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ORIGINAL ARTICLE

Heart rate variability in individuals with thoracic spinal cord injury

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Study design: Cross-sectional study.

Objectives: The main goal of our study was to explore the differences in heart rate variability (HRV) while sitting between able-bodied (AB) participants and paraplegic (P) individuals.

Setting: The study was conducted in the Physical Therapy department and the Physical Education and Sports department of the University of Valencia and Vall d'Hebrón Hospital.

Methods: To record the HRV, a 1000-Hz Suunto Oy t6 heart rate monitor was used. The data were analyzed in the temporal and frequency domains, and nonlinear analysis was performed as well.

Results: We found significant differences between P and AB participants in SDNN: $t(76) = 2.81$, $P < 0.01$; root mean squared of the difference of successive RR intervals: $t(76) = 2.35$, $P < 0.05$; very low frequency: $t(76) = 2.97$, $P < 0.01$; low frequency: $t(41.06) = 2.33$, $P < 0.05$; total power of the spectrum: $t(45.74) = 2.57$, $P < 0.05$; SD1: $t(76) = 2.35$, $P < 0.05$; SD2: $t(76) = 2.82$, $P < 0.01$. Furthermore, there is a reduced variability in the P participants who adopted a sedentary lifestyle as could be observed in detrended fluctuation1 $t(40) = -2.10$; $P < 0.05$.

Conclusion: Although individuals in the P group were more active in sports than the AB group, they had an altered HRV when compared with AB individuals. It could be important to develop more intense sports programs to improve cardiac vagal tone, which in turn produces a decrease in work and oxygen consumption of the heart.

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INTRODUCTION

After a spinal cord injury (SCI), the loss of supraspinal control of the autonomic nervous system below the level of the lesion increases cardiovascular morbidity and mortality,[1] although the most severe symptoms occur with cervical and high thoracic level injuries.

It is assumed that T6 is the lowest level of injury necessary for the development of altered autonomic cardiac control because at lower levels the sympathetic pathways responsible for the autonomic modulation of heart rate remain intact.[2] However, autonomic dysfunction has occurred in some individuals with lesions as low as T8–T10.[3] This may be because autonomic cardiac control can be impaired by the immobility that results from being confined to a wheelchair and from the lifestyle adopted by individuals after SCI.[4]

The analysis of heart rate variability (HRV) can be used as a non-invasive method for quantitatively assessing the relative shifts in autonomic cardiac control.[5] HRV can be measured in the time and frequency domains and assessed using nonlinear methods in individuals with SCI.

Some previous studies have assessed cardiac autonomic function in SCI patients using HRV assessments.[3,6–16] Although participants with high-level SCI, primarily cervical injuries, present with altered cardiac autonomic control,[6,7] some studies have analyzed the HRV of patients with SCI without considering the level of injury (that is, thoracic or cervical).[9]

As previously reported, cardiac autonomic control can be impaired due to immobility resulting from injury and the sedentary lifestyle adopted after injury. For this reason, in contrast with the classifications of other studies,[3,14,15] our study explores HRV only in patients with thoracic SCI because these patients have a similar level of daily activity and use a manual wheelchair, which is enabled by preserved motor function in their upper limbs.

Other studies that also compared HRV between able-bodied (AB) and paraplegic (P) individuals classified their samples into only one P group, but they used a small sample size which compromises the external validity of the results.[8,12,13] Thus, no previous studies have provided all of the pertinent data with a large-enough sample size.

Therefore, it is necessary to provide researchers in this field descriptive data that can be used as a database for future experimental studies or preventive programs for cardiovascular diseases. The main goal of our study is to describe and explore the differences between AB and P participants in HRV while in a sitting position, which is probably the most frequently used posture in the P population during daytime hours. Secondarily, we aim to compare whether the autonomic cardiac control in P is different with varying levels of injury. In addition we wanted to explore the differences in HRV between active and sedentary participants.

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MATERIALS AND METHODS

Participants

The study included 42 P individuals (mean (s.d.), 46.93 (13.68) years old) and 36 AB participants (41.58 (12.33) years old). Sample size was calculated based on a previous study[12] in which differences between groups (that is, P and AB people) of 16.84 ms was measured in root mean squared of the difference of successive RR intervals variable. To achieve an α of 0.05 and β of 0.20 with 80% power, it requires 21 patients in each group of the study. Thirty-six participants in each of the groups of our study would provide 95% power (that is, α and β of 0.05).

At the beginning of the study, a personal interview was conducted with each participant in which questions about the number of hours the individuals participated in different kinds of regular physical activity or sports. P participants were classified as sedentary if they practiced for two or less hours per week and active if they practiced three or more hours per week.

