Effects of compression stockings on sympathetic activity and heart rate variability in individuals with spinal cord injury

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Objective: To investigate whether wearing graduated compression stockings (GCS) could affect the sympatho-adrenergic and heart rate variability (HRV) responses at rest and after a strenuous wheelchair exercise in individuals with spinal cord injury (SCI).

Design: Crossover trial.

Setting: Department of Physical Medicine and Rehabilitation, Saint Etienne, France.

Participants: Nine men with SCI (five with low paraplegia: LP, four with high paraplegia: HP).

Interventions: Two maximal wheelchair exercise tests: with and without GCS (21 mmHg).

Main outcome measures: HRV measurements: high frequency (HF), low frequency (LF), and LF/HF ratio. Norepinephrine (NOR) and epinephrine (EPI), at rest and post-exercise. Secondary measures were: blood pressure, heart rate, maximal power output, oxygen uptake, stroke volume, cardiac output, at rest, during and after exercise.

Results: When wearing GCS: $LF_{nu_{wavelet-post}}$ significantly increased and $HF_{nu_{wavelet-post}}$ significantly decreased ($P < 0.05$) in SCI subjects, leading to an enhance ratio of $LF_{wavelet}/HF_{wavelet}$ and a significantly increased in NOR_{rest} ($P < 0.05$).

Conclusions: GCS induces an enhanced sympathetic activity in individuals with paraplegia, regardless of the level of the injury. Enhanced post-exercise sympathetic activity with GCS may help prevent orthostatic hypotension or post-exercise hypotension.

Keywords: Spinal cord injuries, Paraplegia, Wheelchair, Autonomic nervous system, Heart rate variability, Sympathetic nervous system, Catecholamines, Compression stockings

Introduction

The autonomic nervous system (ANS) is the part of the nervous system that is not under conscious control and regulates individual organ function and homeostasis. It is commonly divided into two usually antagonistic subsystems: the sympathetic and parasympathetic nervous systems. Heart rate variability (HRV) analysis can provide information about the cardiac sympathetic and parasympathetic nervous system (SNS) functions in patients, and provides a quantitative measure to discriminate the influences of these two autonomic

pathways on cardiovascular control.¹ Furthermore, the measurement of blood norepinephrine (NOR) can be used to estimate the SNS activity.² Indeed, the plasma level of free catecholamines, which modulate metabolic and cardiocirculatory reactions as well as adaptation to physical work, constitutes an indicator of sympatho-adrenergic activation with exercise.

Patients with spinal cord injury (SCI) are known to have autonomic ANS imbalance as a result of their spinal lesion.³ As a consequence, sympathetic autonomic activity markers such as HRV or catecholamines will be markedly altered.⁴⁻¹¹ The spinal cord lesion leads to an interruption of pathways from the brain to the peripheral SNS, which results in pathological changes in sympathetic innervation depending on the anatomical

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distribution.^{12,13} SNS dysfunction causes an inability to induce vasoconstriction in the legs and splanchnic area below the level of lesion, as well as a disruption of the catecholamine response. Thus, cardiovascular and metabolic alterations occur at rest and during exercise.¹⁴ The lack of sympathetic vasoconstriction below the lesion and the inability to activate the muscle pump in the legs lead to a disturbance in the redistribution of blood, resulting in venous blood pooling which probably causes a reduced filling pressure, a diminished end-diastolic ventricular volume, and a reduced stroke volume (SV).^{15–17}

Compression stockings are typically prescribed in SCI to prevent deep venous thrombosis or chronic venous insufficiency. Various authors have also explored the possibility of supporting the redistribution of blood in SCI during arm exercise to improve maximal exercise performance or to limit post-exercise hypotension and/or orthostatic hypotension,¹⁸ with anti-gravity garments^{19–22} and with graduated compression stockings (GCS).^{19–21,23}

It has been demonstrated that GCS improve venous hemodynamics. GCS work by increasing the ejection fraction, decreasing reflux and reducing the residual volume fraction, heightening the linear velocity of venous outflow, prevents stasis and venous distension, and enhances emptying of the valvular cusps.^{24–26} Rimaud *et al.* showed that 21 mmHg knee-length compression stockings prevent venous distension in individual with chronic SCI by significantly decreasing venous capacitance in individuals with low or high paraplegia who have a compromised ANS and may not be able to adjust their hemodynamics; and may be as valuable in flaccid as in spastic longstanding SCI. Finally, some investigators have observed an increased SV and cardiac output ($\dot{Q}$) during exercise with lower body positive pressure.^{16,19,21}

Whereas many studies have been conducted to evaluate catecholamine responses to exercise^{2,4,5,8,9} or HRV at rest in subjects with SCI,^{3,10,11,27} few have explored HRV responses to exercise,²⁸ and we have not found any that evaluated the effects of compression therapy on SNS activity.

