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Volume control of the lower limb with graduated compression during different muscle pump activation conditions and the relation to limb circumference variation.

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Volume control of the lower limb with graduated compression during different muscle pump activation conditions and the relation to limb circumference variation.

Short title: Graduated compression in different postural condition.

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ARTICLE HIGHLIGHTS

Type of Research: Single-center prospective crossover study.

Key Findings:

In healthy individuals below-knee 16-20 mmHg graduated compression stockings (GCS) significantly reduce lower limb volume after 30 minutes of standardized walk (-4.4%), sitting (-4.8%) and standing (-4.6%). Bioimpedance analysis demonstrated a significant extracellular water reduction while walking with GCS ($p<0.017$). The interface pressure variation between ankle and calf values can become progressive rather than graduated based on the lower limb circumference variation.

Take home Message: 16-20 mmHg below knee graduated compression stockings significantly reduce healthy subjects lower limb volume after 30 minutes of sitting, standing or standardized walk. Different B-B1 circumferences variations influence the interface pressure gradient significantly.

Table of Contents Summary

This prospective crossover study demonstrates the lower limb volume reduction after 30 minutes of standing, sitting or walking while wearing below knee 16-20 mmHg graduated compression stockings.

Below-knee 16-20 mmHg can effectively control leg edema in standing, sitting and walking, with a major effect in sitting, and independently the leg shape geometry influence on the interface pressure profile.

ABSTRACT

BACKGROUND: Literature supports graduated compression stockings (GCS) use for leg edema. Nevertheless, there is a paucity of data on the GCS effect related to sitting, standing and walking on limb edema. Different limbs shapes data and their impact on GCS exerted pressure are lacking. This investigation provides evidence-based information on GCS effect on edema reduction and the limb circumference gradients impact on GCS pressure.

METHODS: Thirty healthy individuals (15M-15F, mean age 32±5 years) were included. All the subjects underwent lower limb volume (Kuhnke formula) measurement, before and after sitting for 30 minutes, wearing below-ankle non- compressive socks. The same assessment was repeated 7 days later, in the same subjects, but wearing a below-knee 16-20 mmHg GCS. At 7 days interval, one week with below-ankle non-compressive socks and one week with below-knee 16-20 mmHg GCS, all the subjects repeated the same protocol including standing and walking. Ten subjects underwent bioimpedance assessment (Biody Xpert II™) before and after sitting, standing and walking. In the same group, B and B1 interface pressure values were measured.

RESULTS: All 60 limbs completed the data collection. Sitting or walking, without GCS, led to no significant volume changes, while volume was decreased by the use of GCS (-4.8%, $p<0.00001$; - 4.4%,$p<0.00001$, respectively). Standing up, without GCS, led to an increase in volume (2.7%, $p<0.0001$), while limb volume was decreased (4.6%, $p<0.0001$) by use of GCS. Biompedance showed an extracellular water reduction only while walking with GCS (from 40.55±1.66% to 40.45±1.71%, $p<0.017$). Mean interface pressure was 19±5 mm Hg (B) and 16±5 mmHg (B1). The interface pressure variation from B to B1 was not homogenenous among participants (mean percentage variation of -13±25%, ranging from -54% to 16%). A negative linear trend between pressure variation and circumference percentage increase was found, the sub-analysis excluding the two outliers shows a strong negative linear correlation

(Pearson's coefficient: r=-0.96).

CONCLUSION: GCS lead to a significant limb volume reduction irrespective of limb position and muscle pump function. However, extracellular fluid is only mobilized during muscle contraction while walking with GCS. Interestingly, different lower limb circumferences variations influence the interface pressure gradient, indicating the importance of proper fitting of both B and B1 during prescription. These data provide a foundation to future investigations dealing with GCS effect on fluid mobilization and with limb geometry impact on compression performance.

Keywords

Compression, Volume, Bioimpededance, Edema.

