

# Is the use of computerized electrical stimulation associated with cycloergometrics in individuals with medullary lesion beneficial for the muscular parameters?

Igor Kaoru Naki<sup>1</sup>, Marcelo Riberto<sup>2</sup>, Maria Cecília dos Santos Moreira<sup>3</sup>, Linamara Rizzo Battistella<sup>4</sup>

## ABSTRACT

The aim of this study was to determine whether the use of FES produces muscular benefits for individuals with spinal cord injuries. **Method:** A review of the literature was done in the electronic database MEDLINE, PubMed, LILACS and SciELO, without limitation of time or language. The PICO strategy has been used for this research. **Results:** 554 articles were found. From these, 432 were excluded by title, resulting in 122 articles left. Out of these articles the duplicates were excluded resulting in 73 articles; 36 were then excluded after reading the abstract and 33 more after reading the full text. Four studies were selected. Two articles included males and females in their studies and two only included males. Three studies included quadriplegics and paraplegics in the same study; one included only quadriplegics. One of the studies used a more frequent training routine, seven times a week; three trained only three times a week. The duration of the studies was varied considerably, from six weeks to one year. The resulting measurements for strength and resistance evaluation were performed in different manners, by muscle transverse section area measurement, limb circumference, and muscle biopsy; however, all studies presented at least one of the measurements provided by the equipment, power output or work output. Improvement of the power output and work output has been shown in all studies. Despite the heterogeneity encountered in these studies, the outcomes evaluated by them indicate a significant increase in the power output and work output after training periods, with gains starting from six weeks of training at least three times a week. **Conclusion:** Future studies are needed to assess different responses in different groups of subjects, paraplegics or quadriplegics, under different frequencies and periods of training, and thereby provide the elaboration of more directed training protocols.

**Keywords:** electric stimulation, exercise, paraplegia, quadriplegia, spinal cord injuries

<sup>1</sup> Physical Therapist at the Instituto de Medicina Física e Reabilitação do Hospital das Clínicas da Faculdade de Medicina da USP (Physical Medicine and Rehabilitation Institute at the Clinical Hospital, Medical School of the University of São Paulo -IMREA/HCFMUSP).

<sup>2</sup> Psychiatrist, Ph.D., Professor at the School of Medicine of Ribeirão Preto, USP.

<sup>3</sup> Physical therapist, Master's Degree, Director of the IMREA/HCFMUSP.

<sup>4</sup> Psychiatrist, Lecturer, Associated Professor at the Medical School, USP.

Mailing address:  
Instituto de Medicina Física e Reabilitação HCFMUSP  
- Serviço de Fisioterapia  
Rua Diderot, 43 - Vila Mariana  
São Paulo - SP  
CEP 04116-030  
E-mail: iknaki@usp.br

Received on October 8, 2011.

Accepted on November 25, 2011.

DOI: 10.5935/0104-7795.20110009

## INTRODUCTION

Spinal cord injuries affect approximately 32 people per million and about 7,800 people a year in the United States.<sup>1</sup> Worldwide, the variation is from 12.1 to 57.8 cases per million people.<sup>2</sup> It occurs predominantly with males, in about 82% of the cases and with the average age of 33.4 years.<sup>1</sup>

In general, 85% of the patients who survived after the first 24 hours of injury are still alive 10 years later.<sup>1</sup> Projections suggest the need to expand the capacity of attendance/treatment of patients with spinal cord injury and the need to prepare for the aging of this population.<sup>3</sup> Advances in technology and in medicine have provided greater longevity<sup>4</sup> for patients with spinal cord injuries. However, these patients become susceptible to diseases related to aging. Studies indicate that the occurrence of asymptomatic cardiovascular diseases in people with spinal cord injuries is between 25 and 50%,<sup>5,6,7</sup> while the occurrence of symptomatic cardiovascular diseases varies from 30 to 50%.<sup>6,8,9</sup> Nevertheless, among people without spinal cord injuries the rate varies between 5 and 10%.<sup>10</sup> This makes cardiovascular diseases one of the main causes of death in older patients with spinal cord injuries.<sup>11</sup> About a third of individuals with spinal cord injury older than 65 and approximately half of those injured for more than 30 years have died of cardiovascular diseases.<sup>12</sup> Pulmonary and cardiac complications are among the main causes of death 12 years after this type of injury, being the first and the second cause of death, respectively.<sup>13</sup> Mortality in people with spinal cord injury is three times greater than in the general population, when compared by age.<sup>14</sup>

