Original communication

Medical compression stockings on the skin moisture in patients with chronic venous disease

Thea Westphal[1], Wolfgang Konschake[1], Hermann Haase[1], Marcus Vollmer[2], Michael Jünger[1], and Helene Riebe[1]

[1] Department of Dermatology, University of Greifswald, Greifswald, Germany
[2] Department of Bioinformatics, University of Greifswald, Greifswald, Germany

Summary: *Background:* Because of side effects like skin dryness and consecutive symptoms like itching the therapy of chronic venous insufficiency (CVI) with medical compression stockings (MCS) can lead to a diminished wear comfort and restricted compliance. Compression stockings with integrated skin care may have a positive influence on the skin hydration and moreover a positive effect on patients compliance. *Patients and methods:* In this monocentric, randomized prospective, controlled trial a below knee conventional MCS was compared to a medical compression stocking with integrated skin care (MCS-SC), interface pressure range 23–32 mmHg. *Participants:* 50 patients with CVI. *Primary outcome:* skin hydration. *Secondary outcomes*: transepidermal water loss, skin roughness, leg volume, interface pressure and questionnaires about quality of life and wear comfort. *Results:* In patients wearing MCS the skin moisture decreased ($p = 0.021$) and the skin roughness increased significantly ($p = 0.001$), whereas in patients wearing the MCS-SC skin moisture and skin roughness changed only slightly (n.s.). These protective effects of MCS-SC compared to MCS were most common in patients with CVI at stage 3 ($p = 0.046$), in male patients ($p = 0.013$) and patients with initial dry skin ($p = 0.034$). Both MCS reduced lower leg volume, MCS by 80 ml ($p < 0.001$) and MCS-SC by 60 ml ($p < 0.001$), both MCS improved quality of life: leg complaints ($p = 0.0003$); functional status ($p = 0.010$), well-being and life satisfaction ($p = 0.030$). Wear comfort: In terms of tightness, constriction in bond area and strenuous donning the MCS-SC was assessed significantly more comfortable than MCS ($p < 0.001$). *Conclusions:* MCS-SC revealed to be superior to MCS with regard to skin moisture, particularly in patients with low skin humidity, in male patients and in patients with C3, varicose veins accompanied by edema.

Keywords: Chronic venous insufficiency, wear comfort, quality of life, compression therapy, integrated skin care, skin moisture

Introduction

Chronic venous insufficiency (CVI) is a widespread disease and shows high prevalence, especially in industrialized countries with an increasing number of elderly and overweight people [1]. Recent epidemiological data on the German population is obtained from the Bonn Vein Study [2]. Besides surgical procedures, endoluminal ablation and sclerotherapy, compression therapy is considered to be the most important conservative treatment of varicose veins and venous leg ulcers [1, 3]. Medical compression therapy is appropriate to reduce venous reflux and prevents the progression of CVI [4]. Complaints due to venous congestion are reduced by compression, especially in people working in standing position. Individuals working in a standing profession experience swellings, heaviness of the legs and various other disturbances. These symptoms can be alleviated by wearing low-strength medical compression stockings [5]. In addition, serious symptoms such as pain and non-reversible skin changes due to CVI can be prevented by regular application of compression stockings [6, 7]. Compression treatment achieves part of its effect by improving the function of the skin microcirculation [8]. However, the treatment by medical compression stockings can also cause undesired side effects like itchiness, sweating, skin dryness [9] with roughness and scaling [10–12]. Corneometry and TEWL-measurement are the most used and referenced technical methods to investigate the skin hydration and the water household in relation to the function of the skin barrier.

An efficient instrument to measure the hydration of the stratum corneum is the Corneometry. The *Corneometer® CM 825*, (Courage+Khazaka electronic GmbH, Cologne, Germany) is used for capacitance changes of a dielectric medium (stratum corneum), depending on its water content [13, 14]. As shown in previous studies the hydration

level of the skin can be divided in three groups (very dry skin with *Corneometer®* results below 30 AU, dry skin between 30 and 40 AU and normal skin more than 40 AU) [15].

