Effects of Spinal Cord Injury in Heart Rate Variability After Acute and Chronic Exercise: A Systematic Review

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Background: Spinal cord injury (SCI) above T6 is followed by a loss of sympathetic supraspinal control of the heart, disturbing the autonomic balance and increasing cardiovascular risk. Heart rate variability (HRV) is a widely used tool for assessing the cardiac autonomic nervous system and positive adaptations after regular exercise in able-bodied subjects. However, adaptations in SCI subjects are not well known. **Objectives:** To compare HRV between able-bodied and SCI subjects and analyze the effects of chronic and acute exercise on HRV in the SCI group. **Methods:** We searched MEDLINE, Embase, Web of Science, SciELO, and Google Scholar databases to July 2016. We selected English and Spanish observational or experimental studies reporting HRV after training or acute exercise in SCI patients. We also included studies comparing HRV in SCI individuals with able-bodied subjects. Animal studies and nontraumatic SCI studies were excluded. We screened 279 articles by title and abstract; of these, we fully reviewed 29 articles. Eighteen articles fulfilled criteria for inclusion in this study. **Results:** SCI individuals showed lower HRV values in the low frequency band compared to able-bodied subjects. Regular exercise improved HRV in SCI subjects, however time and intensity data were lacking. HRV decreases after an acute bout of exercise on SCI subjects, but recovery kinetics are unknown. **Conclusion:** HRV is affected following SCI. Able-bodied subjects and SCI individuals have different values of HRV. Acute bouts of exercise change HRV temporarily, and chronic exercise might improve autonomic balance in SCI. **Key words:** heart rate variability, paraplegia, posttraumatic myelopathy, tetraplegia

Following spinal cord injury (SCI), disturbance of autonomic balance leads to an increase in cardiovascular risk.^{1,2} While there is strong evidence showing increased cardiovascular risk at higher neurological levels, the relationship with completeness of the injury is less clear.² Sympathetic innervation to the heart is disturbed in injuries above T6 because of the damage in afferent and efferent pathways to sympathetic neurons located on T1-T5 medullar segments. However, the parasympathetic innervation from the vagus nerve remains unchanged, producing a loss of synergic balance between both systems.³ In addition, the stress response from adrenal catecholamines is regulated by preganglionic sympathetic neurons, which may lead to a reduced catecholamine response after exercise.^{4,5} In addition, patients with high SCI levels will have higher perceived exertion with exercise.⁶ Due to

this, strategies aimed to improve neuro-vegetative balance and heart response to efforts are needed.

It has been described that autonomic function may improve after regular exercise in able-bodied subjects,⁷ but it is imperative to achieve equilibrium between training stimuli and rest for obtaining positive cardiovascular adaptations⁸ and avoiding an overtraining effect.⁹ In able-bodied people, tools to optimize workload and training prescription have been described¹⁰; however, the lack of recommendations for monitoring workload in SCI individuals impedes widespread use of these tools.

Heart rate variability (HRV) is a noninvasive tool for assessing the autonomic nervous system.¹¹ It is described as the irregularity in time between each beat of a normal heart, evaluated as the distance between each “R” wave in electrocardiography (R-R interval, described as NN for normal beats).

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Top Spinal Cord Inj Rehabil 2018;24(2):167-176
© 2018 Thomas Land Publishers, Inc.
www.thomasland.com
Published online ahead of print February 12, 2018
doi: 10.1310/sci17-00028

HRV analysis can be made with linear methods (frequency and time domains) and nonlinear methods (detrended fluctuation analysis, Poincaré plot, and approximate entropy, among others).^{11,12} It is commonly accepted that a lower HRV is associated with increased cardiovascular risk and mortality in able-bodied individuals,¹³ but each of the different domains of HRV can be indicative of different functions. In the frequency domain, high frequency (HF), low frequency (LF), very low frequency (VLF), and ultra low frequency (ULF) bands can be analyzed. Whereas HF and time domain are associated with parasympathetic function, LF interpretation is more complex and LF/HF ratio analysis is preferred for sympathetic activity.¹⁴

To date, HRV for exercise monitoring has been widely included in the assessment of able-bodied subjects, where an increase in HRV is associated with positive cardiovascular adaptations and a shift to increased sympathetic tone is associated with overtraining.⁸ However, the use of HRV as a tool for exercise prescription for SCI subjects is less common. The primary outcome of this review is to analyze the effects of acute and chronic exercise on HRV in SCI subjects. The secondary outcome is to compare the differences in rest between able-bodied subjects and SCI individuals.

