LOWER LIMB VOLUME IN HEALTHY SUBJECTS FOLLOWING WALKING WITH COMPRESSION STOCKINGS.

Short title: *Compression effect on leg volume and perceived exertion*

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ARTICLE HIGHLIGHTS

Type of Research: Single-center prospective crossover study.

Key Findings: Continuous aerobic exercise wearing below-knee 20-30 mmHg graduated compression stockings (GCS) leads to a significant lower limb volume decrease from 2466 (670) to 2276 (567) ml (P=.0001), and also to a significantly lower perceived exertion, whereas no significant volume change occurs without GCS.

Take home Message: Standardized continuous walk of 30 minutes in healthy subjects is associated with a significant lower limb volume reduction when applying 24 (2) mmHg GCS use. Wearing this type of compression is also associated with a significant decrease in the perceived exertion, potentially facilitating an even longer walking activity.

Table of Contents Summary

This prospective crossover study analysed the effect of GCS during continuous aerobic exercise on lower limb volume in healthy subjects.

The study suggests that a standardized continuous walk of 30 minutes is associated with a significant lower limb volume reduction together with lower perceived exertion following the use of certified GCS.

ABSTRACT

OBJECTIVE: Despite the modern appeal of wearing compressive garments during physical activities, the literature is lacking in quality data and controversial in the investigations dealing with the pathophysiological mechanism by which graduated elastic compression stockings (GCS) affect the calf pump activation in healthy subjects.

The aim of the present investigation is to provide insight on the clinical effects of GCS use during a standardized walking exercise.

METHODS: Twenty physically active healthy volunteers (mean age: 34±5 years; BMI: 22±2 kg/m^2) underwent lower limb ultrasound scanning in order to exclude vascular impairment.

All subjects performed a continuous aerobic exercise walking for 30 minutes on a treadmill, under cardiac monitoring, at 70% of individual estimated maximal heart rate according to Tanaka equation.

The study population performed the standardized walk without GCS (baseline) and at one week performed the same standardized walk wearing knee-length 20-30 mmHg GCS (compression).

Prior to and after the walk, all subjects underwent a lower limb volume assessment by truncated cone formula, and at the end of the exercise protocol a perceived exertion assessment by means of the validated Borg scale.

RESULTS: All subjects presented normal venous and arterial ultrasound examination. No significant postural defects were reported. Both legs were assessed in all the 20 subjects for a total of 40 cases with and 40 cases without GCS. In baseline group the lower limb volume changed from 2496 (770) ml before exercise to 2512 (805) 2526 ± 404 ml (P=.2597) following exercise. Compression group reported a significant lower limb volume change from 2466 (670) ml before exercise to 2276 (567) ml (P=.0001) following exercise.

Mean perceived exertion was 13 (11) and11 (1) in baseline and compression group , respectively (P=.0001).

The interface pressure exerted by the GCS was 24 (2) mmHg.

No complaints in terms of discomfort were reported by the subjects following the use of GCS.

CONCLUSIONS: In healthy subjects, GCS (24 (2) mmHg) use during a continuous standardized walk of 30 minutes is associated with a significant decrease in lower limb volume and a decrease in the perceived exertion. The mechanism by which GCS impart their effect during physical activity may involve improved muscle pump function and reductions in inflammatory pathways. Further study will need to validate the mechanisms of the function of GCS used during physical exercise.

Keywords

Stockings, compression, volume, exertion, aerobic exercise.

Conflict of interest No conflict of interest to declare. No funding was provided for this investigation. Graduate compression stockings were offered by MEDI GmbH & Co KG, Bayreuth - Germany.

INTRODUCTION

A recent review of the literature has underlined that graduated compression stockings (GCS) have scientific validity in the management of lower limb venous and lymphatics drainage impairment.[1] GCS use benefits have also been reported in healthy subjects involved in occupational activities that require prolonged standing,[2-3] in physiological conditions such as pregnancy,[4-5] and in individuals subjected to prolonged flights.[6]

Of significant interest, the use of stockings in the sport's world is rapidly increasing. However, there is a lack of evidence-based validity regarding the related impact on the physical performance and on the lower limb parameters variations.