The *Tewameter® MPS 580* (Courage+Khazaka electric GmbH, Cologne, Germany) is a sufficient instrument to measure the transepidermal waterloss. The TEWL can be influenced by external and environmental factors such as air temperature or humidity [16]. Low humidity, high air temperature and high sun exposure lead to an increased TEWL and generate chapped, rough and dry skin. Previous studies showed that patients aged 65 or older have a lower TEWL than younger patients (aged 18–64 years) [17]. One possible explanation is that increasing corneocyte surfaces cause increasing stratum corneum transit times for water in older people [17]. As pointed out by Mohammed et al. [18] skin areas with larger corneocytes are associated with lower TEWL-values. A further reason for decreased TEWL values in old age seems to be the reduced circulation of the aging skin [19]. Another influence on TEWL could be the thickness of the stratum corneum. As described in a previous study by Marks et al. [20] there is evidence that the stratum corneum's thickness decreases in aged individuals.

Skin changes under compression therapy such as skin roughness can be well measured with the *FOITS® Camera* (Fast optical in vivo topometry of human skin, AICON 3D Systems GmbH). The advantages are based on a high reproducibility and accuracy as well as the Fast 3 D image acquisition.

To improve wearing comfort side effects should be avoided. The present, prospective, clinical study was carried out to examine if skin desiccation is avoided by MCS with integrated skin care in patients with CVI.

Patients and methods

Study design

The prospective, randomized, controlled trial (RCT) was conducted and carried out at the Department of Dermatology at the University Medicine Greifswald, Germany. All investigations were carried out after written consent by the patient was given (ethic approval BB 025/17, 21.02.2017; German Clinical Trials Register-ID: DRKS 00012258). By using a parallel group comparison, half of the recruited patients received conventional medical compression stockings (MCS) and the other half received the medical compression stocking with an integrated skin care (MCS-SC). Skin hydration was considered as the primary outcome of the trial. Secondary outcomes are the skin barrier, transepidermal water loss (TEWL) and skin roughness. In addition, the wearing comfort and the effect of compression therapy in terms of volume reduction of the lower leg were determined. During the study period, additional skin care and shaving of the study leg were not allowed, only pH-neutral shower lotion was handed out to the patient for daily use. Wearing a compression stocking before the start of the study did not constitute an exclusion criterion.

Table I. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
Age 18–80 years	Age < 18 years
CEAP C_1–C_5	Non-compliance of the subject
Patients of both genders	Acute deep venous thrombosis
Written consent declaration	Peripheral arterial disease (anamnesis, clinical signs, palpation of pedal pulse)
German language skills	Diabetic neuropathy (anamnesis and clinical signs)
	Limited mobility
	Not signed consent
	Pregnancy
	Participation in another study
	Ulcus cruris venosum (CEAP C_6)

Participants

Patients of both genders with CVI (CEAP C_1–C_4) were included into the study. The diagnosis had to be confirmed by a recent duplex ultrasound. In addition, several inclusion and exclusion criteria were taken into account (Table I).

Study procedure

The study was performed between March and August 2017. A total of three visits took place: screening visit, visit 1 (day 0), visit 2 (day 28). The compression stocking had to be worn daily between visit 1 and visit 2 (28 days, 8 hours a day).

The screening visit took place in the mornings and included anamnesis, a clinical examination, checking for inclusion and exclusion criteria and determining the study leg. The severity of the CVI was determined via medical history and clinical examination, particularly inspection and palpation. Venous hemodynamics was measured by a duplex ultrasound. The patients were informed about the purpose and course of the study and written consent had to be given. Leg volume of each participant was determined by using *Bodytronic® 600* and the adequate size of the compression stockings was defined. The allocation of patients to the respective group (MCS/MCS-SC) was randomized.

Visit 1 took place in the afternoon on day of admission. The leg volume, skin moisture, transepidermal waterloss and skin roughness were measured. The compression stocking was handed to the subject and put on first time to measure the interface pressure. The compression stocking had to be worn for the rest of the day, at least 8 hours. The questionnaires on quality of life and wear comfort were explained and handed over by the principal investigator. A special laundry detergent, washing instructions and a pH-neutral shower lotion was given to the patient. Each patient received the same pH-neutral shower lotion to avoid falsification of results by additional care ingredients. Additional skin care (shower gel, body lotion, bath supplements) was not allowed to use.