From the cardiovascular point of view, when compared to a healthy person, the individual with spinal cord injury presents alterations that interfere with his or her capacity to take in large quantities of oxygen (VO<sub>2</sub>). In the healthy person, blood is redistributed from inactive tissues to supply muscular activity. This vasoregulation is attributed to the action of the sympathetic nervous system, which in the patient with spinal cord injury is totally or partially absent according to the level of injury. This results in the reduction of cardiac frequency and of the myocardial contractibility, limiting the cardiac output and maximum volume ejected, which reduces the potential to improve the cardiovascular performance.

Nevertheless, muscular atrophy and increase in body fat occur soon after the injury and continue to increase with aging. These

changes in the body composition and inactivity predispose people with spinal cord injuries to metabolic abnormalities and accelerate the development of cardiovascular diseases.<sup>15</sup>

Including these cardiovascular and vasoregulatory mechanisms in patients with spinal cord injuries, the publication of studies that use computerized functional electrical stimulation (CFES) has increased in order to evaluate physiological responses and to develop efficient therapies for the cardiorespiratory conditioning of these patients.

The CFES is a method for therapeutic purposes that stimulates peripheral nerves modulated by a computer through electrodes attached to the skin. It is a form of coordinated electrical stimulation that provokes sequential contraction of the quadriceps femoris, ischiotibial, and gluteus muscles, reproducing the pedaling of a bicycle.

Its greatest advantage lies in the possibility of producing the pedal movement of a cycle ergometer through the active contraction of the lower limbs muscles mediated by the electrical stimulation effect. This makes such activity possible even for the individual without any control of these muscles. In the course of training, there is an adaptive response by the individual and the resistance to the movement in the pedals can be modified, provoking more aerobic overload and better cardiovascular conditioning. The improvement of cardiorespiratory conditioning with the CFES is related to the improvement of training load parameters (resistance imposed by the cycle ergometer). In a study with 20 subjects with spinal cord injuries, Glaser<sup>15</sup> compared the physiological responses of healthy people submitted to the same treatment as the injured subjects, and observed the gradual increase of VO<sub>2</sub> concomitant to the load increase. In a study with five quadriplegic patients, Hjeltnes<sup>16</sup> evaluated the alterations in body composition after training in the CFES and he observed an increase of VO<sub>2</sub> with the load increase, which is in agreement with the study mentioned before. Figoni<sup>17</sup> evaluated the responses to the exercise in quadriplegic patients, observing the increase of VO<sub>2</sub> and of the cardiac output with load increase from 9 W.

CFES is an interesting alternative to aerobic training for people with spinal cord injuries, with the muscular component having an important role in the performance of this training.

## OBJECTIVE

This study seeks to determine whether the use of CFES produces beneficial muscular outcomes for individuals with spinal cord injuries.

## METHOD

### Inclusion criteria

The inclusion and exclusion criteria are defined based on the question that guides the review:

- Without limiting the period of publication;
- Without limiting the language

### Types of studies

We reviewed published studies of controlled and random clinical tests, semi-random and controlled clinical tests, controlled clinical tests, series of cases, and case studies.