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

GCS are classified according to the interface pressure exerted at the B point, which is defined as the ankle point of minimum girth.[1]

According to the international standards, in graduated hosiery the interface pressure should decrease while moving from the ankle toward the knee.[2]

Literature has already shown that, in vivo, this graduated gradient is not always present and that an inversion of the pressure profile can be found, presenting a higher pressure at the calf than at the ankle (so called progressive compression).[3-5]

Importantly, whenever properly prescribed, both graduated and progressive compression stockings have demonstrated to deliver a positive effect on the limb drainage, with the progressive ones even improving the ejection fraction compared to the graduated hosiery.

In 2002, Aryal et al. assessed the interface pressure in healthy subjects wearing 23-32 mmHg below knee GCS while lying supine and in standing. Data showed that the interface pressure values at the ankle and below the knee correspond to the ones declared by the manufacturer, but that in supine and even to a greater extent in the standing position, at the mid-calf, the interface pressure was higher than at the ankle: a phenomenon that is much more evident at the medial than at the lateral aspect of the leg.[7]

The finding of significant pressure variations along the leg based on the body position was confirmed by Liu et al research.[8] These investigations indicate how body postures may be one of the most important factors influencing the skin pressure profiles.

However, homogeneous data collection reporting eventual differences in compression performance in the sitting, standing, and walking position/activities are missing.

One of the few published reports on the topic is from De Godoy research group, and highlights how GCS generate oscillatory pressure profiles during walking, with larger pressures producing larger variations during muscle activity. Yet the investigation focused only on the walking scenario, without comparison with the standing and/or sitting position.[9]

An evaluation of the postural impact on GCS pressure profiles was performed by Wildin, assessing the same patient in the supine, sitting and standing positions. Only in the standing and in the supine positions were appropriate median pressure profiles obtained. In sitting, the flexed knee was associated with an interface pressure in excess of 28 mmHg at the popliteal level. Moreover, progressive rather than graduated pressure was reported in up to 70% of cases.[4]

To the best of our knowledge, no investigations have correlated the lower limb circumferences variations with interface pressure gradients along all of the different leg sectors, with a lack of data regarding the different performance of GCS on different limbs conformations.[10] Graduated compression stockings (GCS) represent a fundamental tool in the management of subjects affected by or at risk of lower limb edema.[11]

The present work is aimed at evaluating the effect on lower limb volume variation of 16-20 mmHg GCS in the sitting, standing, and walking positions/activities, both by volumetry and bioimpedance assessment.

Secondary endpoint is the correlation among the lower limb circumference variations and the related interface pressure values every 4 cm along the leg (defined circumferential sectors measured on the medial aspect of the leg).

METHODS

Thirty healthy individuals (15M-15F, mean age 32±5 years) were included in the study.

Inclusion criteria were age from 18 to 75 years, body mass index <35 kg/m^2.

Exclusion criteria were cardiac comorbidity (e.g. congestive heart failure, cardiomyopathy, coronary artery disease), chronic venous disease, lower limb arterial disease, use of drugs affecting venous volume (e.g. diuretics, antihypertensives), lymphedema, previous varicose vein treatments, moderate or severe biochemical alterations (e.g. diabetes mellitus, hypothyroidism), chronic kidney disease, sport professionals, and postural musculoskeletal defects.

All the subjects underwent lower limb ultrasound evaluation to exclude venous, arterial, and lymphatic impairment. Lymphatic disease exclusion was determined by clinical examination and by ultrasound scanning reporting absence of the following findings: dilated lymphatic collectors, thickened dermis, thickened and high-echoic subcutis, or reduced echo-contrast between the dermis and subcuticular fat. A weight-bearing analysis excluded significant postural defects potentially altering the limb drainage.[12]

All the subjects performed the following activity protocol, always in the same sequence, with each activity separated by a one week period:

a. Sitting for 30 minutes, wearing below-ankle non-compressive socks.

b. Sitting for 30 minutes, wearing GCS.

c. Standing still for 30 minutes, wearing below-ankle non-compressive socks.

d. Standing still for 30 minutes, wearing GCS.

e. Walking for 30 minutes at a standardized pace, wearing below-ankle non-compressive socks.

f. Walking for 30 minutes at a standardized pace, wearing GCS.