Visit 2 after 28 days took place at the same time as visit 1 in the afternoon. The compression stockings were pulled off immediately before the measurement in the presence of the investigator. All examinations of the first visit were

repeated. The questionnaires were returned to the principal investigator and checked for completeness.

Patient compliance to wear compression stockings was evaluated by questionnaire. All patients wore the devices according fully to the study protocol, data not shown.

All examinations and measurements were carried out in temperature-controlled rooms. The optimal temperature was 20 °C and 40–60 % relative humidity. Before the measurements took place the patient had 10 to 20 min to acclimate in case the patient had exercised beforehand.

Compression materials

The medical compression stockings were distributed to two equally sized patient groups (n = 25).

MCS

Conventional medical compression stockings with an interface pressure 23 to 32 mmHg (Ccl 2), knee-high stocking (AD), *Venotrain® micro* (Bauerfeind AG, Zeulenroda, Germany).

MCS-SC

Medical compression stocking with integrated skincare substances, interface pressure 23 to 32 mmHg (Ccl 2), knee-high stocking (AD), *Venotrain® cocoon* (Bauerfeind AG, Zeulenroda, Germany). The lipophilic substances are applied to the skin throughout the time that the compression stocking is worn. The MCS-SC is made from cellulose and cotton on the inside of the compression stocking with maximum contact with the skin. The cellulose part of the fiber is loaded with the lipid skincare complex and is applied little by little to the skin when the compression stocking is worn.

Measurement of skin hydration

Skin hydration was measured with the *Corneometer® CM 825*, (Courage+Khazaka electronic GmbH, Cologne, Germany). It is made of two finger-type metal plates with an approximate measurement depth of 30 µm [13]. The measured values of the skin moisture are indicated in arbitrary units (AU) from 0 (no water at all) to 120 (water). The measurement was carried out at the lateral lower leg 15 cm close to the planta pedis, while the subject was in lying position. The exact location was marked to measure repeatedly in the same area. Constant room temperature was ensured at all measurement time points [15].

Measurement of transepidermal water loss (TEWL)

The *Tewameter® MPS 580* (Courage+Khazaka electric GmbH, Cologne, Germany) was used to identify the transepidermal water loss (TEWL). Transepidermal water loss is a physiological characteristic, which measures the efficiency of the skin barrier [21]. It is based on Fick's diffusion law indicating the amount of water evaporating and being transported in a defined area and time period. The values are given in $g/m^2/h$ [22].

Similarly to the skin moisture measurements, the measurements for TEWL were always carried out in the same place on the lateral lower part of the respective study leg 15 cm above the sole of the foot proximal the malleolus lateralis.

Measurement of skin roughness

Measurement of skin microstructures (profilometry, microtopography) was performed by means of the contact-free optical topometry measurement – *FOITS®* (Fast optical in vivo topometry of human skin, AICON 3D Systems GmbH). The measuring principle is based on a combination of a gray code and phase shift technique. The measurement system consists of a projection unit and a CCD camera. In the grey-shift method, several grids are projected sequentially with a different brightness distribution. In addition, only one grid is used in the phase shift technique, which is then projected repeatedly with various phase lengths. The addition of volumes above or below a set level results in a positive and negative volume in mm^3 (roughness parameters) [23]. Similarly to skin moisture measurements, the measurements were carried on the lateral lower part of the respective study leg 15 cm above the bottom of the foot.

Volume measurements

The *Bodytronic600®* (Bauerfeind AG, Zeulenroda, Germany) was used to measure leg volume. The subject stood on a slowly rotating platform, while a three-dimensional reconstruction of the legs was done by three-dimensional photography using infrared cameras. For error-free measurement the same level of lighting as well as a fixed position of the test subject was required [7].

Measurement of interface pressure

Interface pressure was measured using *Picopress®* (Microlab Elettronica, Ponto S. Nicolo, Italy). As previously described by Riebe et al. [24] the interface pressure of the compression stocking was determined in a standing position. By means of a special pressure sensor (air-filled silicone sensor) the interface pressure between the compression stocking and the skin was measured at the lateral lower leg 15 cm above the sole of the foot proximal the malleolus lateralis. The value was measured in mmHg.

Questionnaires

Quality of life and wearing comfort were recorded by means of questionnaires.