### Participant characteristics

Adult individuals with traumatic spinal cord injury, *defined as a penetrating or non-penetrating spinal cord injury resulting from external forces.*

### Types of intervention

The use of computerized electrical stimulation (CFES) in patients with spinal cord injuries, defined as the use of *computerized electrical stimulators. This is equipment that generates low intensity pulses transmitted by surface electrodes, causing coordinated contractions in the large muscles of the legs. It has sensors that provide continuous feedback for the proper control of the muscular contractions and for the resistance of the pedal.*

### Outcomes

Muscular trophic alterations

### Search method to identify the studies

The research had no limitations of data or language

### Electronic data bases

- Medline
- Pubmed
- Lilacs
- Portal SciELO

The search strategy was based on questions structured in the P.I.C.O. form ("*Paciente*" "Patient", "*Intervenção*" "Intervention", "*Controle*" "Control", "*Outcome/Desfecho*" "Outcome"). The following descriptors were

utilized: (*Spinal Cord Injuries* OR *Quadriplegia* OR *Paraplegia*) AND (*Electric Stimulation*) AND (*Ergometry*); (*Spinal Cord Injuries* OR *Quadriplegia* OR *Paraplegia*) AND (*Electric Stimulation*) AND (*Bicycling*); (*Spinal Cord Injuries* OR *Quadriplegia* OR *Paraplegia*) AND (*Electric Stimulation*) AND (*Exercise*); (*Spinal Cord Injuries* OR *Quadriplegia* OR *Paraplegia*) AND (*Electric Stimulation*) AND (*Exercise test*); *Tetraplegia* AND *Estimulação elétrica*; *Paraplegia* AND *Estimulação elétrica*; *Traumatismos da medula espinal* AND *Estimulação elétrica*.

### Definitions of descriptors

*Spinal Cord Injuries/ Traumatismos da medula espinal*: Traumas to the spinal cord: penetrating and non-penetrating injuries to the spinal cord resulting from external traumatic forces (e.g. wounds from firearms, whiplash traumas, etc.)

*Electric Stimulation/ Estimulação elétrica*: Use of electrical currents or potentials to obtain biological responses.

*Quadriplegia/Tetraplegia*: Severe or complete loss of motor function in all the four limbs that may result from cerebral diseases, spinal cord diseases, peripheral nervous system diseases, neuromuscular diseases, or, rarely, from muscular diseases.

*Paraplegia/Paraplegia*: Severe or complete loss of motor function in the lower extremities and portions of the trunk. This affliction is more frequently associated with spinal cord diseases, cerebral diseases, peripheral nervous system diseases, neuromuscular diseases, or, rarely, from diseases that can also cause bilateral weakness of the legs.

*Exercise Test/Teste de esforço*: Controlled physical activity, more active than resting, performed to allow the evaluation of physiological functions, especially, cardiovascular and pulmonary, but also of aerobic capacity. Generally, the maximum exercise (more intense) is demanded, but the sub-maximum exercise is also used. The intensity of the exercise is frequently graduated using criteria such as frequency of the work done, consumption of oxygen, and cardiac frequency.

*Exercise/ Exercício*: Physical activity generally regular and done with the intention of improving or maintaining physical fitness or health. It is different from physical effort, which is directed mainly to physiological and metabolic responses to the use of energy.

*Bicycling/ Ciclismo*: The use of a bicycle for transport or recreation. This does not include the use of the bicycle in the study of body responses to physical exercises.

*Ergometry/Ergometria*: Any method to measure the quantity of work done by an organism, generally during physical effort. Ergometry also includes measurements of strength. Some instruments used in these determinations include the manual crank and ergometric bicycle.

The selection of the studies was made through the evaluation of titles and abstracts. When the title and abstract were not clarifying, the entire article was sought out, in order not to leave important studies out of the systematic review. The disagreements that occurred were resolved by consensus.

The data was extracted from each study through a standardized form, with information on the age of the subjects, number of subjects included in the study, type of intervention, the duration, number, and frequency of sessions, types of results measured, and authors' conclusion on the outcomes of the interventions.

## RESULTS

The initial search identified 554 articles (Table 1), from which any duplicates were excluded. The reading of the title (432) and of the abstract (36) excluded 468 articles. From the 37 remaining, after reading the complete text, only 4 satisfied the inclusion criteria in this review.