The standardized pace was performed on a treadmill, under heart frequency monitoring, at a speed related to the 70% of individual estimated maximal heart rate (208-0.7 x age) according to the Tanaka equation.[12] Each assessment was performed at 7 day intervals for all of the activities (a-f above).

GCS used was a below-knee 16-20 mmHg (Mediven Elegance, MEDI GmbH & Co KG, Bayreuth, Germany). The GCS were sized by one of the investigators (EM) at the enrollment visit. Measures were taken between 8 and 9 am, with the subject standing up barefoot, measuring the limb circumference at the ankle, at the largest point of the calf and the length from the ground to the knee. The male population received 10 III, 4 IV and 1 V GCS sizes, while the female population received 12 II and 3 III.

All of the tests were performed in the same room with controlled temperature set at 23 ºC, between 3 PM and 5 PM.

During the different activities, all of the subjects were instructed to always wear the same comfortable sport shoes and to report eventual discomfort associated with GCS use.

Before and after all of the above reported activities (a-f above), in all patients, lower limb volume was calculated by the mathematical truncated cone formula of Kuhnke ($V_{limb} = \sum X^2/\pi$) assessing the leg circumference with a centimeter tape (Gulick Anthropometric Tape, Alimed), starting from above the malleolar level all the way up to the knee every 4 cm, for a total of eight segments (sectors).[14,15]

Bioimpedance measurement (Biody Xpert II™) was performed before and after all of the above reported activities (a-f above) in 10 subjcets, the extracellular water rate was calculated according to the following formula: (extracellular water/extracellular + intracellular water)*100.

At the beginning of the first session wearing GCS, the same 10 volunteer underwent also interface pressure measurement at the B and B1 point (area at which the Achilles tendon changes into the calf muscles).[16]

The protocol and the informed consent were approved by the Institutional Ethics Committee at the University of Ferrara, all the individuals signed a proper informed consent.

Statistical analysis:

InStat GraphPad (GraphPad Software, Inc.La Jolla, CA 92037 USA) was used for statistical analysis. The data were expressed as mean ± standard deviation, or percentage. Kolmogorov-Smirnov test was used to assess the data distribution.

The differences between volume values in the different postural condition with and without GCS were performed using Student's t-test, Wilcoxon Signed-Ranks Testwhen appropriate. Pearson's correlation coefficient was used to calculate the linear correlation between interface pressure variation and leg circumference percentage increase. The difference among the baseline volume of each sessions and the volume reductions associated with GCS use were calculated using One-way ANOVA test for repeated measures.

Statistical significance was defined as $p < 0.05$.

RESULTS

All 60 limbs presented neither vascular nor postural alterations and completed the data collection.

Sitting or walking, without GCS, led to no significant volume changes (from 2534 ± 402 to 2547 ± 380 mL (0.5%) P=.333; from 2513 ± 406 to 2525 ± 413mL (0.4%) P=.096) respectively, while volume was significantly decreased by the use of GCS (from 2483 ± 400 to 2362 ± 406 mL (-4.8%) P<.00001) in the sitting, and (from 2469 ± 432 to 2361 ± 416 mL (- 4.4%) P<.00001) in the walking position/activity.

Standing up, without GCS, led to a significant increase in volume from 2493 ± 399 to 2561 ± 392 mL (2.7%, P<.0001), while limb volume was significantly decreased from 2497 ± 386 to 2381 ± 367 mL (4.6%, p<0.0001) by use of GCS during the standing position, (Table I).

The trend of the single cases of all the GCS sessions volume changes is reported in Figure 1.

The baseline lower limb volume showed no significant difference at the beginning of every session (P=.2541)No significant difference was reported in the volume reduction associated with GCS use in standing, sitting and walking (P=.6971).

Biompedance analysis showed a significant extracellular water reduction only while walking with GCS (from 40.55±1.66% to 40.45±1.71%, P<.017).