Methods

Search strategy

A literature search was performed on August 2016 in MEDLINE, PubMed, Embase, and Web of Science databases by 2 authors independently. MeSH terms used were “heart rate variability” [AND] “spinal cord injury” and “heart rate variability” [AND] “spinal cord injury” [AND] “exercise.” For Spanish publications and gray literature, SciELO and Google Scholar databases were searched for terms “variabilidad del ritmo cardíaco” “lesión medular” and “variabilidad de la frecuencia cardíaca” “lesión medular.” Search restrictions were used for gray literature according to the recommendations of Mahood et al.¹⁵

Article selection

Observational or experimental articles including linear HRV analysis on SCI individuals and

one of the following reports were included: (1) comparison with able-bodied subjects, (2) comparison of active and inactive SCI subjects or inactive SCI individuals initiating an exercise intervention, (3) HRV acute response or recovery after exercise in SCI subjects. Additional inclusion criteria were articles in Spanish or English, published between 1998 and July 2016. A total of 279 articles were identified. After duplicates were removed, the titles and abstracts were screened independently by 2 reviewers (D.B, C.C.). Animal studies and nontraumatic SCI articles were excluded according to PRISMA methods.¹⁶ When there was disagreement in selection, a third reviewer (R.S.) resolved it. A total of 29 articles were fully reviewed, and 11 of them were discarded due to inclusion criteria. Eighteen articles were selected for the final review (**Figure 1**).

Quality measure

No quantitative analysis was performed. Risk of bias was assessed independently by 2 authors using the National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (<https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/cohort>) or the Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group (<https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/tools/before-after>). Results of the assessment were presented with an adaptation of the Cochrane risk of bias summary figure¹⁷ for better understanding.

Results

HRV differences between SCI subjects and able-bodied people

A total of 8 cross-sectional studies were included. Because the NIH assessment tool gives a lower score to cross-sectional studies compared to cohort studies, all included studies were identified as low quality. However, we decided to adjust the tool, removing items designed only for cohort studies (exposure assessed prior to outcome, sufficient timeframe to see an effect, and follow-up rate) due to the difficulty in performing studies

Figure 1. Search strategy.

other than cross-sectional for this outcome. Risk of bias classification is summarized in **Figure 2**.

Most studies found significant differences in rest LF values with a fair risk of bias, but there was a high level of variability within study subjects in regard to neurological level. Two studies used a 24-hour ECG recording,^{18,19} one study used a 4-hour recording,²⁰ and 5 studies performed a short HRV recording of 15 minutes or less.²¹⁻²⁵ Data are summarized in **Table 1**.

Most studies did not report differences in parasympathetic HRV values compared with able-bodied individuals; however, one study found lower values of HF in tetraplegics,²² whereas Krstacic et al found higher HF and time domain values in thoracic SCI patients.¹⁹ In summary, most studies with a fair risk of bias showed lower LF absolute power values with no major differences in HF and time domain HRV.

HRV training adaptations

A total of 4 quasi-experimental and 3 cross-sectional studies were included for qualitative analysis. For analysis of quasi-experimental studies, the NIH assessment tool described above was used, but questions 11 and 12 were not included because of multiple outcome measures and group level interventions. Risk of bias assessment is summarized in **Figure 3**. Most studies were classified as fair risk of bias, mainly because sample size determination and blinding were not described. Nonetheless, the authors agreed that this did not invalidate the results. Only one cross-sectional study was classified as a fair risk of bias, however all of them were identified as low or very low quality for this outcome due to the intrinsic lower quality of observational studies and the feasibility of performing experimental or quasi-experimental studies for this outcome. Results of

Figure 2. Risk of bias of studies comparing rest heart rate variability (HRV) between healthy and spinal cord-injured individuals. Adapted from National Institutes of Health Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies with permission. Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.