Bibliographic review articles, studies where the subjects were not adults, studies with associated therapies (strengthening protocol with functional electrical stimulation and computerized electrical stimulation, for example), studies on subjects with incomplete spinal cord injuries and motor activity (ASIA C, D, E), and studies about metabolism and muscle oxygen consumption were excluded. Articles that used non-stationary cycle ergometers were included.

Despite the concern with selecting more homogeneous studies in relation to the characteristics of the injury (complete or incomplete), type of intervention, and type of measurements, some studies presented certain heterogeneity, as presented on Table 2.

Two articles included males and females in their studies,<sup>18,19</sup> two other articles, only males. Three studies included quadriplegic and paraplegic subjects in the same study,<sup>18-20</sup> one other study included only quadriplegic subjects.<sup>16</sup> Two studies included at least one subject with incomplete injury in the study,<sup>19,20</sup> two other studies included only one subject with complete injury.<sup>16,18</sup> One of the

studies used a greater training frequency, seven times a week,<sup>16</sup> three others used a three times a week frequency.<sup>18-20</sup> The duration of the studies varied greatly, from six weeks<sup>20</sup> to one year.<sup>19</sup>

The studies' population samples presented a reduced number of subjects<sup>16,18-20</sup> and no studies of random and controlled clinical tests were found.

The result measurements for evaluating strength and resistance were taken by various forms, by measuring the cross-section of muscles<sup>16,19</sup> (both studies observed significant increases in the cross-sections), by circumference of the limb<sup>19,20</sup> (one of the studies reported an increase of thigh circumference,<sup>19</sup> while another reported maintenance of circumference),<sup>20</sup> and by muscular biopsy,<sup>18,19</sup> (one of the studies reported an increase in the muscle fibers' area,<sup>18</sup> while another study did not observe any alteration),<sup>19</sup> however, all the studies presented at least one of the measurements supplied by the equipment, the evaluation of potency (power output) or of the work performed (work output).<sup>16,18-20</sup>

## DISCUSSION

Despite the wide research done in this study, the number of articles selected was reduced. The use of keywords and broad terms like these in the search for articles is justified, for the studies on computerized electrical stimulation could be associated with various descriptors. Even though the technology associated with CFES is not recent, the availability of equipment is not easy and the demand for regularity in the training requires supplementary efforts by the users to obtain the cardiovascular and musculoskeletal responses desired, which may have contributed to reduce the final number of articles that satisfied the criteria defined.

Thus, the number of articles that really were about the CFES muscular effects was not great. Davis et al<sup>21</sup> made a literature review on various outcomes with the use of CFES, muscle morphology and biochemistry, cardiac and hemodynamic responses, bone density, functional changes in the capacity to perform the exercise, psychosocial aspects, and generalized metabolic responses, finding a total of 865 articles, and selecting 177 articles. Peng et al.<sup>22</sup> made another literature review evaluating cardiovascular, bone, and muscular aspects, among others. Eight articles were selected regarding the muscular aspect, including evaluations

**Table 1.** Number of articles found/selected, by association of descriptors

Descriptors	Spinal cord trauma	Paraplegia	Quadriplegia	Spinal cord injuries OR quadriplegia OR paraplegia	Total
Electric stimulation AND exercise test	*	*	*	93/24	93/24
Electric stimulation AND exercise	*	*	*	301/50	301/50
Electric stimulation AND bicycling	*	*	*	57/17	57/17
Electric stimulation AND ergometry	*	*	*	90/31	90/31
Electric stimulation	08/00	02/00	03/00	*	13/00
Total	08/00	02/00	03/00	*	554/122