Mean interface pressure was 19±5 mm Hg (B) and 16±5 mmHg (B1).

The interface pressure variation from B to B1 was not homogeneous among participants (mean percentage variation of -13±25%, ranging from -54% to 16%).

Figure 2 shows a negative linear trend between pressure variation and circumference percentage increase. The sub-analysis excluding the two outliers shows a strong negative linear correlation (Pearson's coefficient: r=-0.96).

No complaints were reported after the GCS use in terms of discomfort.

DISCUSSION

The present work data demonstrated that without GCS lower limb oedema occurs after just 30 minutes in the standing position in normal healthy individuals, while during the same amount of time the phenomenon is not observed in neither the sitting or walking conditions.

Interestingly, in standing, sitting, and walking, application of 16-20 mmHg GCS are able to significantly reduce the lower limb volume, with the maximum effect been observed in the sitting position.

This finding is of particular importance considering that a recent Cochrane review pointed out the need of further data related to the use of non-pharmacological interventions for preventing venous drainage impairment in standing and sedentary workers.[17] In another published work from our group, the use of 20-30 mmHg below-knee GCS in healthy subjects showed a significant leg volume reduction by 7.7 and a decreased in perceived exertion after a 30 minutes standardized walk.[18]

Castilho et al. tested the effect of 20-30 mmHg GCS on 10 healthy runners, focusing on the air-plethysmographic parameters variation, showing a hemodynamic improvement. Also this investigation points out the importance of further research in the evaluation of the relationship between total limb volume, its different intra and extra-vascular components and the related eventual edema.[19]

In the herein presented study 16-20 mmHg GCS were used and the lower limb volume decreased by 4.4%, and with our previous work demonstrating a 7.7% volume reduction while wearing 20-30 mmHg GCS, suggest a dose-dependent mechanism between compression values and oedema reduction: a phenomenon in line with observed plethysmographic evidence of a dose-effect mechanism of compression on venous empyting.[20]

The clinical impact is not the endpoint of the herein reported investigation that is focused in providing new evidence in graduated compression mechanism and related impact on lower limb volume control. Yet, variations of few hundreds of milliliters in healthy leg volume have been associated with an improvement of the perceived exertion after 30 minutes of standardized walk.[18]

Previously published investigations demonstrated the possible utility of adequate compression in prolonged standing up and/or sitting workers with minimal supporting evidence, yet, to our knowledge, this is the first investigation assessing in the same subjects in homogenous conditions, the effects of GCS in the sitting, standing, and standardized walking position/activity.[21,22]

The herein reported study population showed a homogeneous trend in lower limb variation in the different conditions of sitting, standing and walking. A less homogeneous trend was reported in

an interesting paper by Goddard demonstrating that approximately two fifths of women experience substantial pooling in the calf region whenever in a dependent position.[23]
Apart the only female population, other significant differences characterize the Goddard investigation by the herein presented one: Goddard measured the pooling by air plethysmography focusing just on the calf part covered by the plethysmographer calf, while our investigation used lower limb volumetry by validated Kuhnke formula.[14] The different findings of the two studies highlight also the importance of future investigations focused on the different components of lower limb volume (intra vs extravascular compartment).
Interestingly this study shows a slightly more pronounced GCS effect on oedema formation in the sitting position. The rationale could be associated with the smaller hydrostatic column compared to the standing position, with consequent lower hydrostatic pressure to be counteracted by GCS.[24]
Yet no statistical significance was reached in the present study population, so making further wider data collection on the topic needed.
The investigation also confirms that high pressure values are not needed to control lower limb oedema formation.[25,26]
Bioimpedance represents a useful and still underused evaluation tool in lower limb oedema formation and GCS related control.[27,28] The herein reported data demonstrated that only after walking with GCS a significant decrease in extracellular fluid was reported, but not with standing or sitting while wearing GCS. The possible interpretation is that the combined effect of calf muscle pump activation and GCS is needed to generate a significant extracellular fluid movement. Indeed, lower limb volume change does not overlap with venous ejection.
Future research lines will have to clarify the relationship of lower limb volume and extracellular

fluid components in the determination of the total volumetry during different limb activities (i.e. sitting, standing, and walking).