quasi-experimental studies are summarized in **Table 2**. Some studies did not find an association between regular physical activity and HRV adaptations in time^{18,24,26,27} and frequency domain,^{18,24,27,28} but other studies have found associations in nonlinear parameters of HRV^{24,26,27,29} and some frequency domain values.^{26,29,30}

In quasi-experimental articles, Ditor et al²⁸ did not find changes on HRV in paraplegics after 4 months of training in a body weight-supported treadmill (BWST). The same group described a significant decrease in LF/HF ratio due to lower LF power after 6 months of BWST in tetraplegics following a similar protocol.³¹ Similarly, Millar et al²⁷ compared HRV after BWST or tilt training protocol in a cross-over design. After 4 weeks of training, only BWST resulted in a significant increase in nonlinear HRV values and a trend to a decrease of LF and HF normalized units power. In contrast, Brizuela Costa et al²⁹ described an increase in time and frequency domains in

patients with tetraplegia after 8 weeks of training in arm ergometer at maximal tolerated intensity. However, an unclear definition of the intervention raises the risk of bias of this study.

As previously described, 3 studies evaluated differences in rest HRV between physically active and inactive SCI subjects in a cross-sectional design. Higher parasympathetic-associated HRV values were found in active SCI compared with sedentary SCI and neurological intact subjects,^{26,30} but the lower intrinsic quality of observational studies does not allow the generalization of this finding.

Acute HRV response and recovery

A total of 7 quasi-experimental articles were included. Five studies evaluated HRV after a single session of aerobic exercise and 2 of them after an isometric exercise. Risk of bias is summarized in **Figure 4**. No sample size justification and lack of blinding are the main biases of included studies. However, the authors agreed that, although interpreted with caution, studies could be considered as a fair risk of bias for internal validity.

Included articles evaluating HRV acute response to aerobic exercise are summarized in **Table 3**. Wecht et al³² analyzed HRV recovery in active and inactive individuals with paraplegia with lesions below T6 after a maximal effort test in arm ergometer. Successive measurements during a 90-minute period post workout showed a significant decrease in HF, LF, and LF/HF ratio values immediately after exercise, as previously reported.^{4,21,25,33}

HRV response to other exercise modalities has also been described. Takahashi et al³⁴ reported a decrease in LF and HF immediately after static arm exercise in patients with tetraplegia, with a recovery to normal values in 90 seconds. In another study,²³ a decrease in LF with no alterations in HF was reported 5 minutes after hand grip exercise. However, definitive conclusions cannot be made due to heterogeneity and limited number of studies.

Discussion

Implications of findings and suggestions for future research

HRV is a noninvasive tool that can be used to evaluate the autonomic tone in SCI. The objective of

Table 1. Heart rate variability differences among spinal cord injury and healthy subjects

Study	N	Lesion level	Parameters	Results
Bunten et al ¹⁸	SCI = 6	C1-C8	HF, LF	↓ LF in LM, HF N/D
	SCI = 7	T1-L5		
	Ab = 13			
Castiglioni et al ²¹	SCI = 33	T5-L4	LF, HF, LF/HF	↓ LF in LM, HF N/D
	Ab = 33			
Claydon et al ²²	SCI = 14	C4-C7	LF, HF, LF/HF	↓ LF cervical, ↓ HF thoracic
	SCI = 12	T2-T11		
	Ab = 17			
Krstacic et al ¹⁹	SCI = 40	C5-T1, L2-S1	RMSSD, SDANN, SDSD, pNN50, LF, HF, LF/HF	↑ RMSSD, ↑ SDANN, ↑ SDSD, ↑ pNN50, ↑ HF, ↓ LF
	Ab = 40			
Agiovlasitis et al ²³	SCI = 20	T6-L5	LF, HF, LF/HF	LF and HF N/D
	Ab = 20			
Serra-Ano et al ²⁴	SCI = 42	T2-T12	SDNN, HF, LF, SD1, SD2	↑ LF, HF N/D
	Ab = 36			
Abreu et al ²⁵	SCI = 7	C6-C7	SDNN, rMSSD, pNN50, LF, HF, LF/HF, SD1, SD2	↓ pNN50, ↓ LF, ↓ HF
	Ab = 8			
Rodrigues et al ²⁰	SCI = 22	C1-C8	LF, HF, LF/HF	↓ LF, HF N/D, ↓ LF/HF
	SCI = 24	T1-S5		
	Ab = 44			