Moreover, there is a disparity in performance between the use of commercially developed certified graduated compression products and stockings generally used during physical exercise or sport.[7]

The available literature is showing a positive effect of compression garments mainly on the delayed onset of muscle soreness, without reporting significant data regarding the required compression features in terms of pressure and stiffness.[8-9]

Importantly, studies published more than 70 years ago reported a significant decrease in ambulatory venous pressure by walking, suggesting the activation of the muscle pump improving lower limb drainage. With many decades spent in the use of GCS, no study reported the ideal duration and speed of a walk aimed to improve lower limb drainage, making the current indication of walking for an unspecified time based more on empiric observation rather than on scientific evidence.[10]

In a previous investigation of our group we analyzed the lower limb volume and perceived exertion variations in healthy subjects undergoing an intermittent walk without and with below-knee GCS of different pressure levels. The results showed that at least 23 mmHg were needed to significantly decrease the lower limb volume. To the contrary, 18 mmHg were associated with no significant variation of the lower limb volume, while subjects wearing sham stockings experienced a leg volume increase. Interestingly, only the group wearing 23 mmHg GCS reported a significant decrease in the perceived exertion.[11]

The purpose of the current study is to evaluate the effects of GCS on limb volume and perceived exertion during standardized exercise. We hypothesize that the use of GCS will reduce limb volume and perceived exertion during a controlled standardized walking exercise. The aim of the present investigation is to assess the lower limb volume variation and the perceived exertion after a standardized continuous walk of 30 minutes with and without below-knee GCS.

METHODS

Population

Twenty healthy volunteers, underwent lower limb ultrasound scanning in order to exclude arterial and venous vascular impairment, and weight bearing analysis to rule out postural defects potentially altering venous return.[12] The cohort was constituted by 10 female and 10 male with mean age 34 ± 5 years and BMI: 22±2 kg/m^2, all the subjects were defined physically active since they used to perform regular not sport professional physical activity at least 3 times per week, familiar with walking on a treadmill.

Inclusion criteria were:

1. Age from 18 to 75 years
2. BMI<35 kg/m^2

Exclusion criteria were:

1. Cardiac co-morbidity
2. Chronic Venous Disease
3. Lower limb arterial disease
4. Use of drugs affecting venous volume
5. Lymphedema
6. Previous varicose veins treatments
7. Moderate or severe biochemical alterations
8. Postural defects

Study protocol

In a room with controlled temperature ranging from 21° to 22°C and always between 3 pm and 5 pm, all the subjects walked continuously on a treadmill for 30 minutes, under heart frequency monitoring, at 70% of individual estimated maximal heart rate (208 – 0.7xAGE) according to the Tanaka equation.[13]

The study population performed the standardized walk without GCS (Baseline group) and at one week, at the same time of the day, the same subjects performed the same standardized walk wearing below knee 20-30 mmHg GCS (Compression group). Since we did not use custom-sized garments, in order to determine the correct GCS size all the subjects were measured with a centimeter tape at the ankle and calf level and as per manufacturer specification was assigned the most appropriate size (mediven plus 20-30 mmHg, MEDI GmbH & Co KG, Bayreuth - Germany). All individuals were instructed to wear comfortable athletic shoes for the examination and standardized walk, and the same shoe for the same individual as a participant for baseline group and compression group.

All the subjects were asked to report eventual discomfort associated with the use of GCS.

The protocol has been approved by the Institutional Review Board at the University of Ferrara, and all the subjects signed the informed consent (approval n°170476).