Indeed, it can be hypothesized that in the sitting position GCS are acting more in the reduction of the venous volume component, so that the lower hydrostatic load facilitates their action.

However, while walking, GCS could maximize their massage effect on the extracellular space, so favouring extracellular fluid reabsorption, as indicated by the bioimpedance analysis. Further investigations are needed in order to clarify this interesting finding.

The interface pressure assessment in B and B1 demonstrated that the mean pressure values correspond to the ones declared by the manufacturer.

At the same time, a significant heterogeneity in the B-B1 pressure gradient was reported, ranging from -54% to 16%. Interestingly, a linear trend has been noticed between the interface pressure values and the leg circumferences, demonstrating that lower limb circumference variations can impact the GCS pressure gradient profiles.

These data point out the importance of a proper lower limb sizing including not just the ankle measurement but also the calf area and leg length, so to allow for a proper GCS prescription.

Moreover, such interface pressure variability urges future scientific data collection to always include the report of how much pressure is exerted by the specific GCS both in B and in B1.

Lack of this information in future data collection could represent the bias of analyzing different scenarios that are not reflecting homogenous conditions, and making data comparison difficult.

The importance of a better awareness and understanding of the interface pressure has been recently reported also in sport compression stockings showing how in vivo and ex vivo pressure profiles can present significant heterogeneity.[29]

This has been also confirmed by Lurie et al. showing the significant variability in B1 interface pressure with the use of different GCS brands;[30] similar differences among GCS brands were reported also by Ma et al.[31]

Importantly, from the results of this study, it would be imperative for future data analysis related to compression to report exactly what interface pressure is obtained on the specific patient, since different patients with different circumference variations between B and B1, wearing the same GCS could actually present different interface pressure values and gradients (i.e. graduated vs. progressive).

As previously reported in the literature,[3,4] the present investigation confirms that a significant number of patients presents with a progressive rather than graduated profile moving from the ankle up, while wearing a GCS. This finding doesn't diminish the value and efficacy of GCS in lower limb oedema control and drainage facilitation. Indeed, previous investigations have already shown that a progressive rather than graduated compression can be extremely beneficial in terms of oedema reduction[32] and calf ejection fraction.[6] These data support the notion that GCS are important in leg oedema reduction in a number of different postural positions and activities, and that further research is required to understand the mechanism of interstitial fluid (extracellular) mobilization induced by GCS while ambulating. Importantly, proper measurement of the limb is required to maximize the effect of GCS, and that limb circumference variations affect the interface pressure when measured during GCS wear at B and B1.

CONCLUSIONS

In conclusion, this investigation demonstrates that lower limb oedema is generated after just 30 minutes of standing position, and that 16-20 mmHg GCS are able to significantly reduce the

lower limb volume in the standing, as well as the sitting and walking conditions.
Walking with GCS is also associated with a significant decrease of the extracellular fluid, as demonstrated by a bioimpedance analysis.
The leg circumference variations is a fundamental parameter to be taken into consideration in GCS pressure profiles, with potential inversion of the gradient from graduated to progressive in a significant number of cases, based on the different limb sectors circumferences. Further research on the in vivo GCS performance and related fluids shifts is needed.

References

1. 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.
2. Lim CS, Davies A. Graduated compression stockings. CMAJ 2014 Jul 8; 186(10): E391–E398.
3. Byars EF, Hopkins GR, Tarnay n. Effectiveness of elastic stocking decompression. Arch Surg 1977; 112:335-9.
4. Wildin CJ, Hui AC, Esler CN, Gregg PJ. In vivo pressure profiles of thigh-length graduated compression stockings. Br J Surg 1988; 85:1228-33.13.
5. Coleridge Smith PD. Compression treatment: still incompletely understood. Phlebology 1999; 14:1-2.
6. Mosti G, Partsch H. Compression stockings with a negative pressure gradient have a more pronounced effect on venous pumping function than graduated elastic compression

stockings. Eur J Vasc Endovasc Surg 2011; 42:261e6.