Wearing comfort

- The questionnaire to assess the wearing comfort was handed to the patients at visit 1 and the same

questionnaire at visit 2. The questionnaire included 34 items and was divided into three parts: Leg complaints (19 items), additional foot complaints (8 items) and 7 additional questions about wearing comfort. A variety of complaints were obtained: constrictions, tightness, cold and warm sensations, sweating, burning, tingling, itching, dry skin and slipping of the stocking.
- Answers to the questions could be given on a visual scale that was 10 cm long (0 = no complaints at all, 10 = very strong complaints).

Quality of life

- One questionnaire was given to evaluate CVI-related complaints before compression therapy at visit 1 and the same questionnaire at visit 2 to assess the change in CVI-related complaints under daily compression stocking therapy. The selection of different scales and related Items was based on the "Tübinger Questionnaire for measuring Quality of Life in patients with CVI (TLQ-CVI)" by Klyscz et al. [6].
- Part 1 of the questionnaire was related to leg complaints before/under compression therapy and contained 14 items such as tired legs, feeling of tension, pain while sitting/lying, heavy legs, feeling of numbness in den legs. Patients could answer the questions in six different ways equal to a score ranging from 0 (I didn't have these complaints till 5 (I had these complaints and suffered from them strongly.
- Part 2 of the questionnaire was about restrictions in everyday life due to venous suffering (functional status) before/under compression therapy and contained 9 items, such as long standing, climbing stairs, putting on shoes, walking, carrying and lifting of heavy weights. Answers could be given on a 10 cm VAS (0 = the complaints didn`t affect me at all; 10 = the complaints affected me very much).
- Part 3 asked questions on the satisfaction with the venous disease before/under compression therapy and contained 10 different items, such as physical condition, mood, stress, anxiousness and general well-being. Answers could be given on a visual analogue scale that was 10 cm long (0 = very dissatisfied, 10 = very satisfied).

Photo documentation

At the beginning and at the end of the wearing period (visit 1 and visit 2 after 28 days) a photograph of the study leg and a close-up of the test field on the lateral lower leg 15 cm above the sole of the foot were taken.

Statistical analysis

Previous knowledge from an unpublished study by M. Mayer (change of skin moisture under wearing stockings VM vs. VMB) was the basis for a power analysis to obtain the necessary sample size. In this study the skin hydration showed a group mean of –9.4 ± 7.5 (n = 25) for VM and –3.6 ± 5.4 (n = 25) for VMB. Using the R package "powerAnalysis", sample sizes were obtained at 5 % significance level and 80 % statistical power. N = 22 for both stocking arms were regarded as sufficient.

To adjust for drop outs, the group size was increased by three, so that the calculated group size was 25 for each group. We used the mean, standard deviation (SD) and the median as descriptive statistics and grouped boxplots illustrates the sample distributions (median, 25 % quantile, 75 % quantile, maximum, minimum). For all measures (Corneometry, TEWL, skin roughness, interface pressure, leg volume) the mean and the 95 %-confidence intervals were calculated at both measurement times at day 0 and day 28 for both groups (MCS and MCS-SC). Treatment effects of variables measured in the same patient at both visits were tested by a paired t-test with the hypothesis $\mu = 0$ within the same group. The difference between the groups (MCS and MCS-SC) was tested by Welch's t-test.

The randomization was done by a blocked randomization (R package "blockrand") with block sizes 2, 4, 6 and 8 such that the sums of the block sizes is equal to the sample size.

Results

Demography

A total of 50 subjects with CVI (CEAP C1–C4) were included in the study. All participants completed this study (no drop outs). Table II shows clinical stages of CVI, the gender distribution in the two groups (MCS or MCS-SC) as well as average age. The youngest participant was 22 and the oldest 78 years old.

Skin moisture

The following graph depicts trends and changes in skin hydration during the 28 day wearing phase (Figure 1).

The MCS-SC diminished the undesirable side effect of skin dehydration. Skin moisture decreased only slightly ($p = 0.057$) by 2.6 AU in patients with MCS-SC, whereas in patients with MCS skin moisture decreased significantly ($p = 0.021$) by 3.6 AU. Comparing the two groups, there is no significant difference ($p = 0.601$).