Outcome parameters

Prior to and after the walk, all subjects underwent a lower limb volume assessment by measuring the leg circumference with a centimeter tape starting immediately above the malleolar level and continuing measurements every 4 cm for 8 leg segments.[14]

Using an excel data base the leg volume was calculated by the mathematical truncated cone formula,[15] (Kuhnke formula: $V_{limb} = \Sigma X^2 / \pi$)[16] (Figure 1).

At the end of the exercise protocol a perceived exertion assessment by means of the original Borg scale was performed.

The rating of perceived exertion (RPE) scale is a validated assessment tool used in clinical practice to measure perceived exertion. RPE is a widely used and reliable indicator to monitor and guide exercise intensity. The scale allows individuals to subjectively rate their level of exertion during exercise, and it can be used as an indicator of impending fatigue.[17]

In RPE scale the verbal expressions are anchored to the correct positions on a visual scale. The original Borg scale starts at number 6 where the subject has no difficulty at all (perceived exertion: very, very light) and progresses through to number 20 where the effort is maximal (perceived exertion: very, very hard). [17-19] All the subjects were invited to give their personal score. The interface pressure values between the compression devices and the skin were measured in standing position right before and right after the exercise.

A pneumatic pressure transducer (Picopress Microlab Italia, Padua, Italy) connected to a pressure probe of 5 cm in diameter and < 1 mm in thickness filled with 2 mL of air during measurement, was attached on the ankle skin minimum girth point (B). The sensor was never positioned on a bony prominence.[20]

This device has been shown to provide accurate, linear, and reproducible measurements.[21]

Statistical Analysis

InStat GraphPad (GraphPad Software, Inc.La Jolla, CA 92037 USA) was used for statistical analysis. The data were expressed as median (IRQ). Kolmogorov-Smirnov test was used to assess the data distribution.

The differences between volume values, Borg scale, interface pressure were tested using nonparametric Wilcoxon matched-pairs test. Statistical significance was defined as $p < 0.05$.

RESULTS

All subjects presented normal venous and arterial ultrasound examination. No significant postural defects were reported. Both legs were assessed in all the 20 subjects for a total of 40 cases with and 40 cases without GCS. The started leg volume (measured before exercise) was 2496 (770) and 2466 (670) for baseline and compression group respectively, showing no statistically significant difference (p=7829). In baseline group the lower limb volume changed from 2496 (770) ml before exercise to 2512 (805) ml (P=.2597) following exercise. The compression reported a significant lower limb volume change from 2466 (670) ml before exercise to 2276 (567) ml (P=.0001) following exercise (Figure 2).

Mean perceived exertion was 13 (1) and 11 (1) in baseline and compression group, respectively (P=.0001) (Figure 3).

The interface pressure exerted by the GCS at prior to walk was 24 (2) mmHg, while following exercise the interface pressure measured in the same point was 24 (1) mmHg (P=.0831).

No complaints in terms of discomfort were reported by the subjects following the use of GCS.

DISCUSSION

The calf muscle pump activation is considered so beneficial in lower limb drainage, and has been defined as a "peripheral heart".[22]

The activity of walking has such potential in reducing the venous pressure that in the past a dedicated "walking venous pressure test" was used in lower limb drainage assessment. Nevertheless, despite some preliminary clinical data about the benefits for chronic venous disease patients walking for 50 minutes with 20-30 mmHg GCS,[23] to the best of our knowledge, no data are available in the literature regarding the effect of a standardized walk with and without GCS on healthy subjects lower limb drainage and perceived exertion.

The present investigation demonstrated that 30 minutes of a continuous standardized walk without GCS, was unable to significantly impact the reduction in lower limb volume value in healthy subjects. To the contrary, GCS exerting at least 24 (2) mmHg were able to significantly decrease lower limb volume. The use of the same GCS was also associated with a significant improvement in fatigue control during the physical exercise, by having decreased value of perceived exertion.

These data related to a continuous walk are in accordance with the one previously published regarding the lower limb volume variation and the perceived exertion reduction following the use of at least 23 mmHg below knee GCS after an intermittent walk.[11]

Compliance to a correctly prescribed GCS demonstrated to be high, with no uncomfortable feeling being reported by the users.