None of the participants showed symptoms of cardiorespiratory disease or other pathological conditions, such as diabetes or hypertension that could affect autonomic cardiovascular control. This condition was checked by a team of specialist physicians responsible of the patient's management (with clinical histories).

Menstrual status was controlled for by asking women about their menstrual cycle status. Following the protocol of Bai *et al.*,[17] we only included women in the follicular phase in our analysis.

All patients in the P group were in a stable clinical condition (that is, the event occurred at least 2 years before the study started). Their level of injury was between T2 and T12 and all were manual wheelchair users. The level and completeness of SCI were determined by a complete neurological examination that was conducted by expert physicians using the AIS (American Spinal Injury Association Impairment Scale). All participants were motor complete with an AIS score of either A or B.

All participants provided written informed consent, and all procedures were conducted in accordance with the principles of the World Medical Association's Declaration of Helsinki and the protocols were approved by the ethical committee of the Vall d'Hebrón Hospital.

HRV measurements

All participants were asked to refrain from ingesting beverages containing caffeine or alcohol during the 48 h preceding the tests and also to abstain from smoking for 12 h. The HRV was recorded at 8:00 am, after an adaptation period of 10 min. Participants were seated, with participants in the P group in their wheelchair and the AB group in a chair with armrests and a backrest. As in previous studies,[3,18] we explored the HRV in the sitting position because this is the most commonly used position by P individuals during daytime hours.

To record the HRV, a t6 heart rate monitor (Suunto Oy, Vantaa, Finland, 1000 Hz) was used. The validity of this device, was compared with an electrocardiogram, is intraclass correlation coefficient > 0.99.[19] Data acquisition lasted 15 m and were performed in a room with a temperature between 20 and 22 °C, with no noise or uncomfortable atmosphere. The participants were asked to remain silent and attempt to maintain their breathing rate as low as possible, without speaking or moving.

The HR data were stored in a personal computer using Suunto Training Manager Software (version 2.3.0). Signal processing was performed using Kubios HRV analysis software (version 2.1, Biosignal Analysis and Medical Imaging Group, Department of Physics, University of Kuopio, Finland) and the analysis was performed in the time, frequency and nonlinear domains.

In the HRV time domain, the following measures were obtained: the mean of the RR interval (MEANRR) and its s.d. (SDNN), the mean heart rate (MEANHR) and its s.d. (SDHR), the RMSSD and the number and percentage of consecutive RRs that differed by > 5 ms each (NN50 and pNN50, respectively).

A Fast Fourier Transform of the RR signals was used for the HRV frequency domain analysis. The spectral response provided by the system was broken down into three bands: very low frequency (vLF) from 0.003 to 0.04 Hz, low frequency (LF) from 0.04 to 0.15 Hz and high frequency (HF) from 0.15 to 0.4 Hz. Power was expressed in absolute and normalized units (power/total power > 0.04 Hz).

The nonlinear analysis techniques used in this study included the Poincaré Plot, detrended fluctuation analysis and sample entropy. The Poincaré diagrams were obtained by plotting the RR values of n on the *x* axis, and the RR values of $n+1$ on the *y* axis. The SD1 axis indicates short-term variability, while the SD2 axis indicates long-term variability. With the detrended fluctuation analysis, we obtained the degree to which the R–R interval pattern is random or correlated. By analyzing the sample entropy, we analyzed the overall complexity and predictability of the time series.

Statistical analysis

The descriptive data are presented as the mean and s.e. and the 95% confidence intervals.

To compare the means of the dependent variables in the two groups (AB and P) we conducted independent-measures Student's *t*-tests.

When the sample size is large, small differences in group variances can produce a significant Levene's test, which indicates a violation of the assumption of homoscedasticity. When we obtained significant Levene's test values, we calculated Hartley's F_{Max}. When homoscedasticity was assumed, we used the *t*-test ratio. In the case of heteroscedasticity, we used the Satterthwaite approximation that adjusted the degrees of freedom.

To address the secondary aims of the study, we used independent-measures Student's *t*-tests to compare the mean HRV between sedentary and active individuals with P, and between participants with high and low injury levels.

RESULTS

The clinical profile of the participants is presented in Table 1. In the AB group, 69.4% were male and in the P group, 83.3% were male. There were no statistically significant differences in age and body mass ($P > 0.05$) between the groups.

We found significant differences between P and AB participants in some variables in the time domain, frequency domain and nonlinear analyses. Overall, P group values obtained indicated reduced variability compared with the AB group. The mean descriptive data and *t*-test results are presented in Table 2.