7. K. Aryal, S. R. Dodds, R. Chukwulobelu. Effect of Posture on the Pressure Exerted by Below-Knee Class II Compression Stockings on Normal Subjects. Phlebology 2002; 17:32-35

8. Liu R, Kwok YL, Li Y, Lao TT, Zhang X, Dai XQ. Objective evaluation of skin pressure distribution of graduated elastic compression stockings. Dermatol Surg. 2005; 3:615-24.

9. de Godoy JM, Braile DM, Perez FB, Godoy Mde F. Effect of walking on pressure variations that occur at the interface between elastic stockings and the skin. Int Wound J. 2010; 7:191-3.

10. Partsch H. Compression therapy: clinical and experimental evidence. Ann Vasc Dis. 2012; 5:416-22.

11. 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.

12. Uhl JF, Chahim M, Allaert FA. Static foot disorders: a major risk factor for chronic venous disease? Phlebology. 2012; 27:13-8.

13. Tanaka H, Monahan KD, Seals DR. Age-predicted maximal heart rate revisited. J Am Coll Cardiol 2001;37:153-56.

14. Kuhnke E. Volumenbestimmung aus Umfangmessungen. Folia Angiolica 1976; 24:224-32.

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. Partsch H, Clark M, Bassex S, Benigni JP, Becker F, Blazek V, et al. Measurement of Lower Leg Compression In Vivo: Recommendations for the v of Measurements of Interface Pressure and Stiffness. Dermatol Surg 2006; 32:224–33
17. Robertson L, Yeoh SE, Kolbach DN. Non- pharmacological interventions for preventing venous insufficiency in a standing worker population. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD006345. DOI: 10.1002/14651858.CD006345.pub3.
18. Gianesini S, Mosti G, Sibilla MG, Maietti E, Raffetto JD, Diaz J, et al. Lower limb volume in healthy individuals after walking with compression stockings. J Vasc Surg Venous Lymphat Disord, 2019 ;7:557-561.
19. Castilho Junior OT, Dezotti NRA, Dalio MB, Joviliano EE, Piccinato CE. Effect of graduated compression stockings on venous lower limb hemodynamics in healthy amateur runners. J Vasc Surg Venous Lymphat Disord. 2018;6:83-89.
20. Lattimer CR, Kalodiki E, Kafeza M, Azzam M, Geroulakos G. Quantifying the degree graduated elastic compression stockings enhance venous emptying. Eur J Vasc Endovasc Surg. 2014;47:75-80.
21. Blazek C, Amsler F, Blaettler W, Keo HH, Baumgartner I, Willenberg T. Compression hosiery for occupational leg symptoms and leg volume: a randomized crossover trial in a cohort of hairdressers. Phlebology. 2013; 28:239-47.
22. Krijnen RM, de Boer EM, Adèr HJ, Osinga DS, Bruynzeel DP. Compression stockings and rubber floor mats: do they benefit workers with chronic venous insufficiency and a standing profession? J Occup Environ Med. 1997;39:889-94.

23. Goddard AA, Pierce CS, McLeod KJ. Reversal of lower limb edema by calf muscle pump stimulation. J Cardiopulm Rehabil Prev. 2008;28:174-9.

24. Groothuis JT, Poelkens F, Wouters CW, Kooijman M, Hopman MT. Leg intravenous pressure during head-up tilt. J Appl Physiol (1985). 2008; 105:811-5.

25. Partsch H, Damstra RJ, Mosti G. Dose finding for an optimal compression pressure to reduce chronic edema of the extremities. Int Angiol. 2011;30:527-33.

26. Partsch H, Winiger J, Lun B. Compression stockings reduce occupational leg swelling. Dermatol Surg. 2004;30:737-43

27. Pichonnaz C, Bassin JP, Currat D, Martin E, Jolles BM. Bioimpedance for oedema evaluation after total knee arthroplasty. Physiother Res Int. 2013;18:140-7.