Skin moisture – subgroup analysis

1) Skin humidity: 13 out of 50 subjects (7 subjects with MCS, 6 subjects with MCS-SC) had low skin moisture initially (≤ 19 AU). Especially patients with low baseline moisture benefitted from MCS-SC and showed a significant increase in skin moisture compared to MCS ($p = 0.034$) (Figure 2).

2) Stages of CVI: Particularly patients with an advanced stage of CVI (C3-Varicose with edema) (n = 26) benefitted from MCS-SC and showed a significant increase in skin

Table II. Clinical characteristics.

Subjects	50
Gender	
Male	13 8 = MCS; 5 = MCS-SC
Female	37 17 = MCS; 20 = MCS-SC
Age (years)	
Median	49
Median range	22–78
CEAP – clinical classification	
C1	10
C2	12
C3	26
C4	2
C5	0

moisture compared to those C3-patients who wore the MCS (p = 0.046).

3) Gender: The study showed a significant impact of gender on skin moisture. Male participants (n = 13) (mean 19.9; SD 5.1) had a significantly drier skin than female participants (n = 37) (mean 24.6; SD 7.2) as an initial finding (p = 0.016). Male subjects who wore MCS-SC showed a significant increase in skin moisture compared to male subjects with MCS (p = 0.013).

Transepidermal water loss (TEWL)

The TEWL decreased equally for MCS (Δ -0.1) (p = 0.902) and MCS-SC (Δ -0.2) (p = 0.822). This result suggests that skin barrier function has improved in both groups. There was no significant difference between the groups (p = 0.804).

Skin roughness

Whereas skin roughness in patients with MCS increased significantly by 3.2 mm^3 (p = < 0.001), patients with MCS-SC showed only a slight increase by 1.0 mm^3 (p = 0.211) (Figure 3). There was no significant difference between the groups (p = 0.067).

Interface pressure

For both groups interface pressure was initially optimal (MCS 26.0 mmHg at visit 1; MCS-SC 24.8 mmHg at visit 1). At day 28, the interface pressure had decreased by 1.9 mmHg in MCS (p = 0.027) and by 3.2 mmHg in the MCS-SC (p = 0.002). The intended interface pressure range (23 to 32 mmHg) was still maintained by both medical compression stockings after the wearing of 28 days.

Leg volume

Both patient groups reduced their lower leg volume significantly (MCS −0.08 l (p = < 0.001) and MCS-SC −0.06 l (p = < 0.001). There was no significant difference between the groups (p = 0.361).

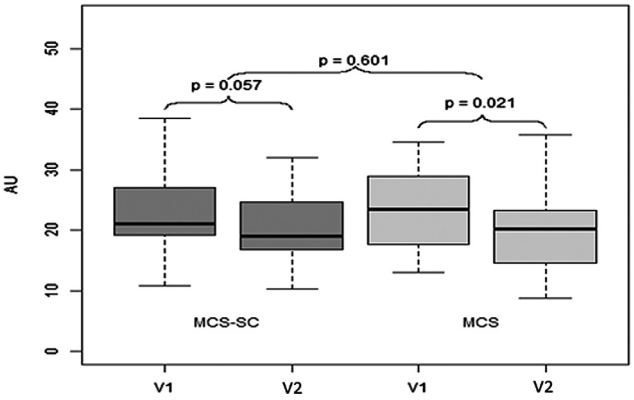

Figure 1. Skin moisture before and after the wearing period (V1, V2) for both stocking types, data in AU (Arbitrary units).

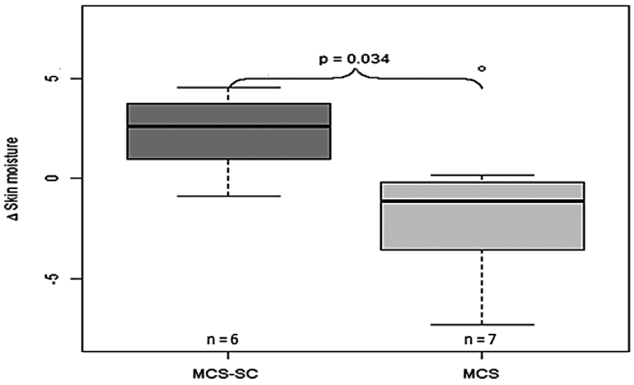

Figure 2. Patients with low baseline moisture benefitted from MCS-SC and showed a significant increase in skin moisture compared to MCS (p = 0.034).