When power was normalized, there were no significant differences between both the groups ($P > 0.05$). The LF band value in P group was 62.33 (2.59) % and 68.81 (2.37) % for AB group, and HF band value was 37.67 (2.59) % and 31.19 (2.37) %, respectively.

In addition, we assessed whether the level of injury (above or below the T6) was responsible for the differences in autonomic cardiac control, and we did not see statistically significant differences between the groups ($P > 0.05$).

Table 1 Participants' clinical profile

	Paraplegic group	Able-bodied group
Age (years)	46.93 (13.68)	41.58 (12.33)
BMI (kg m^{-2})	24.54 (3.12)	24.72 (3.15)
Sports practice (h)	4.02 (4.69)	0.92 (1.31)
Time since injury (years)	16.23 (11.50)	
Level of injury (N)		
High ($>$T6)	22	
Low ($<$T6)	20	
Etiology (N)		
Traumatic	42	
Others	0	

Abbreviation: BMI, body mass index.
The data are presented as mean (s.d.) for age, body mass index (BMI), sports practice and time since injury. For the level of injury and etiology, the number of participants is presented. No differences ($P > 0.05$) were obtained between the groups in age and BMI variables.

Table 2 Comparison of the values obtained in the linear and nonlinear analyses of the heart rate variability between the able-bodied and paraplegic participants

	Able-bodied participants		Paraplegic participants		Differences (t-test)
	Mean (s.e.)	95% CI	Mean (s.e.)	95% CI	
Time domain					
MEANRR (ms)	878.13 (16.37)	844.89–911.38	841.07 (22.30)	796.03–886.11	t(72.45) = 1.340; P = 0.185
SDNN (ms)	53.07 (4.72)	43.49–62.64	37.69 (3.04)	31.55–43.84	**t(76) = 2.81; P = 0.006**
MEANHR (b.p.m.)	69.49 (1.33)	66.79–72.18	73.80 (2.12)	69.53–78.08	t(67.40) = − 1.73; P = 0.089
SDHR (b.p.m.)	4.20 (0.31)	3.57–4.83	3.69 (0.51)	2.65–4.72	t(76) = 0.82; P = 0.413
RMSSD (ms)	34.96 (4.31)	26.21–43.71	23.89 (2.32)	19.21–28.57	**t(76) = 2.35; P = 0.021**
NN50 (count)	39.92 (8.53)	22.60–57.23	22.29 (5.39)	11.40–33.17	t(60.34) = 1.75; P = 0.086
PNN50 (%)	12.01 (2.67)	6.58–17.44	6.69 (1.66)	3.33–10.05	t(59.69) = 1.69; P = 0.096
Frequency domain					
vLF (Hz)	1232.99 (148.69)	931.14–1534.85	662.44(124.13)	411.76–913.12	**t(76) = 2.97; P = 0.004**
LF (Hz)	1402.54 (375.12)	641.01–2164.08	491.06 (110.38)	268.16–713.97	**t(41.06) = 2.33; P = 0.025**
HF (Hz)	686.95 (208.05)	264.59–1109.32	299.10 (58.98)	179.99–418.21	t(40.63) = 1.79; P = 0.080
Totpow (Hz)	3323.85 (677.29)	1948.87–4698.83	1452.93 (266.45)	914.82–1991.04	**t(45.74) = 2.57; P = 0.013**
Nonlinear analysis					
SD1 (ms)	24.76 (3.05)	18.56–30.96	16.92 (1.64)	13.61–20.23	**t(76) = 2.35; P = 0.021**
SD2 (ms)	70.32 (6.06)	58.03–82.62	50.18 (4.09)	41.92–58.44	**t(76) = 2.82; P = 0.006**
DFA1 (n.u.)	1.25 (0.03)	1.18–1.31	1.19 (0.04)	1.11–1.27	t(73.15) = 1.05; P = 0.296
DFA2 (n.u.)	0.95 (0.04)	0.86–1.04	0.96 (0.03)	0.90–1.02	t(64.23) = − 0.16; P = 0.876
Sampen (n.u.)	1.41 (0.04)	1.33–1.50	1.38 (0.05)	1.27–1.49	t(76) = 0.54; P = 0.590

Abbreviations: b.p.m., beats per minute; DFA1, short-term fluctuation slope of the detrended fluctuation analysis; DFA2, long-term fluctuation slope of the detrended fluctuation analysis; HF, high-frequency band; LF, low-frequency band; MEANHR, mean of the heart rate; MEANRR, mean of the RR interval; NN50, number of consecutive RRs that differed by >5 ms each; n.u., no units; pNN50, percentage of consecutive RRs that differed by >5 ms each; RMSSD, root mean squared of the difference of successive RR intervals; Sampen, sample entropy; SDHR, standard deviation (s.d.) of the heart rate; SD1, the s.d. of the perpendicular axis of the Poincaré plot; SD2, the s.d. of the longitudinal axis of the Poincaré plot; SDNN, s.d. of the RR interval; vLF: very low frequency band; Totpow, total power of the spectrum; 95% CI, 95% confidence intervals.
The data are presented as mean (s.e.). Significant differences (independent Student's t-test) are in bold.