Note: Ab = able-bodied subjects; N/D = no differences; HF = high frequency; LF = low frequency; pNN50 = percentage of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording; rMSSD = root mean square of the successive differences of NN; SCI = spinal cord injury subjects; SD1 = standard deviation of points perpendicular to axis in a Poincaré plot; SD2 = standard deviation of points along the axis in a Poincaré plot; SDNN = standard deviation of NN; SDSD = standard deviation of differences between adjacent NN intervals.

Figure 3. Risk of bias of quasi-experimental (A) and cross-sectional (B) studies that compare heart rate variability adaptations to exercise in spinal cord injury subjects. Adapted from National Institutes of Health Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group and for Observational Cohort and Cross-Sectional Studies with permission. Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.

Table 2. Heart rate variability adaptations after exercise training in spinal cord injury subjects

Study	N	Lesion level	Parameters	Results
Ditor et al ²⁸	SCI = 6	C4-T12	LF, HF, LF/HF	N/D
Ditor et al ³¹	SCI = 8	C4-C5	LF, HF, LF/HF	↓ LF/HF, ↓ LF
Millar et al ²⁷	SCI = 7	C5-T10	rMSSD, pNN50, LF, HF, LF/HF	N/D
Brizuela Costa et al ²⁹	SCI = 11	C4-C6	rMSSD, LF, HF, LF/HF	↑ HF, ↑ LF, ↑ rMSSD

Note: HF = high frequency; LF = low frequency; N/D = no differences; pNN50 = percentage of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording; rMSSD = root mean square of the successive differences of NN; SCI = spinal cord injury subjects; SD1 = standard deviation of points perpendicular to axis in a Poincaré plot; SD2 = standard deviation of points along the axis in a Poincaré plot; SDNN = standard deviation of NN; SDSD = standard deviation of differences between adjacent NN intervals.

Figure 4. Risk of bias of quasi-experimental studies that evaluate heart rate variability acute responses to exercise in spinal cord injury subjects. Adapted from National Institutes of Health Quality Assessment Tool for Before-After (Pre-Post) Studies With No Control Group with permission. Source: National Heart, Lung, and Blood Institute; National Institutes of Health; U.S. Department of Health and Human Services.

this review was to analyze the effects of SCI on HRV compared with able-bodied subjects and determine how HRV is modified with acute and chronic exercise in SCI subjects. In the reviewed articles, lower rest LF values were observed in SCI subjects compared with neurological intact controls independently of recording time. Unfortunately, these findings could not be interpreted as an alteration in autonomic balance because of difficulties interpreting LF and inconsistency in other HRV parameters. Despite

some authors who suggested that LF could be used as a marker of sympathetic tone, it is now believed to reflect sympathetic and parasympathetic tone in neurologically intact and SCI subjects.^{14,34} Also, the lack of homogeneity in neurological level and completeness impedes identification of these differences as part of alterations in sympathetic tone, other comorbidities, or as an adaptation to a sedentary behavior. Indeed, the physical inactivity hypothesis could be viable considering that HRV values are similar between active SCI and able-bodied subjects in observational studies.^{26,30} However, these findings are not validated by higher quality studies. If lower HRV values in individuals with paraplegia below T6 are a consequence of low physical activity, it could be expected that chronic training could improve autonomic tone. Furthermore, if improvement in HRV values occurs in SCI subjects with an interruption of sympathetic pathways, exercise could be an important therapeutic tool independently of previous autonomic injury. Indeed, while no differences in HRV have been reported between injuries above T6 and those below T6,²⁴ alterations in sympathetic innervation in high SCI subjects should be considered for future studies with larger sample size.