We speculate that if GCS have an effect on vascular hemodynamic and cardiovascular function (i.e. application of GCS is supposed to shift the blood centrally to the heart, producing an increment in the preload and cardiac filling and then an increase in SV), it could have an impact on the SNS function. Since SNS dysfunction is one of the principal factors influencing orthostatic hypotension occurrence in SCI,¹⁸ this could have potential clinical relevance on the treatment of post-exercise hypotension and orthostatic hypotension

which affect SCI patients.^{18,29} Indeed, orthostatic hypotension is a frequent complication, very difficult to control, and severely impairs the quality of life of individuals with SCI. Also, the symptoms associated with acute hypotension significantly interfere with the rehabilitation of these patients. Orthostatic maneuvers performed during physiotherapy and mobilization are reported to induce blood pressure (BP) decreases, diagnostic of orthostatic hypotension in 74% of patients with SCI, and symptoms of orthostatic hypotension (such as lightheadedness or dizziness) in 59% of individuals with SCI.^{30,31}

From a medico-economic point of view, non-pharmacological management of orthostatic hypotension should be the first line of therapy.^{18,32} Then, the application of compression bandages and/or support stockings (i.e. by decreasing capacitance of the vasculature beds in the legs, which are the major area of blood pooling during standing)^{18,30} is a prevention therapy commonly prescribed, even if they can only partially control the symptoms associated with orthostatic hypotension.³²

The purpose of the present study was, therefore, to investigate if routinely prescribed GCS in SCI could affect sympatho-adrenergic activity and HRV at rest and after a strenuous wheelchair exercise in individuals with SCI. We also intended to measure changes in SV, $\dot{Q}$, total peripheral resistance (TPR), $\dot{V}O_{peak}$, BPs, and heart rate (HR) during and after a maximal wheelchair exercise test with GCS.

Methods

Subjects

Nine trained male subjects with traumatic SCI participated in the study (four high-level paraplegia (HP) with lesion above T6 and five low-level paraplegia (LP) with lesion below T6) (Table 1). All subjects were at least 2 years post-injury and underwent a clinical examination, which included a medical history and screening questionnaire, cardiac and pulmonary auscultation, as well as a neurological evaluation. None of the subjects had cardiovascular, pulmonary or metabolic diseases, or took any medications that could affect the study results. Eight of the subjects were well-trained individuals who competed regularly at the national or international level. All subjects gave written informed consent. The study was approved by the institutional Ethics Committee.

Experimental protocols

All subjects performed two maximal wheelchair exercise tests, using their personal wheelchairs. One test was done with and the other without GCS. The tests were assigned in random order following a counter-balanced

Table 1 Anthropometric and neurological characteristics of individuals with SCI

Patient	Age (years)	Weight (kg)	Height (cm)	Injury level	Lesion	Duration of lesion (years)	Trouble	Sport	Hours of training per week
1	31	63.5	179	T12	Complete	2	Flaccid	Swimming	6
2	33	75	184	T10	Complete	14	Spastic	Basket-ball	8
3	24	60	170	T12	Complete	4	Flaccid	Skiing	5
4	53	58	175	T12	Complete	34	Flaccid	Basketball	2
5	25	82	177	L1	Complete	9	Flaccid	Basketball	4
6	34	61	176	T4–T5	Complete	9	Flaccid	Racing	8
7	27	63	175	T4–T5	Complete	4	Spastic	Basketball	6
8	27	105	181	T5–T6	Complete	10	Spastic	Recreational activities	2
9	54	70	169	T5–T6	Complete	3	Flaccid	Recreational activities	2
Mean $\pm$ SD	34.2 $\pm$ 11.5	71.8 $\pm$ 15.8	176.2 $\pm$ 4.8			9.9 $\pm$ 9.9			4.8 $\pm$ 2.4

design, and were conducted at the same time of the day (11:00 a.m.), on the same day of the week, exactly 1 week apart. For all subjects, the last meal was taken 2 hours before the test. At least 4 hours prior to each test, the subjects refrained from taking caffeine, alcohol, or nicotine, and they were asked to avoid vigorous activity 24 hours before testing.