28. Gaw R, Box R, Cornish B. Bioimpedance in the assessment of unilateral lymphedema of a limb: the optimal frequency. Lymphat Res Biol. 2011;9:93-9.

29. Reich-Schupke S, Surhoff S, Stücker M. Pressure profiles of sport compression stockings. J Dtsch Dermatol Ges. 2016;14:495-506.

30. Lurie F, Kistner R. Variability of interface pressure produced by ready-to-wear compression stockings. Phlebology. 2014;29:105-8.

31. Ma H, Blebea J, Malgor RD, Taubman KE. Variability in leg compression provided by gradient commercial stockings. J Vasc Surg Venous Lymphat Disord. 2015;3:431-437.

32. Mosti G, Partsch H. Occupational leg oedema is more reduced by antigraduated than by graduated stockings. Eur J Vasc Endovasc Surg. 2013;45:523-7.

Figure 1-PRINT

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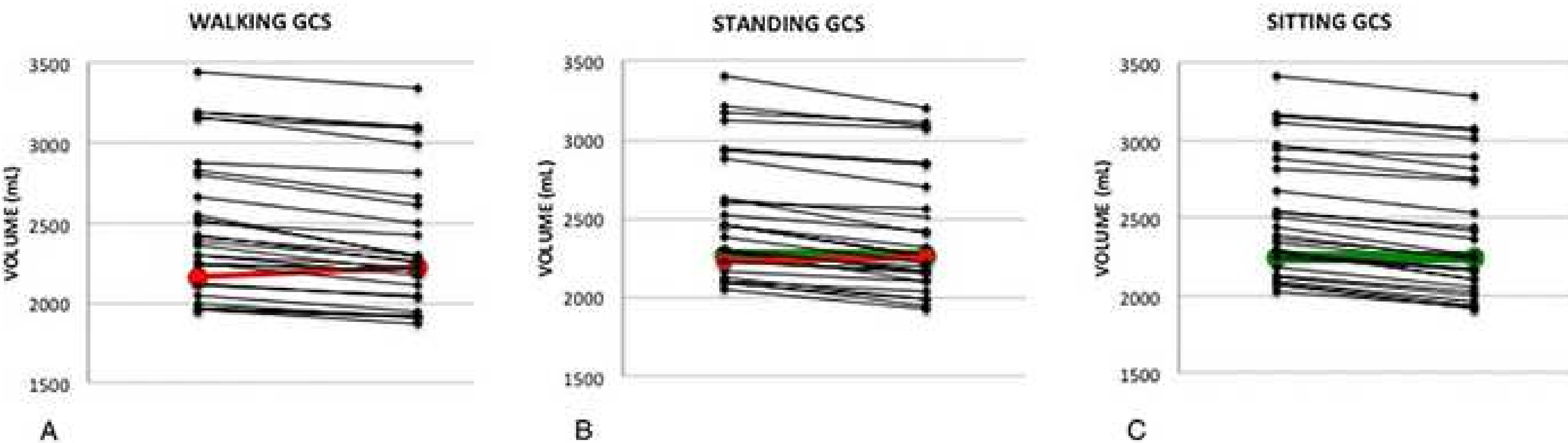