The interface pressure assessment in this study confirmed that the range values stated by the GCS manufacturer corresponded to the in vivo measurement.

Noteworthy is the fact that after the physical exercise, the GCS maintained their elastic properties and the interface pressure features, in compression group that demonstrated a significant decrease in lower limb volume.

Previous literature has showed that compression is usually not associated with causing a significant increase in the ejection fraction: 30.5 mmHg GCS were associated with a moderate non-significant improvement of the ejection fraction of 17%.[24]

Considering that the herein presented data show that 24 mmHg were able to significantly reduce the lower limb volume and the perceived exertion, an open question remains on the driving force responsible for the improved venous drainage. If we exclude the possibility of an improved muscle pump function, we could assume that GCS are able to improve the drainage by decreasing the deep veins calibre and not the superficial ones, according to the so called "compression paradox" described by Uhl.[25]

According to this theory, GCS are acting on the muscular-fascial structure of the leg, directly in contact with the deep veins that are consequently reduced in calibre, differently from the more superficial ones that are surrounded by loose subcutaneous tissue. Such hypothesis is in accordance with our data considering that the intramuscular pressure measured by Uhl significantly decreased when using 22 mmHg GCS.

A potential bias of the investigation is represented by the subjects having first the baseline walk and one week after the walk with GCS, thus eventually perceiving less exertion because more familiar with the specific physical activity. On the other hand, all the study population was composed by active individuals used to walk on a treadmill, so limiting the same possible bias.

Another potential limit of this investigation is the lack of a sham GCS use. At the same time, differently from a previous investigation of our group[11] in which we compared different subjects with different garments, in this specific case the same subject was tested in two different conditions (without and with compression). Adding a sham GCS in this scenario could have equally introduced a bias in the form of feeling the different compression level.

Further investigations should explore the biochemical impact of GCS during exercise, and correlate the clinical findings with biochemical and pathophysiological mechanisms in edema reduction and reduced exertion.

CONCLUSIONS

The present investigation offers the evidence-based demonstration that, in healthy subjects, a standardized continuous walk of 30-minutes while wearing 24 (2) mmHg GCS is associated with a significant lower limb volume reduction and with a significant decrease in the perceived exertion, so potentially facilitating an even longer walking activity.

This study's clinical evidence provides a foundation to assess GCS in physical activity and sports.

Current sports literature reports evidence showing a role for compressive garments delaying muscle soreness after exercise. The present data add the effect of a reduced perceived exertion following the use of certified GCS. Continued research in the mechanism of GCS effects on limb volume and exertion is needed to fully understand the beneficial affects of limb compression during activity.

References

1. Rabe E, Partsch H, Hafner J, Lattimer C, Mosti G, Neumann M, et al. Indications for medical compression stockings in venous and lymphatic disorders: An evidence-based consensus statement. *Phlebology* 2018;33:163-184.