HRV adaptations to regular exercise in able-bodied subjects have been well defined,^{35,36} however these adaptations are less understood in SCI individuals due to few quasi-experimental studies.^{18,24,26-30} Most articles had a small sample size and lack of standardization in exercise intensity and duration, which affected their external validity. Some studies found a trend to an improvement in HF values post training, but exercise intensity was

Table 3. Heart rate variability acute response to exercise in spinal cord injury subjects

Study	N	Lesion level	Parameters	Results after exercise
Wecht et al ³²	SCI-A = 18	Below T6	LF, HF, LF/HF	↓ LF, HF, LF/HF. Recovery in 90 min only in SCI-A
	SCI-S = 9	Below T6		
Merati et al ⁴	SCI = 7	C6 - T4	LF, HF, LF/HF, rMSSD, pNN50	↓ LF, HF, LF/HF
	SCI = 9	T5 - L4		
	Ab = 20			
Castiglioni et al ²¹	SCI = 33	T5 - L4	LF, HF, LF/HF	↓ LF y HF
	Ab = 33			
Romero et al ³³	SCI = 9	C5 - C7	SDNN, rMSSD, HF, LF, LF/HF	↓ SDNN, rMSSD, LF y HF. LF/HF N/D
	Ab = 9			
Takahashi et al ³⁴	SCI 6	C6 - C7	LF, HF, LF/total, HF/total	↓ LF y HF
	Ab = 9			
Agiovlasitis et al ²³	SCI = 20	T6 - L5	LF, HF, LF/HF	↓ LF, HF S/D, ↓ LF/HF
	Ab = 20			
Abreu et al ²⁵	SCI = 7	C6 - C7	SDNN, rMSSD, pNN50, LF, HF, LF/HF, SD1, SD2	↓ SDNN, rMSSD, LF, HF, SD1, SD2
	Ab = 8			

Note: Ab = able-bodied subjects; N/D = no differences; HF = high frequency; LF = low frequency; pNN50 = percentage of pairs of adjacent NN intervals differing by more than 50 ms in the entire recording; rMSSD = root mean square of the successive differences of NN; SCI = spinal cord injury subjects; SCI-A = active spinal cord injury subjects; SCI-S = inactive spinal cord injury subjects; SD1 = standard deviation of points perpendicular to axis in a Poincaré plot; SD2 = standard deviation of points along the axis in a Poincaré plot; SDNN = standard deviation of NN; SDSD = standard deviation of differences between adjacent NN intervals.

limited by spasticity and the training protocol did not meet the SCI recommendations for physical activity.³⁷ If these articles are compared,^{27-29,31} it could be interpreted as indicating that a higher intensity²⁹ or a longer period of training in protocols of low intensity³¹ is required to obtain positive cardiovascular adaptations in subjects with an altered sympathetic innervation. Furthermore, time and frequency domains could have low sensitivity in early phases, and nonlinear parameters might be more adequate at short term.^{24,26,27} Positive adaptations were observed even in high SCI, which reinforces the idea of maintained exercise as a feasible option to decrease cardiovascular risk in persons with tetraplegia with sympathetic compromise. Future training protocols with controlled exercise variables and standardized characteristics of SCI subjects are encouraged to obtain better conclusions.

The autonomic nervous system has a key role in cardiac functioning and hemodynamics during acute exercise, helping in the delivery of oxygen and glucose for muscular contraction.³⁸ During exercise,

a decrease in parasympathetic tone and an increase in sympathetic response is maintained even during recovery due to mechanisms in which mechano- and baroreceptors are involved.³⁹ In able-bodied subjects, HRV changes immediately after exercise have been described,⁴⁰⁻⁴² however few studies and heterogeneous protocols of exercise in the SCI population make it difficult to extrapolate results to clinical practice. Indeed, only one recent study evaluated HRV response after continuous exercise at 50% and 80% of heart rate reserve,²⁵ which is more related to clinical practice. In the articles reviewed, HRV values decreased immediately after exercise,^{4,21,25,32,33} but recovery kinetics are unclear. It has been described that a rise in endocrine catecholamines is involved in the decrease of HRV during exercise⁴³ and is proportional to exercise intensity,⁴⁴ which can explain the sympathetic response to exercise in persons with tetraplegia. Regarding recovery kinetics, Wecht et al³² reported that 90 minutes post exercise, only active SCI subjects return to normal HRV values compared to inactive SCI subjects. The authors attributed these