The progressive wheelchair test started with a 30-minute rest period on a wheelchair ergometer (VP100H-HEF Tecmachine, Andrezieux Boutheon, France)³³ to stabilize the various cardiorespiratory variables and to collect blood samples. Microfibers-2 tights with grip-top, graduated compression knee-length stockings (Olympique®, Tournier-Bottu S.A., Gibaud Products, Saint-Etienne, France) were used in this study. The stockings were knitted so as to create the greatest amount of elastic pressure at the ankle, and a gradual decrease in pressure up the lower leg. The pressure levels generated by the stockings varied between 21 mmHg (at the ankle) and 15 mmHg (at the top of the calf). They are available in small, medium, and large sizes, depending on the ankle, calf, and thigh circumferences of the subjects.

This was followed by a 6-minute warm up at a constant speed (comfortable speed) with no load. The load was then increased by 10 W increments for LP and 5 W increments for HP every 2 minutes until volitional exhaustion, or until the subjects were no longer able to maintain the required speed, despite strong verbal encouragement from the examiners. The highest load that could be maintained at a constant speed for 1 minute was taken as the $W_{\max}$. $\dot{V}O_{2\text{peak}}$ was determined as the highest $\dot{V}O_2$ recorded in a 30-second average. The two tests were performed at the same speed determined by the patient as their comfortable speed.

The test was followed by inactive recovery period: after the exercise, the subjects were instructed to rest on the wheelchair ergometer for 30 minutes.

Cardiovascular measurements

During the tests, $\dot{V}O_2$ and $\dot{V}CO_2$ (ml/minute/kg) were measured continuously by means of a metabolic analyzer (Medgraphics, TI CPX/D System, St Paul, MN, USA). The O_2 and CO_2 analyzers were calibrated with a known reference gas mixture before and after each session.

HR (beats/minute) was monitored continuously at rest, during exercise, and during the 30-minute recovery period by Holter monitoring (Vista, Novacor, Rueil-Malmaison, France).

Finger arterial blood pressure, SV, $\dot{Q}$, TPR, and BP, were monitored continuously by means of a Portapress (Portapress Model-2, TNO-TPD Biomedical Instrumentation, Amsterdam, The Netherlands). The plethysmographic cuff was placed around the middle phalanx of the finger, and the cuff pressure was modulated to maintain transmural pressure at an effective zero. This monitoring has proven to be a reliable beat-to-beat measurement of systolic blood pressure (SBP) in a wide variety of autonomic testing conditions when compared with intra-arterial monitoring.³⁴

HR variability

The ECG Holter recordings were analyzed on a Novacor system (UltimaHolter soft model, Rueil-Malmaison, France) equipped with a HRV module. To obtain the R–R interval, we determined the time when each QRS complex occurred by detection software. The quality of the electrocardiogram (ECG) recording and the accuracy of the computerized R-wave detection were verified by visual inspection of

the data, and the few erroneously detected R waves were removed manually. Ventricular and supraventricular ectopic beats and artifacts were removed. A R–R interval was interpreted as a premature beat if it deviated from the previously qualified interval value by more than a tolerance level of 30%. Next, a cubic spline was used to interpolate the irregular R–R series into a regular grid. It must be noted that cubic spline interpolating smoothed the R–R series and also the first derivative one.

Wavelet transform (WT): using a 5-minute window, the wavelet coefficients were calculated on sets of 256 R–R intervals giving seven separate levels of analysis named 2, 4, 8, ..., 128. Then, the variability power level by level was calculated as the sum of the squares of the coefficients. Thus, for each segment, the variability power for each level was obtained. The sum of wavelet-power coefficients at levels 2, 4, and 8 (HF_{wavelet}) approximately corresponds to the high frequency (HF) and is considered an index of parasympathetic activity. The wavelet-power coefficients at levels 16 and 32 (LF_{wavelet}) roughly correspond to the low frequency (LF). The wavelet-power coefficients at levels 64 and 128 (VLF_{wavelet}) correspond to the VLF. The $LF_{\text{wavelet}}/HF_{\text{wavelet}}$ ratio and the $LFnu_{\text{wavelet}}$ and the $HFnu_{\text{wavelet}}$ were also calculated.