Figure 2-PRINT

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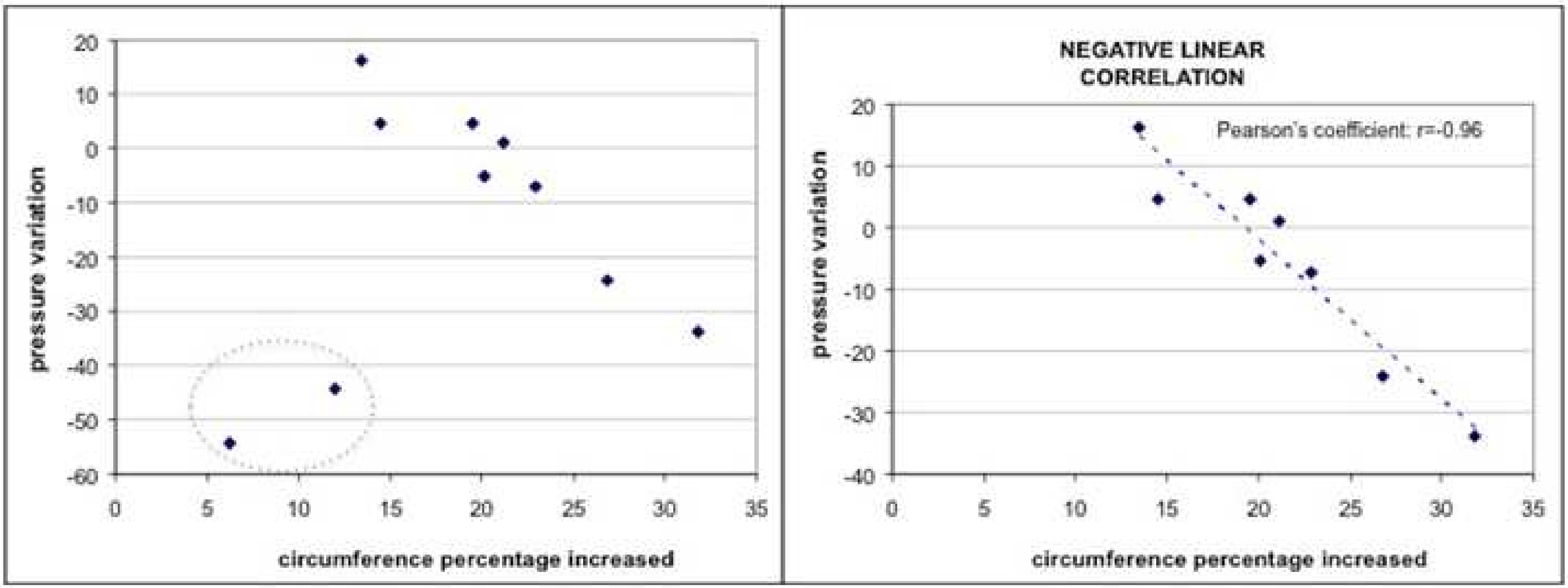

Table I.

	Limb Volume (mL) Pre Sampling (mean±SD)	Limb Volume (mL) Post Sampling (mean±SD)	Mean variation (mL) (95%CI)	Mean % variation	P value	
WALKING NO GCS	2513 ± 406	2525 ± 413	+10 (-2 – + 21)	0.4%	.096	—
WALKING GCS	2469 ± 432	2361 ± 416	-108 (-133 – -84)	- 4.4%	<.00001	↓
STANDING NO GCS	2493 ± 399	2561 ± 392	+68 (+45 – + 90)	2.7%	<.0001	↑
STANDING GCS	2497 ± 386	2381 ± 367	-116 (-139 - -93)	- 4.6%	<.0001	↓
SITTING NO GCS	2534 ± 402	2547 ± 380	+13 (-14 – +41)	0.5%	.333	—
SITTING GCS	2483 ± 400	2362 ± 406	-120 (-135 – -105)	- 4.8%	<.00001	↓

Figure/Table Legend:

Figure 1: The trend of the single cases of all GCS sessions volume changes. A) Single volume changes in walking with GCS. In red the single case showing an increased volume. B) Single volume changes in standing with GCS. In red the case showing an increased volume. In green the case showing no volume change. C) Single volume changes in sitting with GCS. In green the single case showing no volume changes.

Figure2: Negative linear trend between pressure variation and circumference percentage increase. The sub-analysis excluding the two outliers shows a strong negative linear correlation (Pearson's coefficient: r=-0.96).

Table I: Lower limb volume (mL) assessment by truncated cone formula (Kuhnke formula), pre and post exercise (walking) or postural condition (standing and sitting), with and without graduated compression stockings (GCS).