**Table 2.** Description of articles used in this review

Author	Number of participants (males/females)	Average age in years $\pm$ standard deviation (variation in years)	Level of injury	Average time of injury in years $\pm$ standard deviation (variation in years)	Complete injury (C) Incomplete injury (I)*	Equipment
Chillbeck 1999 <sup>18</sup>	6 (5 males, 1 female)	(31-50)	C5-T8	(3-25)	All C	ERGYS 2 (Therapeutic Alliances Inc., Ohio, USA)
Gerrits 2000 <sup>20</sup>	7 (males)	40,4 $\pm$ 11,0(28-61)	C5-T8	9,8 $\pm$ 10,0(1 -27)	5C and 2 I	ERGYS 2(Therapeutic Alliances Inc., Ohio, USA)
Hjeltnes 1997 <sup>16</sup>	5 (males)	35 $\pm$ 6,1	C5-C7	10,2 $\pm$ 7,6 (4-23)	All C	ERGYS1 (Therapeutic Alliances Inc., Ohio, USA)
Mohr 1997 <sup>19</sup>	10 (8 males, 2 females)	35,3 $\pm$ 7,2 (27-45)	C6-T4	12,5 $\pm$ 6,2 (3-23)	9 C and 1 I	REGYS 1 (Therapeutic Alliances Inc., Ohio, USA)
Description of randomization	Training frequency per week	Duration of each session	Duration of training	Losses reported?	Type of measurement	
Non-randomized	3	30 min	8 weeks	No	Muscle biopsies of the lateral vastus muscle, obtained before and after training. Work output.	
Non-randomized	3	30 min	6 weeks	No	Circumference of thigh, measured at 5 and 20 cm from the patella. Work output	
Non-randomized	7	30 min	8 weeks	Yes, and justifies losses	Transversal section through computerized tomography of gluteus maximus and medius, ischiotibial muscles, and quadriceps. Power output.	
Non-randomized	3	30 min	12 months	No	Circumference of thigh, measured at 10 and 20 cm from the patella. Transversal section of thigh muscle, medium portion, by functional magnetic resonance; and muscle biopsy of the lateral vastus muscle. Power output.	
Results				Author's conclusion		
Average increase of 23% in the muscle fibers area and of 39% in the number of capillaries				Eight weeks of training 3x/week of CFES promotes the proportional increase of the fibers' area and of the number of capillaries. These changes can increase functional parameters, such as muscle resistance in individuals with spinal cord injuries.		
Six weeks of training in the FES-LCE did not alter the thigh circumference significantly. Measured at 5 and 20 cm from the patella. Respectively, 40.2 $\pm$ 3.2 centimeters before, and 40.4 $\pm$ 2.5 centimeters; and 47.8 $\pm$ 2.9 centimeters before, and 48.0 $\pm$ 3.4 centimeters after the training. Significant increase of work output with average of 4 $\pm$ 5 kJ to 13 $\pm$ 14 kJ.				The present study shows clearly that 6 weeks of training in the FES-LCE can improve the physiological properties of the quadriceps in individuals with SCI in relation to resistance to fatigue.		
Significant increase of muscles' cross-section at 22% or 58 cm <sup>2</sup> Increase in the load (6W) to (22.4W). Four subjects were able to perform the training session in the CFES for 30 min with loads varying from 6W(subjects 3 and 4) to 12.2W (subject 2) and 18.3W (subject 1), but subject 4 felt fatigue after 20 min at 6W.				The training done 7x/week for 8 weeks promoted significant increase in muscular resistance in quadriplegic patients.		
The thigh circumference, at 20 cm from the patella, increased 0.9 $\pm$ 0.2 cm ( $p < 0.05$ ) after 6 months and 0.9 $\pm$ 0.2 cm ( $p < 0.05$ ) after 12 months, respectively 3 and 5% increases. Increase of 5% in the cross-section of the thigh muscles. There was no significant increase of the muscle fiber areas.				The musculoskeletal changes that occurred in the subject with spinal cord injury after the injury can be reverted. The training of legs with electrostimulation is an effective rehabilitation tool.		

\* Complete injury, sensory and motor complete; incomplete injury, sensory incomplete, but motor complete

on muscular tropism and spasticity, not excluding those studies with subjects who had incomplete injury. These authors observed that the use of CFES promoted increases in the muscle mass and resistance, reduced the frequency and the duration of muscle spasms, increased sensitivity to insulin, increased ventilatory parameters, and increased oxygen consumption.