$LFnu_{\text{wavelet}}$ and $HFnu_{\text{wavelet}}$ were calculated as $100 \times LF_{\text{wavelet}}$ and HF_{wavelet} divided by P_{tot} (total power)– VLF_{wavelet} . The $LF_{\text{wavelet}}/HF_{\text{wavelet}}$ ratio was also calculated. Overall, the VLF_{wavelet} represents parasympathetic activity, LF_{wavelet} and $LFnu_{\text{wavelet}}$ represent both sympathetic and parasympathetic activity, and HF_{wavelet} and $HFnu_{\text{wavelet}}$ represent parasympathetic activity.

Catecholamines

Blood samples (10 ml) were collected from the antecubital vein at rest and immediately after the exercise tests to measure NOR and epinephrine (EPI) concentrations. All venous samples were collected into heparinized tubes (Lithium Heparin 170 IU tubes, BD Vacutainer®, TX, USA) with sodium metabisulfite as antioxidant, and promptly placed on crushed ice until centrifugation at 4°C. The plasma was stored at –80°C until later analysis.

Catecholamines from 2 ml of plasma were extracted into 30 mg alumina acid (type WA-4) with 1.0 ml of Tris-HCl buffer pH 8.6, EDTA 2%, in 5 ml conical test tubes. 3,4-Di-hydroxybenzylamide (DHBA) was used as an internal standard to correct for absolute recovery variations in catecholamines. After washing three times with H₂O, the catecholamines were eluted into 200 µl of an acetic acid 0.3 M solution into

special microtubes (Microtube Ultrafree®, Millipore Corporation, Milford, CA, USA). Catecholamines in the eluates were then measured by high-performance liquid chromatography with electrochemical detection (Kontron Instruments, Zürich, Switzerland). Injections were realized on a reverse phase C-18 Waters Symmetry Shield® column (Milford, CA, USA), 150 mm × 3.9 mm ID, with a particle size of 5 µm. For calibration purposes, EPI, NOR, and DHBA standards (Sigma, St Louis, MO, USA) were treated in the same way as the samples. External Quality Controls (Lyphochek Endocrine Control) were purchased from Bio-Rad Laboratory (Pleasanton, CA, USA).

Statistical analysis

Values are given as means ± SD. The Wilcoxon's test for non-parametric paired random data (two-tailed test) was used to determine differences between the two tests with and without GCS for all parameters. The level of significance was set at $P < 0.05$. We tested the null hypothesis (H_0): no relationship between GCS and HRV, catecholamines, and all cardiovascular responses. The null hypothesis was rejected if GCS resulted in a significant difference in the study variable. Significance was set at $P < 0.05$.

Results

Cardiovascular responses

Cardiovascular responses to wheelchair maximal exercise are described in Table 2. No significant differences were seen in $\dot{V}O_{2\text{peak}}$, W_{max} , HR, or blood pressure, with GCS compared to without GCS in all groups.

HRV analysis

Statistical comparisons were made for HRV measurements with and without GCS (Table 3). Post-exercise HRV responses were evaluated from 3 to 8 minutes after the end of the maximal exercise.

Post-exercise normalized LF_{wavelet} ($LFnu_{\text{wavelet-post}}$) were significantly higher (+11%, $P < 0.05$) and post-exercise normalized HF_{wavelet} ($HFnu_{\text{wavelet-post}}$) were significantly lower (–27%, $P < 0.05$) with GCS.

Similarly, the ratio of $LF_{\text{wavelet}}/HF_{\text{wavelet}}$ tended to be higher at rest or post-exercise when wearing GCS (+44% at rest; +40% post-exercise, NS); and so did P_{tot} (+42% at rest; +26% post-exercise, NS), LF_{wavelet} (+55% at rest; +31% post-exercise, NS), HF_{wavelet} (+67% at rest, NS; no changes in post-exercise), although these differences failed to reach statistical significance.