Finally, we compared the HRV of the P group when subdivided into sedentary and active groups. Twenty-two of the participants were enrolled in some sport for three or more hours per week, whereas the rest of them did not practice any sport. We only observed significance differences between the groups in DFA1 (detrended fluctuation) t (40) = − 2.10; P = 0.042. The rest of the variables did not achieve the level of statistical significance (P > 0.05).

Because our main goal was to describe and explore the differences between the groups in HRV with the goal of providing researchers with data to conduct further studies, all individual values for both the groups are included in the Supplementary Data Set.

DISCUSSION
The results of this study provide information about the different patterns of HRV observed in AB and P individuals with the orthostatic load produced by the sitting position, which is the most commonly used posture in the P population during the daytime.

With respect to the HRV time domain parameters, we found a significantly lower SDNN in the P compared with the AB group, which means that the s.d. of all normal RR (NN) intervals were reduced, and a significantly lower RMSSD, which is an indirect measure of the vagal tone.

As presented in Table 2, the mean (s.e.) of the SDNN for the AB group is 53.40 (5.41) and for SCI is 37.69 (3.04). Some previous studies of participants who did not have SCI (that is, patients with previous acute myocardial infarction) have reported that the risk of mortality in patients with an SDNN < 50 ms was 2.8 times greater than those with an SDNN ⩾ 50 ms.[20] The SDNN is an estimate of the overall HRV. This higher risk might occur because a reduced SDNN is, in general terms, a reduction in the variability. The mean value measured in our P group was < 50 ms. This can be explained by the fact that the sympathetic nervous system is altered in this population, although some of the P individuals had a level of injury below T6.

In addition, we obtained a significantly lower RMSSD of P participants, compared with the AB group, which is in agreement with previous studies.[15] The RMSSD estimates the short-term components of the HRV and is considered an indirect measure of the vagal cardiac tone.

We found a reduction in both SDNN and RMSSD, consistent with the results of Krassioukov et al.,[5] whose paper provided information about dysfunction of the autonomic nervous systems, both sympathetic and parasympathetic, after SCI. This notion is supported by the view that the sympathetic and parasympathetic systems do not always act reciprocally, but may also act synergistically and complementarily.

Regarding the frequency domain analysis, we saw a reduction in the LF bands. The HF band reflects the ventilator modulation of the RR intervals with the efferent impulses of the cardiac vagal nerve, and the LF band appears to be modulated by baroreflexes, with a combination of sympathetic and parasympathetic efferent nerve traffic to the sinoatrial node.[21] However, the exact physiological mechanisms of the vLF band are not precisely known. Some previous studies suggest that the vLF band reflects parasympathetic efferent pathway activity, whereas others suggest that it reflects thermoregulation or vasomotor activity.[22]

The decrease in the lower bands is interpreted as predominantly a consequence of sympathetic denervation, uninfluenced by the degree

of physical activity.[7] Even though it is at a low level, the SCI affects specific components of spontaneous blood pressure variability, such that it also affects the LF component of HRV and the baroreflex control of the heart, despite the intact cardiac baroreflex arc and the intact cardiac autonomic innervations. This could be because the autonomic dysfunction is not only due to the disruption of spinal cord communication but also because of the lifestyle adopted, reliance on the wheelchair, venous muscle pump impairment and muscle paralysis.