Wear comfort

In terms of tightness, constriction in bond area and strenuous donning the MCS-SC was assessed significantly more comfortable than MCS (p < 0.001). Easier donning was associated with increased slipping down the MCS-SC. Furthermore, the tightening of the MCS-SC was significantly faster (p < 0.001).

The fit of MCS in the ankle area in terms of tightness, constriction and reduced mobility received a significant better rating compared to MCS-SC (p = 0.001).

Quality of life

The quality of life improved significantly under compression therapy with MCS and MCS-SC (Leg complaints: p < 0.001; functional status: p = 0.010; well-being and life satisfaction: p = 0.030). The quality of life was compared before and after compression therapy (day 28) (Figure 4).

Leg complaints under compression therapy with the MCS and MCS-SC have improved equally. There was no significant difference between the groups (p = 0.424).

The functional status improved slightly more with MCS compared to MCS-SC (n.s.).

Well-being and satisfaction under compression therapy with both stocking types have improved similarly. There

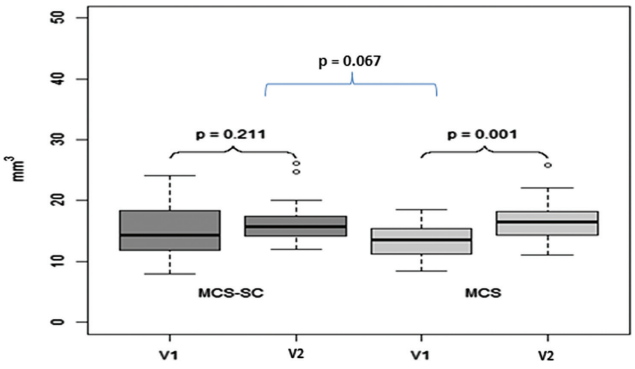

Figure 3. Skin roughness before (Visit 1) and after 28 days (Visit 2) for both groups. Skin roughness in patients with MCS-SC showed only a slight increase (p = 0.211) compared to patients with MCS skin roughness increased significantly (p = < 0.001). The Difference between MCS-SC and MCS did not reach significance (p = 0.067).

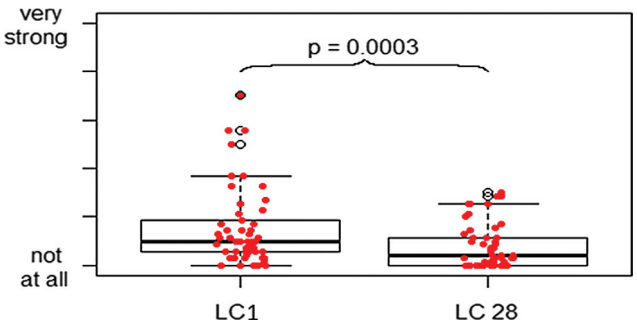

Figure 4. Significant improvement in leg complaints under compression therapy with MCS and MCS-SC (p = 0.0003). (0 = no leg complaints at all; 5 = very strong leg complaints). (LC 1 = leg complaints before compression therapy; LC 28 = leg complaints after 28 days of compression therapy).

was no significant difference between the groups (p = 0.447).

Discussion

The aim of the study was to determine the effect of integrated skin care in medical compression stockings compared to conventional compression stockings on skin humidity and wear comfort in patients with CVI. The primary outcome was skin moisture. Further, physiological changes of the skin such as TEWL and skin roughness were evaluated. Quality of life, adverse effects and wear comfort were also evaluated. All these aspects play a significant role in a long-term compression therapy and for patient's compliance. Previous work has shown that patients with chronic venous disease can benefit from compression stockings with integrated emollients [25]. Skin aging and the associated loss of function reduce the resilience of the skin, especially in the elderly. The skin is more sensitive and less resistant to external influences [26]. Therefore, in aging societies in industrial nations and a growing number of CVI patients, it is important to develop medical compression stockings with integrated skin care to reduce unwanted side effects and to improve quality of life, comfort and compliance.