Without GCS, patients with SCI exhibited, immediately after exercise, a statistically significant decrease in mean relative risk (RR) (–24%, $P < 0.0002$), P_{tot}

Table 2 Cardiovascular and catecholamine responses at rest and after wheelchair maximal exercise of subjects with SCI

		Without GCS	With GCS	Difference with/without (%)
VO _{2peak} (ml/minute/kg)		23.4 ± 7.4	22.4 ± 6.9	-4
W _{max} (W)		82 ± 33	82 ± 34	0
Lactates 3' post-exercise (mmol/l)		12.0 ± 5.1	11.3 ± 4.0	-6
HR (beat/minute)	Rest	78.5 ± 16.1	78.1 ± 14.9	-1
	Peak	175.8 ± 14.8	175.9 ± 17.8	0
SBP (mmHg)	Rest	136 ± 18	138 ± 25	+1
	Peak	123 ± 26	135.2 ± 24	+10
DBP (mmHg)	Rest	85 ± 16	87 ± 19	+2
	Peak	78 ± 18	81 ± 20	+4
SV (ml)	Rest	50.6 ± 12.2	58.8 ± 23.9	+16
	Peak	48.9 ± 17	46.5 ± 16	-5
Q (l/minute)	Rest	4.0 ± 1.7	4.5 ± 1.8	+13
	Peak	5.0 ± 2.0	4.6 ± 1.7	-8
TPR (MU)	Rest	1.5 ± 0.7	1.6 ± 0.8	+7
	Peak	1.3 ± 0.5	1.7 ± 1.4	+31
NOR (pg/ml)	Rest	382.8 ± 173.3	*493.4 ± 265.3	+29
	Peak	†1771.3 ± 1063.5	†2192.3 ± 1542.5	+24
EPI (pg/ml)	Rest	68.3 ± 39.6	67.0 ± 38.5	-2
	Peak	†209.7 ± 122.0	†273.3 ± 193.7	+30

Mean ± SD.

P* < 0.05: significantly different compared to without GCS.†*P* < 0.01: significantly different compared to rest.Table 3 Mean results of HRV measures**

		Without GCS	With GCS	Difference with/without (%)
Mean RR (milliseconds)	Rest	777.8 ± 140.4	768.7 ± 139.2	-1
	Post-exercise	†593.2 ± 87.3	†623.4 ± 143.4	+5
P _{tot} (millisecond ² /Hz)	Rest	3333.3 ± 2350.3	4734.4 ± 5083.7	+42
	Post-exercise	†576.8 ± 525.9	†725.3 ± 561.6	+26
VLF _{wavelet} (millisecond ² /Hz)	Rest	1328.6 ± 1067.3	1537.2 ± 1696.1	+16
	Post-exercise	†223.8 ± 167.6	†304.7 ± 190.5	+36
LF _{wavelet} (millisecond ² /Hz)	Rest	1283.1 ± 747.2	1988.5 ± 1870.7	+55
	Post-exercise	†230.9 ± 239.1	†301.6 ± 282.2	+31
HF _{wavelet} (millisecond ² /Hz)	Rest	721.7 ± 180.5	1207.8 ± 1767.1	+67
	Post-exercise	†122.1 ± 186.5	†119.0 ± 180.7	-3
LF _{nu} _{wavelet} (%)	Rest	68.7 ± 10.9	72.2 ± 14.8	+5
	Post-exercise	71.8 ± 15.4	*79.5 ± 10.2	+11
HF _{nu} _{wavelet} (%)	Rest	31.2 ± 10.8	27.8 ± 14.8	-11
	Post-exercise	28.2 ± 15.4	*20.5 ± 10.2	-27
LF _{wavelet} /HF _{wavelet} (%)	Rest	2.5 ± 1.1	3.6 ± 2.5	+44
	Post-exercise	3.5 ± 2.1	4.9 ± 2.9	+40

Mean ± SD.

**P* < 0.05: significantly different compared to without GCS.†*P* < 0.01: significantly different compared to rest.

(-83%, *P* < 0.004), LF_{wavelet} (-82%, *P* < 0.0007), and HF_{wavelet} (-83%, *P* < 0.04).

In the same way, with GCS, SCI patients exhibited, immediately after exercise, a statistically significant decrease in mean RR (-19%, *P* < 0.02), P_{tot} (-85%, *P* < 0.04), LF_{wavelet} (-85%, *P* < 0.02), and HF_{wavelet} (-90%, *P* < 0.02).

