of carotid intima-media thickness was investigated in a comparative study between spinal cord injured individuals with neurological level between C4-T12 and healthy individuals.¹⁵

In a recent study, heart rate variability was analyzed in 60 patients with spinal cord injury divided into 2 groups (above and below the T6 level) in relation to the control group. The evaluation was done from the waveforms and spectral analysis of the electrocardiogram. Statistical data showed that both groups of patients had some degree of autonomic dysfunction. However, the group of patients with spinal cord injury above the T6 level presented an increased risk of comorbidity and morbidity.¹⁶

Manogue et al,¹⁷ in a recent review have noted that both acute and chronic SCIs are often followed by cardiac abnormalities, characterized by impairment of the Sympathetic Nervous System, with dominance of the Parasympathetic counterpart. Episodes of bradycardia, sinus arrest or total heart block are observed in the acute phase. In the chronic phase, there are episodes of autonomic dysreflexia and paroxysmal hypertension, which are frequently initiated by vesical distensions or other stimuli below the lesion, and may be followed by bradycardia or tachycardia. They also note that the prognosis of these individuals tends to improve due to new technological advances and improved professional care.¹⁷ We believe our contribution here shows that cardiovascular function is essentially normal in chronic paraplegia.

Bar-On et al¹⁸ evaluated, in paraplegic patients, the relationship between heart rate and O₂ consumption at maximal physical effort: they report that, in individuals with SCI below T3, the interaction within the Sympathetic Nervous System is intact, because a linear correlation between heart rate and O₂ consumption occurs due to increased exercise load. However, they do suggest the presence of some other compensatory mechanism in the regulation of cardiac control.

It is known that individuals with acute or chronic SCI exhibit cardiac impairment due to the lack of harmonization within the autonomic nervous system, especially when patients with a neurological level above T6 are considered,^{14,16,18} suggesting the presence of a compensated sympathetic impairment.^{16,18} In our study neither systolic nor diastolic pressure were significantly different between the three groups in response to exercise, with or without NMES treatment. However, in the comparison between exercise phases, significant differences for systolic and diastolic pressures were found. Systolic pressure became higher during the test itself (fatigue) due to the increasing

speed imposed by the test and consequently the increase of the force of ventricular contraction and cardiac output during the exercise.¹⁹ On the other hand, diastolic pressure was lower at the end of the exercise itself. The values were significant in relation to the phase and were consistent with a drastic drop in resistance to peripheral blood flow during exercise.¹⁹

Petrofsk²⁰ investigated the systolic and diastolic blood pressure and heart rate responses in paraplegics having complete and incomplete injuries and healthy volunteers during fatiguing isometric contraction of the grasp and quadriceps muscles. All subjects performed voluntary grasp and presented pressure and heart rate increasing from rest to fatigue. Quadriceps contraction was generated by functional electrical stimulation in patients, and their systolic and diastolic responses were similar to the healthy controls. However, the heart rate of healthy controls reached 127 beats/min at the end of the contraction, while the paraplegic group presented an average increase of 6 beats/min. According to these findings, the control of blood pressure is peripheral in origin and heart rate seems to be centrally mediated.

This study also shows that NMES treatment did not generate sympathetic hyperexcitability and a possible hypertensive peak, nor did it cause cutaneous stimuli below the lesion level. Therefore, NMES is a safe and effective treatment for this group of individuals.

Healthy controls presented a lower heart rate when compared with the paraplegic patients, with no difference between treated and untreated groups. This difference is very likely a consequence of the severe deficit of active musculature in paraplegic individuals, placing them at the disadvantage in relation to the control group, a fact already expected by the study. Nonetheless all three groups exhibited the physiologically expectable tachycardia during exercise, further confirmation of the harmless action of NMES.

Study Limitations. The sample is small because of the smallness of the group of patients treated with NMES in our Institution. Recruitment of paraplegic patients (levels T2 – T6) who had not undergone NMES treatment was even more difficult. Although this study has demonstrated that NMES is an effective and safe strategy of treatment, future studies with more volunteers will be necessary to confirm these results. However, to the best of our knowledge, no published report covers this specific aspect of the management of paraplegia.

■ CONCLUSION

This study showed that the paraplegic patients with lesions above T6 are normotensive and remain hemodynamically stable during an exertion test coupled with Neuromuscular Electrical Stimulation. As a consequence of sedentarism and deficient muscular masses, paraplegic patients presented

higher basal heart rates vs healthy controls. Overall, this study showed that NMES is a safe and effective form of treatment for individuals with high level paraplegia, although more studies should be done towards a better understanding of the role of NMES in autonomic dysfunctions.