Coincidentally, in this review, the studies selected used the same brand of equipment, Ergys (Therapeutic Alliances Inc, Ohio, USA), which allows us to affirm that the results have a greater consistency. However, other CFES equipment, or cycle ergometer equipment associated with another electrical stimulation apparatus was also already used. Kakebeeke et al.<sup>23</sup> used StimMaster (ELA,

Dayton, OH), while Berry and col used Mobile Recumbent Tricycle (Inspired Cycle Engineering Ltd., Falmouth, Cornwall, UK) adapted for coupling with electrical stimulation. Duffel et al.<sup>24</sup> made their study using the tricycle Trice (Inspired Cycle Engineering, Ltd., UK) and the Stanmore stimulator as an electrical stimulator, Scremin et al.<sup>25</sup> used REGYS (Therapeutic Alliances Inc., Ohio, USA).

The CFES devices were introduced into the market in the 1980s with the first commercialized equipment - REGYS (Therapeutic Alliances Inc.). Since then other companies have introduced new CFES or cycloergometer models and protocols into the market associated with other electrical stimulation devices. Nevertheless, the high cost and maintenance of the equipment, and the clinical complications inherent to the population studied, may have contributed to the reduced number of studies made.

The evaluation measurements used in the studies of this review were the muscular microstructure evaluation by biopsy, the measurement of limb circumference (thigh), the evaluation of the muscle cross-section (thigh), work output, and power output.

The evaluation of muscle cross section used in two studies<sup>16,19</sup> showed an increase in area of the muscle fibers examined. However, this increase in the muscle fiber areas was not observed through the muscular biopsy.<sup>19</sup> According to the authors of this study, muscle fiber areas smaller than 200 $\mu\text{m}^2$  were not counted, for they could be confused with artifacts, this could justify this controversial finding. Conversely, Chilibeck et al.<sup>18</sup> evaluated the muscle fiber areas by biopsy and observed an increase in the fibers' areas after the period of training.

The thigh circumference measuring was used by Mohr et al.<sup>19</sup> and Gerrits et al.<sup>20</sup> the former observed an increase of this measurement, while the latter did not observe any such change. Gerrits et al.<sup>20</sup> report that this result may be associated with the fact of this measurement not being sensitive and subject to measurement errors, despite its easy application.

The work output and power output parameters used in these studies indicate the productivity of the exercise, that is, the capacity of the individual to perform the exercise. The work output parameter refers to the quantity of energy spent during the exercise, measured in Joules (J). The power output parameter refers to the velocity at which the quantity of energy is spent per unit of time during the exercise, measured in Watts (W). Fignon<sup>17</sup> correlated cardiorespiratory improvement in quadriplegic individuals submitted to exercise based on their performance at the potency of 9 W (210 Kcal/hour), compared to a walk at the velocity of 3.2 km/h for people without spinal cord injuries. In another study<sup>22</sup> the authors identified that individuals with spinal cord injuries trained in the CFES presented maximum peak of  $\text{O}_2$  consumption

equivalent to an individual without spinal cord injury walking at 4.8 km/h or pedaling at 50 W.

Spinal cord injuries create important alterations in the muscle tissue over time. There is an important muscular atrophy in the paralyzed muscles in the first year after the injury, maintaining a "stationary state" of tropism after that.<sup>26,27</sup> Nevertheless, in the paralyzed muscles of these individuals with SCI, there is a transformation of fibers type I (slow twitch and resistant to fatigue) into muscle fibers type IIB (fast twitch and quick to fatigue), with the consequent predominance of muscular fibers type IIB (fast twitch and quick to fatigue) in relation to muscle fibers type I and type IIA (fast twitch and resistant to fatigue).<sup>28</sup>

Training with CFES is capable of partially reversing these alterations in the muscle tissue. Morh et al.<sup>19</sup> observed a reversal of muscular atrophy and a reduction of adipose tissue, with a significant increase in muscle fibers type IIA in relation to fibers type IIB.