Catecholamine responses

NOR_{rest} was significantly higher (+29%, *P* < 0.05) with GCS than without (Table 2, Fig. 1). No significant differences were found in EPI_{rest} and EPI_{peak} with and

without GCS, even if EPI_{peak} with GCS was 30% higher than EPI_{peak} without (Table 2, Fig. 2).

EPI increased significantly with exercise (+207% without GCS, +308 with GCS, *P* < 0.01). In the same way, NOR increased significantly with exercise (+363% without GCS, +344% with GCS, *P* < 0.05).

Discussion

Our study showed an increase in sympathetic activity and a decrease in parasympathetic activity after a maximal exercise in individuals with SCI when wearing GCS as shown by the increase in LF_{nu}_{wavelet}

Figure 1 NOR responses to incremental exercise in subjects with SCI. * $P < 0.05$: significantly different between with and without GCS; † $P < 0.01$: peak significantly different compared to rest.

Figure 2 EPI responses to incremental exercise in subjects with SCI. † $P < 0.01$: peak significantly different compared to rest.

and decrease in HFnu_{wavelet} components. These results are further supported by an enhanced sympathetic activity at rest in SCI, as demonstrated by a significant increase in noradrenergic response when wearing GCS.

Sympathetic activity at rest

Results showed a significant increase in NOR_{rest} (+29%, $P < 0.05$) with GCS. This is linked with a consistent increase in SV during compression stockings application, which is thought to be a result of an increase in central blood volume. Then, application of GCS is

supposed to reduce the venous pooling in the lower limbs and to shift the blood centrally to the heart, producing an increment in the preload and cardiac filling and then an increase in SV, according to the Frank–Starling mechanism. We speculate that the consequence of this increase in the cardiac filling induced by GCS could be an increase in the myocardial wall stress. The myocardial mechanoreceptors, induced by increased cardiac filling, would be expected to produce a noradrenergic response (NOR) similar to that initiated at the beginning of the exercise.

Sympathetic activity after maximal exercise

Our study showed that post-exercise responses (i.e. in terms of catecholamines and HRV components) were different with or without compression stockings with regard to sympathetic activity.

The innervation of the adrenal medulla, the primary source of circulating EPI, derives from the T5–T9 spinal levels.⁸ Due to a very short half-life, the measurement of free plasma catecholamines reflects the current sympathetic activity, whereas the plasma level of NOR is more, the result of a spillover from sympathetic nerve endings than a release from the adrenal medulla. It is a direct reflection of impulse traffic within the nerve. An increase in free plasma EPI is a good evidence of adreno-medullary stimulation.^{12,13} The present study shows that our subjects with partially or completely intact adrenal medulla innervation were able to increase EPI and NOR during exercise; and this increase in sympathetic activity with exercise was enhanced when wearing GCS regardless of the level of the injury (even if the differences were not statistically significant).

The mechanisms through which GCS generates an increase in NOR and EPI remain unclear. Since spinal reflexes, driven by afferent signals from mechanoreceptors in contracting skeletal muscle or by an increase in sympathetic outflow in response to muscle acidosis, seem to play a role in the increase in plasma EPI in SCI,^{35,36} the occurrence of higher excretion of catecholamines with GCS in our study is possibly caused by the condition of spinal reflexes, uninhibited by supraspinal centers, in response to external compression stimuli on the lower limbs. Furthermore, metaboreflex, during dynamic supine leg exercise in healthy subjects, moderate muscle metaboreflex activation induced by the application of lower body positive pressure (LBPP) (35 mmHg), produced significant increases in NOR and EPI.³⁶ For Nishiyasu *et al.*³⁷ these results would support the idea that metaboreflex activated the efferent sympathetic pathways when LBPP was applied during dynamic exercise.

In addition, the likelihood of enhanced noradrenergic output driving the increase in sympathetic activity with GCS is further supported by our HRV findings.