■ ACKNOWLEDGEMENTS

We thank the support by grants from São Paulo Research Foundation (FAPESP), Coordination of Improvement of Higher Level Personnel (CAPES) and National Council for Scientific and Technological Development (CNPq), and Fernanda Furtado Camargo for contributing with her knowledge to this study.

■ CONFLICTS OF INTEREST

The authors declare no conflict of interest.

■ AUTHOR PARTICIPATION

Letícia Vargas de Almeida: main researcher of the described work; elaborated the proposed methodology, performed data collection and analyzed the results. Carolina Lins: auxiliary researcher, assisted in the elaboration of the proposed method and in the statistical analyses. Janaina Roland Tancredo: assisted in data collection, including AIS assessment. Renato Varoto: co-author, provided assistance on data interpretation and discussion, text elaboration and revision. Wilson Nadruz Junior: co-author, provided assistance on text elaboration and data interpretation and discussion, based on his expertise on the human cardiovascular system. Alberto Cliquet: academic Advisor, proposed the initial concept for the presented work. Provided guidance and assistance on research development and execution.

PACIENTES COM LESÃO CRÔNICA ALTA DA MEDULA ESPINHAL PODEM SER TRATADOS DE FORMA SEGURA COM ESTIMULAÇÃO ELÉTRICA NEUROMUSCULAR: A FUNÇÃO CARDIOVASCULAR NÃO É AFETADA

OBJETIVO: Identificar mudanças na pressão arterial e frequência cardíaca em indivíduos com paraplegia crônica tratados com estimulação elétrica neuromuscular.

MÉTODO: Estudo prospectivo observacional. **Participantes:** vinte indivíduos com paraplegia crônica (nível neurológico acima de T6) pertencentes a dois diferentes grupos (G1 e G2) foram submetidos a um teste de exercício de membros superiores. Os pacientes do G1 (n = 13) haviam sido tratados com estimulação elétrica neuromuscular (25 Hz, pulsos de 300 µs, 100 V) por 2 anos ou mais, pelo me-

nos uma vez por semana; os pacientes do G2 (n = 7) não receberam o tratamento com estimulação elétrica neuromuscular; os indivíduos do G3 (n = 6) eram voluntários saudáveis. **Procedimentos:** A pressão sanguínea arterial e a frequência cardíaca foram medidas durante quatro fases do teste de exercício: no repouso inicial, durante o aquecimento, durante o exercício e no repouso após o exercício.

RESULTADOS: As pressões arteriais sistólica e diastólica não apresentaram diferença estatística entre os grupos. Na comparação entre as fases do exercício, independentemente do grupo, a pressão sistólica foi significativamente maior e a pressão diastólica significativamente menor no final do exercício, em comparação com todas as outras fases. A frequência cardíaca em repouso foi significativamente menor em controles saudáveis versus G1 e G2, que não foram significativamente diferentes entre eles mesmos. O exercício aumentou a frequência cardíaca em todos os grupos.

CONCLUSÃO: Este estudo mostrou que os grupos são normotensos e homogêneos em seus resultados; a frequência cardíaca foi maior em ambos os grupos paraplégicos em comparação com controles saudáveis, mas nenhuma diferença foi encontrada entre os grupos tratados versus os não tratados. Assim, a estimulação elétrica neuromuscular é uma maneira segura e eficaz de tratar indivíduos com paraplegia crônica.

PALAVRAS-CHAVE: Lesão Medular, Paraplegia, Pressão Sanguínea, Frequência Cardíaca, Estimulação Elétrica Neuromuscular, Disreflexia Autônoma.