2. Partsch H, Winiger J, Lun B. Compression stockings reduce occupational leg swelling. *Dermatol Surg* 2004;30: 737-43
3. Amsler F, Blättler W. Compression therapy for occupational leg symptoms and chronic venous disorders - a meta-analysis of randomised controlled trials. *Eur J Vasc Endovasc Surg* 2008; 35:366-72.
4. Nilsson L, Austrell C, Norgren L. Venous function during late pregnancy, the effect of elastic compression hosiery. *Vasa* 1992;21:203-5.
5. Gray G, Ash AK.A survey of pregnant women on the use of graduated elastic compression stockings on the antenatal ward. *J Obstet Gynaecol* 2006;26:424-8.
6. Clarke M, Hopewell S, Juszczak E, Eisinga A, Kjeldstrøm M. Compression stockings for preventing deep vein thrombosis in airline passengers. *Cochrane Database Syst Rev*. 2006:CD004002. Review.
7. Benigni JP. Compression and Sports. Veins and Lymphatics 2016; 5:5992.
8. Beliard S, Chauveau M, Moscatiello T, Cros F, Ecarnot F, Becker F. Compression garments and exercise: no influence of pressure applied. *J Sports Sci Med*. 201;14:75-83.
9. Engel FA, Holmberg HC, Sperlich B. Is There Evidence that Runners can Benefit from Wearing Compression Clothing? *Sports Med*. 2016;46:1939-1952.
10. Pollack AA, Taylor BE, Myers TT, Wood EH. The effect of exercise and body position on the venous pressure at the ankle in patients having venous valvular defects. *J Clin Invest.* 1949;28:559-63.
11. Gianesini S, Tessari M, Menegatti E, Spath P, Vannini ME, Occhionorelli S, et al. Comparison between the effects of 18- and 23-mmHg elastic stockings on leg volume and fatigue in golfers. *Int Angiol*. 2017;36:129-135.
12. Hartmann BR, Drews B, Kayser T. Physical therapy improves venous hemodynamics in cases of primary varicosity: results of a controlled study. *Angiology* 1997; 48:157-62

13. Tanaka H, Monahan KD, Seals DR. "Age-predicted maximal heart rate revisited". *J. Am. Coll. Cardiol*. 2001; **37** :153–6.

14. Mosti G, Cavezzi A, Partsch H, Urso S, Campana F. Adjustable Velcro Compression Devices are More Effective than Inelastic Bandages in Reducing Venous Edema in the Initial Treatment Phase: A Randomized Controlled Trial. *Eur J Vasc Endovasc Surg*. 2015;50:368-74.

15. Kaulesar Sukul DM, den Hoed PT, Johannes EJ, van Dolder R, Benda E. Direct and indirect methods for the quantification of leg volume: comparison between water displacement volumetry, the disk model method and the frustum sign model method, using the correlation coefficient and the limits of agreement. *J Biomed Eng.* 1993;15:477-80.

16. Kuhnke E. Volumenbestimmung aus umfangmessungen. *Folia Angiolica,* 1976, 24:224-32.

17. Dumke CL. Heath-related physical fitness testing and interpretation. In Riebe D editor. ACSM's: Guidelines for Exercise Testing and Prescription. 10th Ed. Philadelphia: Wolters Kluwer, 2017 p.83-84.

18. Borg G. Psychophysical scaling with applications in physical work and the perception of exertion. *Scand J Work Environ Health.* 1990;16 Suppl 1:55-8.

19. Chen MJ, Fan X, Moe ST. Criterion-related validity of the Borg ratings of perceived exertion scale in healthy individuals: a meta-analysis. *J Sports Sci.* 2002;20:873-99.

20. Partsch H, Clark M, Bassez S, Benigni JP, Becker F, Blazek V, et al. Measurement of lower leg compression in vivo: recommendations for the performance of measurements of interface pressure and stiffness: consensus statement. *Dermatol Surg*. 2006;32:224-32.

21. Partsch H, Mosti G. Comparison of three portable instruments to measure compression pressure. *Int Angiol* 2010;29:426e30.

22. Uhl JF, Gillot C. Anatomy of the veno-muscular pumps of the lower limb. *Phlebology*. 2015;30:180-93.

23. Carvalho CA, Lopes Pinto R, Guerreiro Godoy Mde F, Pereira de Godoy JM. Reduction of Pain and Edema of the Legs by Walking Wearing Elastic Stockings. *Int J Vasc Med*. 2015; 2015:648074.
24. Mosti G, Partsch H. is low compression pressure able to improve venous pumping function in patients with venous insufficiency? *Phlebology*. 2010;25:145-50.
25. Uhl JF, Benigni JP, Cornu-Thenard A, Fournier J, Blin E. Relationship between medical compression and intramuscular pressure as an explanation of a compression paradox. *Phlebology*. 2015;30:331-8.