Further, although the HF band did not significantly differ between the groups, a trend toward a reduction in this band in the P group was observed. As a result, this decrease in all frequency bands is reflected in a significant reduction in the total power of the spectrum, similar to the findings obtained by Uhlir *et al.*[8] and Ditor *et al.*[23]

Regarding the nonlinear analysis, we obtained significant differences only in SD1 and SD2 but not in DFA1, DFA2 or sampen. DFA is a measure of roughness in the time series and predicts fatal cardiovascular events in various populations. Kleiger *et al.*[20] showed that values of $\alpha 1$ near 1 are considered normal. Both of our groups had values of $\alpha 1$ near 1 without differences between them. This could be because neither of the groups had a cardiac disease. With respect to $\alpha 2$, this fractal exponent is not recognized as useful for predicting cardiovascular risk.[20]

The Poincaré graph plots each R–R interval as a function of the next R–R interval. SD1 is considered the short-term beat-to-beat R–R variability from the Poincaré plot (width) and SD2 is the long-term beat-to-beat R–R variability (length). We found significantly lower values for both axes in P, compared with AB individuals. A greater dispersion of the scatter plot is associated with relaxation and a well-balanced autonomic nervous system, whereas a narrower dispersion indicates an imbalance with a predominance of sympathetic activity.[24]

To our knowledge, this is the first study that analyzes the HRV in the time domain, frequency domain and using nonlinear methods, classifies participants in AB and P groups. We conducted the experiment this way for two reasons. The first is that the results of previous studies that tried to establish differences between high- and low-level paraplegia did not find significant differences between levels.[13–15] This concurs with the results obtained from one of our secondary analyses. The other reason is because differences in HRV are not always due to altered or preserved autonomic function, but can be due to long-term use of a wheelchair and/or the lifestyle adopted. Daily activities performed by individuals with a thoracic-level SCI are similar, because they maintain motor function in the upper limbs, and therefore perform daily tasks in a similar way.

It is worthy to note that, for contrasting our secondary goal, in which we explored the possibility of differences between paraplegics who played some sports and who did not, we used a personal interview in which participants reported the number of hours per week they spent practicing their chosen sport. Although this is not an objective method to classify the level of activity and, even though the subdivision of the sample could lead to a risk of a power reduction, we thought that it could be worthwhile knowing whether the sport practice time might be important for improving HRV in this population.

Therefore, when we compared the HRV between P individuals who had an active lifestyle with those who did not, we found lower values in P individuals who were sedentary for DFA1, compared with P individuals who participate in sports. A previous study conducted by Zamunér *et al.*[12] also analyzed the differences in HRV between sedentary P, active P and AB individuals and did not find significant differences in most of the parameters analyzed. They only found a

significant reduction in the complexity of the R–R interval time series when comparing the sedentary P and AB groups. However, the small sample size used in both studies could account for the lack of significant differences. Further studies ought to enlarge the sample size to better understand the influence of the sport practice time on HRV in the P population.

Once the results of our study have been discussed, it is necessary to indicate that we conducted a large number of comparisons because we calculated lineal and nonlineal variables. This may have increased the risk of making a Type I error. Nevertheless we decided to present this large number of variables instead of selecting a reduced number of them because it could be interesting for the researchers in this field.

So far, most of the papers published on this topic have presented a small number of variables, reducing the possibility of making a Type I error but without providing some variables commonly used in other populations.[25] However, the variables reported in our study provided in Supplementary Material can be used by the researchers, allowing for use of more restrictive statistical analysis than those performed in our study (for example, Bonferroni or Holm Bonferroni).

Another limitation of the study is that we used a short-term recording of the HRV. Although 24-h recordings cannot completely be replaced by 15-min recordings, previous studies suggest that the short-term HRV is related to the long-term values.[26] The primary problem with using a short-term recording limits the validity of some parameters, such as entropy or vLF, which depend on a large number of data points.[27] However, using a short-term recording facilitates the use of these devices and protocols at a patient's annual checkup and could provide objective information about cardiovascular risk, to raise awareness of the importance of a healthy lifestyle.

Despite these limitations, the findings of this study could be potentially relevant. The data obtained from this study provide more information about HRV in individuals with P. It should be noted that although the P group in our study was more active in sports than the AB group, they had a lower HRV compared with the AB group, even without increasing their HR. Despite these comments, it is too premature to affirm that HRV is a useful tool to diagnose and prevent cardiovascular pathologies in the P population. Researchers in this field should focus on increasing the descriptive data and conducting prospective studies. Finally, we wish to recognize that sports practice could be important in improving health in the P population, although our data do not allow us to conclude that the HRV is completely influenced by this practice. It may be important to develop more intense sports programs to improve cardiac vagal tone,[28] which in turn produces a decrease in work and oxygen consumption of the heart and provides a survival advantage.

CONCLUSION
Heart rate variability is altered in P individuals, particularly if they lead a sedentary life. The results of this study encourage the use of HRV analysis to screen the risk for cardiovascular disease in this population and encourage the development of remedial actions to prevent further clinical complications.

DATA ARCHIVING
There were no data to deposit.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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Supplementary Information accompanies this paper on the Spinal Cord website (http://www.nature.com/sc)