■ REFERENCES

1. Ahuja CS, Wilson JR, Nori S, Kotter MRN, Druschel C, Curt A, et al. Traumatic spinal cord injury. *Nat Rev Dis Primers*. 2017;3:17018. DOI:10.1038/nrdp.2017.18.
2. Ferro FP, González HJ, Ferreira DM, Cliquet A Jr: Electrical stimulation and treadmill gait in tetraplegic patients: assessment of its effects on the knee with magnetic resonance imaging. *Spinal Cord* 2008;46(2):124-8. DOI:10.1038/sj.sc.3102078
3. Kim D, Tan CO. Alterations in autonomic cerebrovascular control after spinal cord injury. *Auton Neurosci*. 2017. pii: S1566-0702(17)30084-X. DOI:10.1016/j.autneu.2017.04.001.
4. Grove, C C, Poudel, MK, Baniya M, Rana C, House DR, Descriptive study of earthquake-related spinal cord injury in Nepal. *Spinal Cord*. 2017;55(7):705-10. DOI:10.1038/sc.2017.25.
5. Kriz J, Kulakovska M, Davidova H, Silov M and Kobesova A. Incidence of acute spinal cord injury in the Czech Republic: a prospective epidemiological study 2006–2015. *Spinal Cord*. 2017;55(9):870-4. DOI:10.1038/sc.2017.20.
6. Savic G, DeVivo MJ, Frankel HL, Jamous MA, Soni BM and Charlifue S. Long-term survival after traumatic spinal cord injury: a 70-year British study. *Spinal Cord*. 2017;55(7):651-8. DOI:10.1038/sc.2017.23.
7. Partida E, Mironets E, Hou S, Tom VJ. Cardiovascular dysfunction following spinal cord injury. *Neural Regen Res*. 2016;11(2):189-94. DOI:10.4103/1673-5374.177707.
8. Biering-Sørensen F, Biering-Sørensen T, Liu N, Malmqvist L, Wecht JM, Krassioukov A. Alterations in cardiac autonomic control in spinal cord injury. *Auton Neurosci*. 2017. pii: S1566-0702(17)30044-9. DOI:10.1016/j.autneu.2017.02.004.

9. Maynard FM, Jr, Bracken MB, Creasey G, Ditunno JF, Jr, Donovan WH, Duckler TB, et al. International Standards for Neurological and Functional Classification of Spinal Cord Injury. *Spinal Cord*. 1997;35(5):266-74.
10. Kirshblum SC, Burns SP, Biering-Sorensen F, Donovan W, Graves DE, Jha A, et al. International standards for neurological classification of spinal cord injury (Revised 2011). *J Spinal Cord Med*. 2011;34(6):535-46. DOI:10.1179/204577211X13207446293695.
11. Conconi, F; Ferrari, M.; Ziglio P. G.; Droghetti, P.; Codeca, L. Determination of the anaerobic threshold by a noninvasive field test in runners. *J Appl Physiol Respir Environ Exerc Physiol*. 1982;52(4):869-73.
12. Conconi F, Grazzi G, Guglielmini C, Borsetto C, Ballarin E, Mazzoni G, et al. The Conconi Test: Methodology after 12 years of application. *Int J Sports Med*. 1996;17(7):509-19. DOI:10.1055/s-2007-972887
13. Carvalho DCL, Zanchetta MC, Sereni JM and Cliquet Jr A. Metabolic and cardiorespiratory responses of tetraplegic subjects during treadmill walking using neuromuscular electrical stimulation and partial body weight support. *Spinal Cord*. 2005;43(7):400-5. DOI:10.1038/sj.sc.3101730
14. Gallo-Junior L, Maciel BC, Marin-Neto JA, Martins LE. Sympathetic and parasympathetic changes in heart rate control during dynamic exercise induced by endurance training in man. *Braz J Med Biol Res* 1989;22(5):631-43
15. Matos-Souza JR, Pithon KR, Ozahata TM, Gemignani T, Cliquet A Jr, Nadruz W Jr. Carotid intima-media thickness is increased in patients with spinal cord injury independent of traditional cardiovascular risk factors. *Atherosclerosis*. 2009;202(1):29-31. DOI:10.1016/j.atherosclerosis.2008
16. Carvalho-Abreu EM, Dias LP, Lima FP, Paula-Júnior AR, Lima MO. Cardiovascular autonomic control in paraplegic and quadriplegic. *Clin Auton Res*. 2016;26(2):117-26. DOI:10.1007/s10286-015-0339-1.
17. Manogue M, Hirsh DS, Lloyd M. Cardiac electrophysiology of patients with spinal cord injury. *Heart Rhythm* 2017;14(6):920-7. DOI:10.1016/j.hrthm.2017.02.015
18. Bar-On ZH, Nene AV. Relationship Between Heart Rate and Oxygen Uptake in Thoracic Level Paraplegics. *Paraplegia*. 1990;28(2):87-95. DOI:10.1038/sc.1990.11
19. Currie KD, West CR and Andrei V. Krassioukov AV. Differences in Left Ventricular Global Function and Mechanics in Paralympic Athletes with Cervical and Thoracic Spinal Cord Injuries. *Front Physiol*. 2016;7:110. DOI:10.3389/fphys.2016.00110.
20. Petrofsk JS. Blood pressure and heart rate response to isometric exercise: the effect of spinal cord injury in humans. *Eur J Appl Physiol*. 2001;85(6):521-6. DOI:10.1007/s004210100489.