findings to a faster recovery of vagal tone and a better autonomic control post workout with chronic exercise. Preservation of vagal tone and influence of parasympathetic response in exercise is observed in a nonpublished work³³ in which able-bodied and active tetraplegics with sympathetic alterations performed an incremental aerobic exercise test. In addition to a decrease in HRV values immediately after exercise, recovery of parasympathetic-related HRV parameters showed similar values in both groups. This finding could be interpreted as an inhibition and recovery of parasympathetic activity independent of sympathetic compromise, as observed by other authors.³⁴ Even though the interest of aerobic exercise response in this population is increasing, it could be prudent to evaluate continuous protocols at standardized intensities to obtain a better picture in recovery.

Study limitations

The biggest limitation of this systematic review is the vast heterogeneity of included articles regarding characteristics of subjects and exercise protocols. Completeness and lesion level in SCI directly affects autonomic innervation, however actual classification guidelines do not fully differentiate autonomic completeness.² Even if future studies homogenize by the current American Spinal Injury Association Impairment Scale (AIS), it cannot be guaranteed that autonomic innervation follows a similar standardization.

Other limitations are the lack of experimental studies in the literature and the low sample size in quasi-experimental studies. In long-term studies, it is hard to obtain an adequate sample size of subjects with similar characteristics who complete the follow-up; this could be even more difficult if SCI participants require longer periods of training. In addition, studies involving exercise adaptations or acute response to exercise lack standardization of the protocols used. Even if intensity and

duration of exercise is standardized, the HRV changes could be different depending on whether an arm ergometer or a BWST is used, so results of current evidence must be interpreted in the correct context.

Conclusion

HRV values in SCI subjects show differences with able-bodied subjects, specifically in LF, with a low risk of bias. However, it is not possible to attribute these differences to anatomic, functional, or behavior characteristics due to the high heterogeneity of included subjects. In the SCI population, there is a nonsignificant trend toward an improvement in HF values after a training period with a fair risk of bias. Because of small sample sizes and different exercise parameters used among studies, future research is needed with larger sample sizes and with adherence to SCI exercise recommendations. Regarding acute response of HRV to exercise in SCI subjects, all HRV values decrease immediately after exercise with a low risk of bias. Nevertheless, the role of intensity and duration of exercise in this response is unclear. In addition, studies in HRV recovery kinetics to exercise are lacking. Therefore, more experimental studies are needed to evaluate how exercise affects autonomic response and recovery with the purpose of obtaining a tool for monitoring intensity and rest periods during training and rehabilitation. Future studies must standardize AIS to minimize confounding variables in a highly heterogeneous population.

Acknowledgments

We thank Loreto Vergara, Sandra Mahecha, Natalia Gattini, and Erwin Buckel for comments and advice that improved this article.

The authors report no conflicts of interest.