The findings described above may be criticized due to none of the selected studies being randomized, controlled, or masked clinical tests. However, clinical knowledge allows us to declare with confidence that individuals with complete spinal cord injury do not improve their muscular tropism without some kind of direct stimulation to the musculature, such as electrical current, and that the mere passive cyclic movement only results in maintenance of articular amplitude and muscle tone regulation. Since there were no control groups, it would make no sense to randomize the subjects. Finally, masking in clinical studies aims to reduce the impression that there may be bias in the reporting of results by interference from the research subject or from the evaluator. Since the muscle outcomes selected were obtained objectively by equipment or biopsy, interferences of this nature are not expected. Thus, we can affirm that this synthesis of results from literature offers clear answers as to the effect of exercise associated to CFES on muscular parameters, except for it being applied only to a restricted group of patients with complete spinal cord injury.

## CONCLUSION

Despite the heterogeneity found in these studies, the outcomes evaluated indicate that training using CFES in individuals with

spinal cord injuries promotes improvement in the muscle parameters, with a significant increase of power and work output after the periods of training, with gains reported after six weeks,<sup>20</sup> frequency of training starting from three times a week<sup>18,19,20</sup> with 30-minute sessions, which means that these patients better support the overload of imposed physical activity. This study still leaves some questions open: what would be the effect of this type of training on individuals with incomplete injury and what is the dose-response relationship, that is, whether more density in training could be more efficient or if there is a ceiling effect.

## REFERENCES

1. National Spinal Cord Injury Association [homepage on the Internet]. New York: NSCIA; c2009 [cited 2009 Feb 20]. Available from: <http://www.spinalcord.org/>
2. Van den Berg ME, Castellote JM, Mahillo-Fernandez I, de Pedro-Cuesta J. Incidence of spinal cord injury worldwide: a systematic review. *Neuroepidemiology*. 2010;34(3):184-92.
3. Lasfargues JE, Custis D, Morrone F, Carswell J, Nguyen T. A model for estimating spinal cord injury prevalence in the United States. *Paraplegia*. 1995;33(2):62-8.
4. DeVivo MJ, Rutt RD, Black KJ, Go BK, Stover SL. Trends in spinal cord injury demographics and treatment outcomes between 1973 and 1986. *Arch Phys Med Rehabil*. 1992;73(5):424-30.
5. Phillips WT, Kiratli BJ, Sarkarati M, Weraarchakul G, Myers J, Franklin BA, et al. Effect of spinal cord injury on the heart and cardiovascular fitness. *Curr Probl Cardiol*. 1998;23(11):641-716.
6. Washburn RA, Fignon SF. Physical activity and chronic cardiovascular disease prevention in spinal cord injury: a comprehensive literature review. *Top Spinal Cord Inj Rehabil*. 1998;23:16-32.
7. Janssen TW, van Oers CA, van Kamp GJ, TenVoorde BJ, van der Woude LH, Hollander AP. Coronary heart disease risk indicators, aerobic power, and physical activity in men with spinal cord injuries. *Arch Phys Med Rehabil*. 1997;78(7):697-705.
8. Bauman WA, Kahn NN, Grimm DR, Spungen AM. Risk factors for atherogenesis and cardiovascular autonomic function in persons with spinal cord injury. *Spinal Cord*. 1999;37(9):601-16.
9. Levi R, Hultling C, Seiger A. The Stockholm Spinal Cord Injury Study: 2. Associations between clinical patient characteristics and post-acute medical problems. *Paraplegia*. 1995;33(10):585-94.
10. American Heart Association [homepage on the Internet]. Dallas: American Heart Association; c2009 [cited 2009 Feb 25] Available from: <http://www.heart.org/>
11. DeVivo MJ, Black KJ, Stover SL. Causes of death during the first 12 years after spinal cord injury. *Arch Phys Med Rehabil*. 1993;74(3):248-54.
12. Cardús D, Ribas-Cardús F, McTaggart WG. Coronary risk in spinal cord injury: assessment following a multivariate approach. *Arch Phys Med Rehabil*. 1992;73(10):930-3.