The present study demonstrated an impairment of the skin hydration by wearing conventional compression stockings. A significant decrease in skin hydration, a significant increase in skin roughness and a non-significant decrease in TEWL over the 28-day period found for this group.

In comparison, for the group with integrated skin care in compression stockings (MCS-SC) skin barrier function was maintained. Skin moisture decreased slightly, and skin roughness showed only a small non-significant increase. These results confirm the hypothesis that conventional compression stockings can impact negatively on the skin barrier function and medical compression stockings with integrated skin care can keep barrier stable. According to the presented data, particularly male participants, subjects with initially low skin hydration as well as patients with advanced varicose and edema in stage CEAP C3 benefitted most from compression stockings with integrated skin care in terms of skin moisture.

Further the therapeutic effect was measured by volume and interface pressure. Both compression stockings had a diminishing impact on the volume of the lower limb. For both groups the edema was reduced.

Both medical compression stockings showed a slight decrease in interface pressure during 28 days, the intended interface pressure range (23 to 32 mmHg) however was maintained.

Regarding wear comfort, MCS-SC was assessed significantly better with regard to tightness, constriction in bond area and donning, easier and faster donning, however, was correlated with a tendency to slipping in the knee.

These are positive effects, especially for elderly persons and overweight immobile people with CVI, because the inability to apply stockings without help is one of the major reasons for irregular compression therapy.

The quality of life was significantly improved under compression therapy with MCS and MCS-SC. Both compression stockings have achieved comparatively good results. An advantage for the MCS-SC in terms of quality of life could not be shown in this study.

Limitations

Results of TEWL are strongly dependent on external factors such as sweating, skin surface temperature and room air temperature. An increase in air temperature leads to sweating, increase in skin surface temperature and TEWL [16]. These external factors cannot be completely eliminated by air-conditioning and lead to fluctuations in measurement results. Furthermore, both types of compression stockings were not tailor made. Instead standardized models were selected. This could have also influenced the results on wearing comfort for both types of stockings. Another limitation is the small number of patients (n = 50). Especially the exploratory results regarding the subgroups, which were not part of sample size calculations, are to be handled with caution underlining the need for

further studies. It has to be mentioned that our results are only valid for patients with CVI CEAP C1–C4, because no patient with CVI CEAP C5 could be recruited.

Conclusions

The results of the present study show that mainly male patients, patients with dry skin, patients with higher stages f the CVI (varices with edema) benefitted from the medical compression stocking with skin care fibers extracted from cellulose, cotton and lipid skincare complex. The quality of life improved the same as with the conventional MCS.