The LF component of the spectral HRV gives a measure of the sympathetic activity, with some influence from vagal activity, and may be related to baroreflex activity, temperature regulation, and/or maintenance of homeostasis during various cardiovascular stresses.¹ The HF component is almost exclusively mediated by vagal activity, and is usually directly associated with respiratory activity. The LF/HF ratio has been used as an index of the sympathovagal balance of the heart, and reflects sympathetic modulation (a high ratio indicates greater sympathetic activity and a low ratio indicates greater parasympathetic activity).^{9–11,28} LFnu and HFnu represent the relative value of each power component in proportion to the total power minus the VLF_{wavelet} component. The representation of LFnu and HFnu emphasizes the controlled and balanced behavior of the two branches of the ANS. Moreover, the normalization tends to minimize the effect of the changes in total power on the value of LF and HF components.¹ An increased LFnu is observed during 90° tilt, standing, mental stress, and moderate exercise in healthy subjects, and during moderate hypotension and physical activity.¹

Our study shows an increase in sympathetic activity and a decrease in parasympathetic activity (i.e. withdrawal of vagal cardiac influences) after a maximal exercise in individuals with SCI wearing GCS, as shown by the increase in LFnu_{wavelet} (+11%, $P < 0.05$) and decrease in HFnu_{wavelet} (−27%, $P < 0.05$) components, which together tended to increase the LF_{wavelet}/HF_{wavelet} ratio, although this change failed to reach a statistical significance. The cessation of muscular activity after a maximal exercise leads to a reduced sympathetic outflow to skeletal muscle vascular beds, thereby increasing the pooling of blood in the lower body, in turn causing a decrease in blood volume in the central circulation and a consequent unloading of cardiopulmonary and arterial baroreceptors. The vasodilatation of peripheral vessels below the level of the spinal cord lesion cannot be counteracted because of impaired function of the sympathetic nervous system. This chain of events eventually leads to a decrease in central blood volume. Conversely, the use of GCS could lead to an increase in central blood volume by limiting the venous pooling caused by the SNS dysfunction and/or the lack of the muscle pump below the level of the spinal cord lesion. We speculate that this enhancement of central blood volume after exercise with GCS contributes to a persistent tonic sympathetic outflow.

Another possible explanation could be that the LFnu_{wavelet} and LFnu_{wavelet}/HFnu_{wavelet} increase may be caused in part by enhanced sympathetic activity, presumably due to the excitation of the isolated spinal SNS in response to the external stimulus from the periphery below the level of the lesion due to the GCS. Parasympathetic activation is considered to be the main mechanism underlying exponential cardio deceleration after exercise. The rate of decrease in heart beat frequency and the length of time to recovery after moderate to heavy exercise are commonly used as indicators of cardiovascular fitness.^{38,39} In able-bodied subjects, a decrease in sympathetic activity is desired after exercise. However, SCI, particularly lesions above T6, disrupt supraspinal control of the splanchnic bed (and thus to the major capacitance vessels) predisposing to orthostatic instability.

Then, as SCI leads to a disruption of the descending spinal cardiovascular pathways resulting in sympathetic hypoactivity; enhanced post-exercise sympathetic activity with GCS could help prevent orthostatic hypotension or post-exercise hypotension. Wearing compression stockings are often considered an optional treatment, after pharmacological treatment for the therapy of hypotension in patients with SCI. However, under specific conditions whose purpose is not the prevention of deep venous thrombosis or chronic venous insufficiency but to support the redistribution of blood at exercise, GCS have to be a first line of therapy. Indeed, our pilot study showed that wearing adapted compression stockings in terms of pressure and size (graduated custom-made stockings with 21 mmHg at the ankle) can be a substantial help to stimulate the sympathetic response in active SCI subjects after exercise or even during orthostatic challenge.

Finally, the absence of measurements of direct sympathetic function with muscle sympathetic activity was a major limitation of this study. Furthermore, this major finding of a marked increase in sympathetic activity must be confirmed by studies with a larger number of patients, which would lead to more homogeneous samples in terms of age, injury level, injury duration, spasticity, and physical activity level. This would lead to accurate comparisons between these patients' characteristics.

Conclusion

The present study is the first to evaluate the sympathetic activity responses to maximal exercise and compression stockings in individuals with SCI. Results showed that GCS induces an enhanced sympathetic activity in patients with SCI, as seen by the increase in NOR, EPI, LFnu_{wavelet}, HFnu_{wavelet}, HRV components, and

the $\text{LFnu}_{\text{wavelet}}/\text{HFnu}_{\text{wavelet}}$ ratio. This enhanced post-exercise sympathetic activity with GCS may help prevent orthostatic hypotension or post-exercise hypotension.

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