13. Annual reports 9 and 10 for the Model Spinal Cord Injury Care Systems. The National Spinal Cord Injury Statistical Center. Birmingham: University of Alabama; 1992.
14. Van den Berg ME, Castellote JM, de Pedro-Cuesta J, Mahillo-Fernandez I. Survival after spinal cord injury: a systematic review. *J Neurotrauma*. 2010;27(8):1517-28.
15. Glaser RM, Figoni SF, Collins SR, Rodgers MM, Suryaprasad AG, Gupta SC, et al. Physiologic responses of SCI subjects to electrically induced leg cycle ergometry. In: Harris G, Walker C. Proceedings of the Tenth Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE.1988;4:1638-40.
16. Hjeltnes N, Aksnes AK, Birkeland KI, Johansen J, Lannem A, Wallberg-Henriksson H. Improved body composition after 8 wk of electrically stimulated leg cycling in tetraplegic patients. *Am J Physiol*. 1997;273(3 Pt 2):R1072-9.
17. Figoni SF. Exercise responses and quadriplegia. *Med Sci Sports Exerc*. 1993;25(4):433-41.
18. Chilibeck PD, Jeon J, Weiss C, Bell G, Burnham R. Histochemical changes in muscle of individuals with spinal cord injury following functional electrical stimulated exercise training. *Spinal Cord*. 1999;37(4):264-8.
19. Mohr T, Andersen JL, Biering-Sørensen F, Galbo H, Bangsbo J, Wagner A, et al. Long-term adaptation to electrically induced cycle training in severe spinal cord injured individuals. *Spinal Cord*. 1997;35(1):1-16.
20. Gerrits HL, de Haan A, Sargeant AJ, Dallmeijer A, Hopman MT. Altered contractile properties of the quadriceps muscle in people with spinal cord injury following functional electrical stimulated cycle training. *Spinal Cord*. 2000;38(4):214-23.
21. Davis GM, Hamzaid NA, Fornusek C. Cardiorespiratory, metabolic, and biomechanical responses during functional electrical stimulation leg exercise: health and fitness benefits. *Artif Organs*. 2008;32(8):625-9.
22. Peng CW, Chen SC, Lai CH, Chen CJ, Chen CC, Mizrahi J, et al. Clinical benefits of functional electrical stimulation cycling exercise for subjects with central neurological impairments. *J Med Biol Eng*. 2011;31(1):1-11.
23. Kakebeeke TH, Hofer PJ, Frotzler A, Lechner HE, Hunt KJ, Perret C. Training and detraining of a tetraplegic subject: high-volume FES cycle training. *Am J Phys Med Rehabil*. 2008;87(1):56-64.
24. Duffell LD, Donaldson Nde N, Perkins TA, Rushton DN, Hunt KJ, Kakebeeke TH, et al. Long-term intensive electrically stimulated cycling by spinal cord-injured people: effect on muscle properties and their relation to power output. *Muscle Nerve*. 2008;38(4):1304-11.
25. Scremin AM, Kurta L, Gentili A, Wiseman B, Perell K, Kunkel C, et al. Increasing muscle mass in spinal cord injured persons with a functional electrical stimulation exercise program. *Arch Phys Med Rehabil*. 1999;80(12):1531-6.
26. Taylor PN, Ewins DJ, Fox B, Grundy D, Swain ID. Limb blood flow, cardiac output and quadriceps muscle bulk following spinal cord injury and the effect of training for the Odstock functional electrical stimulation standing system. *Paraplegia*. 1993;31(5):303-10.
27. Round JM, Barr FM, Moffat B, Jones DA. Fibre areas and histochemical fibre types in the quadriceps muscle of paraplegic subjects. *J Neurol Sci*. 1993;116(2):207-11.
28. Lotta S, Scelsi R, Alfonsi E, Saitta A, Nicolotti D, Epifani P, et al. Morphometric and neurophysiological analysis of skeletal muscle in paraplegic patients with traumatic cord lesion. *Paraplegia*. 1991;29(4):247-52.