References

1. Reich-Schupke S, Murmann F, Altmeyer P, Stücker M, Compression therapy in elderly and overweight patients. Vasa. 2012;41:125–31.
2. Rabe E, Pannier-Fischer F, Bromen K, Schuldt K, Stang A, Poncar C, et al.Bonner Venenstudie der Deutschen Gesellschaft für Phlebologie. Phlebologie. 2003;32:1–14.
3. Stücker M, Link K, Reich-Schupke S, Altmeyer P, Doerler M, Compression and venous ulcers. Phlebology. 2013;28:68–72.
4. Pfisterer L, König G, Hecker M, Korff T, Pathogenesis of varicose veins-lessons from biomechanics. Vasa. 2014;43:88–99.
5. 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.
6. Klyscz T, Jünger M, Schanz S, Janz M, Rassner G, Kohnen R, Lebensqualität bei chronisch venöser Insuffizienz (CVI) Ergebnisse einer Untersuchung mit dem neu entwickelten Tübinger Fragebogen zur Messung der Lebensqualität von CVI-Patienten (TLQ-CVI). Der Hautarzt. 1998;49:372–81.
7. Blättler W, Thomae HJ, Amsler F, Venous leg symptoms in healthy subjects assessed during prolonged standing. J Vasc Surg. 2016;4:455–62.
8. Klyscz T, Galler S, Steins A, Züder D, Rassner G, Jünger M, The effect of compression therapy on the microcirculation of the skin in patients with chronic venous insufficiency (CVI). Der Hautarzt. 1997;48:806–11.
9. Reich-Schupke S, Murmann F, Altmeyer P, Stücker M, Quality of life and patients' view of compression therapy. Int Angiol. 2009;28:385.
10. Raju S, Hollis K, Neglen P, Use of compression stockings in chronic venous disease: patient compliance and efficacy. Ann Vasc Surg. 2007;21:790–95.
11. Riebe H, Konschake W, Haase H, Jünger M, Advantages and disadvantages of graduated and inverse graduated compression hosiery in patients with chronic venous insufficiency and healthy volunteers: A prospective, mono-centric, blinded, open randomized, controlled and cross-over trial. Phlebology. 2016;33:14–26.
12. Konschake W, Riebe H, Pediaditi P, Haase H, Jünger M, Lutze S, Compression in the treatment of chronic venous insufficiency: Efficacy depending on the length of the stocking. Clin Hemorheol Microcirc. 2016;64:425–34.
13. Alanen E, Nuutinen J, Nicklén K, Lahtinen T, Mönkkönen J, Measurement of hydration in the stratum corneum with the Moisture Meter and comparison with the Corneometer. Skin Res Technol. 2004;10:32–7.
14. Clarys P, Clijsen R, Taeymans J, Barel AO, Hydration measurements of the stratum corneum: comparison between the capacitance method (digital version of the Corneometer CM 825®) and the impedance method (Skicon-200EX®). Skin Res Technol. 2012;18:316–23.
15. Heinrich U, Koop U, Leneveu-Duchemin MC, Osterrieder K, Bielfeldt S, Chkarnat C, et al., Multicentre comparison of skin hydration in terms of physical-, physiological- and product-dependent parameters by the capacitive method (Corneometer CM 825). Int J Cosmetic Sci. 2003;25:45–53.
16. Barel AO, Clarys P, Study of the stratum corneum barrier function by transepidermal water loss measurements: comparison between two commercial instruments: evaporimeter® and Tewameter®. Skin Pharmacol Physiol. 1995;8:186–95.
17. Kottner J, Lichterfeld A, Blume-Peytavi U, Transepidermal water loss in young and aged healthy humans: a systematic review and meta-analysis. Arch Dermatol Res. 2013;305:315–23.
18. Mohammed D, Matts PJ, Hadgraft J, Lane ME, Variation of stratum corneum biophysical and molecular properties with anatomic site. The AAPS J. 2012;14:806–12.
19. Endo K, Suzuki N, Yoshida O, et al.The barrier component and the driving force component of transepidermal water loss and their application to skin irritant tests. Skin Res Technol. 2007;13:425–35.
20. Marks R, Measurement of biological ageing in human epidermis. BJDD. 1981;104:627–33.
21. Gardien KL, Baas DC, de Vet HC, Middelkoop E, Transepidermal water loss measured with the Tewameter TM300 in burn scars. Burns. 2016;42:1455–1462.
22. Camargo FB Jr, Gaspar LR, Maia Campos PM, Skin moisturizing effects of panthenol-based formulations. Int J Cosmetic Sci. 2011;62:361.
23. Piche E, Häfner HM, Hoffmann J, Jünger M, FOITS (fast optical in vivo topometry of human skin): new approaches to 3-D surface structures of human skin. Biomedizinische Technik. Biomed Eng. 2000;45:317–22.
24. Riebe H, Konschake W, Haase H, Jünger M, Interface pressure and venous drainage of two compression stocking types in healthy volunteers and in patients with hemodynamic disturbances of the legs. Clin Hemorheol Microcirc. 2015;61:175–83.
25. Proksch E, Fölster-Holst R, Jensen JM, Skin barrier function, epidermal proliferation and differentiation in eczema. J Dermatol Sci. 2006;43:159–69.
26. Proksch E, Altersspezifische Prinzipien der topischen TherapieAged-related principles of topical therapy. Der Hautarzt. 2014;65:192–96.

History
Submitted: 02.05.2019
Accepted after revision: 06.06.2019
Published online: 31.07.2019

Conflicts of interests
No conflicts of interest exist.

Funding
The authors received no financial support for authorship and/or publication of this article. Compression stockings and a measuring device was funded by Bauerfeind AG, Zeulenroda, Germany

Correspondence address
Prof. Dr. med. Michael Jünger
Department of Dermatology
University Medicine Greifswald
Ferdinand-Sauerbruchstraße 1
17475 Greifswald
Germany

michael.juenger@med.uni-greifswald.de