REFERENCES

- Garshick E, Kelley A, Cohen SA, et al. A prospective assessment of mortality in chronic spinal cord injury. *Spinal Cord*. 2005;43(7):408-416.
- West CR, Bellantoni A, Krassioukov AV. Cardiovascular function in individuals with incomplete spinal cord injury: A systematic review. *Top Spinal Cord Inj Rehabil*. 2013;19(4):267-278.
- Krassioukov A, Biering-Sorensen CF, Donovan W, et al. International Standards to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI), First Edition 2012. *Top Spinal Cord Inj Rehabil*. 2012;18(3):282-296.
- Merati G, Di Rienzo M, Parati G, Veicsteinas A, Castiglioni P. Assessment of the autonomic control of heart rate variability in healthy and spinal-cord injured subjects: Contribution of different complexity-based estimators. *IEEE Trans Biomed Eng*. 2006;53(1):43-52.
- Schmid A, Huonker M, Stahl F, et al. Free plasma catecholamines in spinal cord injured persons with different injury levels at rest and during exercise. *J Auton Nerv Syst*. 1998;68(1-2):96-100.
- Lewis JE, Nash MS, Hamm LF, Martins SC, Groah SL. The relationship between perceived exertion and physiologic indicators of stress during graded arm exercise in persons with spinal cord injuries. *Arch Phys Med Rehabil*. 2007;88(9):1205-1211.
- Laing ST, Gluckman TJ, Weinberg KM, Lahiri MK, Ng J, Goldberger JJ. Autonomic effects of exercise-based cardiac rehabilitation. *J Cardiopulm Rehabil Prev*. 2011;31(2):87-91.
- Smith DJ. A framework for understanding the training process leading to elite performance. *Sports Med*. 2003;33(15):1103-1126.
- Kuipers H, Keizer HA. Overtraining in elite athletes. Review and directions for the future. *Sports Med*. 1988;6(2):79-92.
- Stanley J, Peake JM, Buchheit M. Cardiac parasympathetic reactivation following exercise: Implications for training prescription. *Sports Med*. 2013;43(12):1259-1277.
- Heart rate variability: Standards of measurement, physiological interpretation and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Circulation*. 1996;93(5):1043-1065.
- Aubert AE, Seps B, Beckers F. Heart rate variability in athletes. *Sports Med*. 2003;33(12):889-919.
- Kuo TB, Lin T, Yang CC, Li CL, Chen CF, Chou P. Effect of aging on gender differences in neural control of heart rate. *Am J Physiol*. 1999;277(6 Pt 2):H2233-2239.
- Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: An integrative review of the heart's anatomy and heart rate variability. *Front Psychol*. 2014;5:1040.
- Mahood Q, Van Eerd D, Irvin E. Searching for grey literature for systematic reviews: Challenges and benefits. *Res Synth Methods*. 2014;5(3):221-234.
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *J Clin Epidemiol*. 2009;62(10):1006-1012.
- Higgins J, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. IVersion 5.1.0. 2011. <http://training.cochrane.org/handbook>
- Bunten DC, Warner AL, Brunnemann SR, Segal JL. Heart rate variability is altered following spinal cord injury. *Clin Auton Res*. 1998;8(6):329-334.
- Krstacic A, Krstacic G, Gamberger D. Control of heart rate by the autonomic nervous system in acute spinal cord injury. *Acta Clin Croat*. 2013;52(4):430-435.
- Rodrigues D, Tran Y, Guest R, Middleton J, Craig A. Influence of neurological lesion level on heart rate variability and fatigue in adults with spinal cord injury. *Spinal Cord*. 2016;54(4):292-297.
- Castiglioni P, Di Rienzo M, Veicsteinas A, Parati G, Merati G. Mechanisms of blood pressure and heart rate variability: An insight from low-level paraplegia. *Am J Physiol Regul Integr Comp Physiol*. 2007;292(4):R1502-1509.
- Claydon VE, Krassioukov AV. Clinical correlates of frequency analyses of cardiovascular control after spinal cord injury. *Am J Physiol Heart Circ Physiol*. 2008;294(2):H668-678.
- Agiouvasitis S, Heffernan KS, Jae SY, et al. Effects of paraplegia on cardiac autonomic regulation during static exercise. *Am J Phys Med Rehabil*. 2010;89(10):817-823.
- Serra-Ano P, Montesinos LL, Morales J, et al. Heart rate variability in individuals with thoracic spinal cord injury. *Spinal Cord*. 2015;53(1):59-63.
- Abreu EM, Alves Rde S, Borges AC, Lima FP, Junior AR, Lima MO. Autonomic cardiovascular control recovery in quadriplegics after handcycle training. *J Phys Ther Sci*. 2016;28(7):2063-2068.
- Zamuner AR, Silva E, Teodori RM, Catai AM, Moreno MA. Autonomic modulation of heart rate in paraplegic wheelchair basketball players: Linear and nonlinear analysis. *J Sports Sci*. 2013;31(4):396-404.
- Millar PJ, Rakobowchuk M, Adams MM, Hicks AL, McCartney N, MacDonald MJ. Effects of short-term training on heart rate dynamics in individuals with spinal cord injury. *Auton Neurosci*. 2009;150(1-2):116-121.
- Ditor DS, Macdonald MJ, Kamath MV, et al. The effects of body-weight supported treadmill training on cardiovascular regulation in individuals with motor-complete SCI. *Spinal Cord*. 2005;43(11):664-673.
- Brizuela Costa G, Sinz S, Malavés RA, Navarro IM. Efecto del pedaleo de brazos sobre el sistema cardiorrespiratorio de las personas con tetraplejia. *Revista Internacional de Ciencias del Deporte*. 2010;6(21):297-310.
- Otsuka Y, Shima N, Moritani T, Okuda K, Yabe K. Orthostatic influence on heart rate and blood pressure variability in trained persons with tetraplegia. *Eur J Appl Physiol*. 2008;104(1):75-78.
- Ditor DS, Kamath MV, Macdonald MJ, Bugaresti J, McCartney N, Hicks AL. Reproducibility of heart rate variability and blood pressure variability in

- individuals with spinal cord injury. *Clin Auton Res*. 2005;15(6):387-393.
32. Wecht JM, Marsico R, Weir JP, Spungen AM, Bauman WA, De Meersman RE. Autonomic recovery from peak arm exercise in fit and unfit individuals with paraplegia. *Med Sci Sports Exerc*. 2006;38(7):1223-1228.
 33. Romero Ávila JL, Brizuela Costa GA. *Efecto inmediato del ejercicio sobre la variabilidad de la frecuencia cardíaca en personas con tetraplejia*. Valencia: Departamento de Educación Física y Deportiva, Universitat de València; 2011.
 34. Takahashi M, Matsukawa K, Nakamoto T, et al. Control of heart rate variability by cardiac parasympathetic nerve activity during voluntary static exercise in humans with tetraplegia. *J Appl Physiol* (1985). 2007;103(5):1669-1677.
 35. Bellenger CR, Fuller JT, Thomson RL, Davison K, Robertson EY, Buckley JD. Monitoring athletic training status through autonomic heart rate regulation: A systematic review and meta-analysis. *Sports Med*. 2016;46(10):1461-1486.
 36. da Silva VP, de Oliveira NA, Silveira H, Mello RG, Deslandes AC. Heart rate variability indexes as a marker of chronic adaptation in athletes: A systematic review. *Ann Noninvasive Electrocardiol*. 2015;20(2):108-118.
 37. Ginis KA, Hicks AL, Latimer AE, et al. The development of evidence-informed physical activity guidelines for adults with spinal cord injury. *Spinal Cord*. 2011;49(11):1088-1096.
 38. Koga S, Rossiter HB, Heinonen I, Musch TI, Poole DC. Dynamic heterogeneity of exercising muscle blood flow and O₂ utilization. *Med Sci Sports Exerc*. 2014;46(5):860-876.
 39. Houssiere A, Najem B, Ciarka A, Velez-Roa S, Naeije R, van de Borne P. Chemoreflex and metaboreflex control during static hypoxic exercise. *Am J Physiol Heart Circ Physiol*. 2005;288(4):H1724-1729.
 40. Gladwell VF, Sandercock GR, Birch SL. Cardiac vagal activity following three intensities of exercise in humans. *Clin Physiol Funct Imaging*. 2010;30(1):17-22.
 41. Edmonds R, Burkett B, Leicht A, McKean M. Effect of chronic training on heart rate variability, salivary IgA and salivary alpha-amylase in elite swimmers with a disability. *PLoS One*. 2015;10(6):e0127749.
 42. Raczak G, Pinna GD, La Rovere MT, et al. Cardiovascular response to acute mild exercise in young healthy subjects. *Circ J*. 2005;69(8):976-980.
 43. Breuer HW, Skyschally A, Schulz R, Martin C, Wehr M, Heusch G. Heart rate variability and circulating catecholamine concentrations during steady state exercise in healthy volunteers. *Br Heart J*. 1993;70(2):144-149.
 44. Bahr R, Hostmark AT, Newsholme EA, Gronnerod O, Sejersted OM. Effect of exercise on recovery changes in plasma levels of FFA, glycerol, glucose and catecholamines. *Acta Physiol Scand*. 1991;143(1):105-115.