

Multicomponent compression stockings in chronic venous leg ulcer treatment

A review of the current literature



Ann. Ital. Chir., 2017 88: 67-72
pii: S0003469X17026598

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The role of compression stockings in the treatment of chronic venous disease was amply demonstrated. Concerning patients with chronic venous leg ulcers (VLU), multi-layer bandage is the standard of care. Recently, multicomponent compression stocking (McCS) systems for VLUs treatment and healing nowadays have been proposed. The aim of this review is to describe and analyze current literature evidence regarding McCS used in VLUs treatment.

KEY WORDS: Compression therapy, Compression stockings, Venous leg ulcers

Introduction

Chronic venous leg ulcers (VLU) are a common manifestation of severe venous insufficiency of the lower limbs. Their overall prevalence ranges from 0.06% to 2% among general population¹, increasing to 0.6–3% among people aged over 60 years and to 5% of those aged over 80 years^{2,3}. Reported symptoms include pain, burning, heaviness, aching and itching. VLU promotes important functional and psychological consequences, including an increased risk of major comorbidities^{4,5}, a

decreased quality of life, a diminished mobility and consequently depression and other mood disorders^{5,6}. In addition, the economic costs for the care of patients with VLU is growing worldwide^{7,8}, raising up three times higher than for a patient with chronic venous insufficiency without ulcers⁹⁻¹¹. Although there are several methods of treatment, multilayer bandage (MLB) systems remain nowadays the gold standard, over single component bandage or short stretch bandage (SSB), though degrees and levels of evidence remain suboptimal¹³⁻¹⁶. Compression stockings (CSs) have been investigated in order to evaluate wound healing rate¹⁷⁻²⁰. These are formed by elastic material that wraps the affected leg. They may be available with open or closed toe, usually used below the knee. Compression degree commonly decreases from the ankle to the knee (graduated compression) and it is measured in mmHg. Compression stockings are available in different sizes to fit any type of leg.

Recently, multicomponent compression stocking (McCS) systems for VLUs treatment and healing have been proposed. McCS systems consist of two or more CSs specifically designed to work together, ensuring an accurate compression levels along the index leg and avoiding traumatic lesions of wound and skin. Their role in litera-

Pervenuto in Redazione Ottobre 2016. Accettato per la pubblicazione Dicembre 2016

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ture is currently marginal, although there are studies describing McCS types and comparing McCS *versus* MLB or *versus* other VLUs therapeutic systems.

The purpose of this review is to describe current scientific evidence concerning McCS used as VLUs treatment choice, considering McCS types, kinds of patients enrolled in studies and subjective and objective clinical outcomes.

Methods

Main international scientific databases (PubMed, EMBASE, Scopus) were consulted to find recruitable articles. Terms as “compression stockings”, “compression therapy”, “vein ulcers”, “multicomponent stockings”, “ulcer healing” were combined to form the first articles cluster. Only the articles regarding McCS were considered. Reference list of each article was used for further studies. The articles comparing McCS with any type of bandage or other treatment for VLUs were included. Articles using hand-made McCS, using McCS not for VLUs treatment, not assessing clinical outcomes (healing rate, patient compliance), not published on peer-review journals and with less than 20 patients were excluded. A web research was also conducted for tracing different types of McCS in commerce, through manufacturing companies sites view. Same terms used for the scientific databases research were also used in this step.

Results

Literature research identified 235 articles potentially recruited for analysis. After inclusion and exclusion cri-

teria selection, only 4 articles were included. Web research showed different McCS types actually in commerce (Table I).

McCS TYPES

Depending on the mutual position and role of stockings, it is possible to divide available McCS types into three main groups:

Type 1 - Single-compression systems : consisting of an inelastic under-stockings positioned under an elastic over-stocking.

Type 2 - Multi-compression overlapping systems : consisting of two or more different pressure stockings positioned one above the other.

Type 3 - Multi-compression non-overlapping systems : composed of two different pressure stockings, positioned one at ankle and one at calf, with a minimum overlapping area.

In type 1 McCS, the under-stocking ensures a good containment of ulcer medication, avoiding displacement and simultaneously offering an easy plan for over-stocking application. In type 2, the under-stocking produces a weak pressure (18-20 mmHg) that provides a continuous compression therapy also during the night, when it is sometimes recommended the removal of over-stocking. A particular type 2 McCS kit is equipped with three stockings: a non-elastic under-stocking support and two elastic over-stockings at increasing compression (18-24 mmHg + 30-40 mmHg). The rational of the type 3 McCS is to maintain a graduated compression, greater on the ankle and lower on the calf, or similar in both regions, through the application of two overlapping stockings for a short surface. In several cases, type 1 and

TABLE I - *McCS types*

Type	McCS trademark	Stocking system
1	Venotrain ® Ulcertec Bauerfeind AG (GER)	US + OS 34-39 mmHg or 40-46 mmHg
1	VenoFlow ® Creative Care (USA)	US + III o IV class OS
1	Mediven ulcer kit ® Medi GmbH (GER)	US + OS 40mmHg*
2	Ulcer X ® Sigvaris (CH)	US 15-20 mmHg + OS 23-32 mmHg
2	Multi-Layer Stocking System Carolon (USA)	US 15-20 mmHg + OS 30-40 mmHg o 40-50 mmHg
2	UlcerKit Pro ® GloriaMed (ITA)	US + OS 18mmHg or 24 mmHg + second OS 30-35 mmHg US + OS 18mmHg or 24 mmHg + second OS 35-40 mmHg
3	UlcerKit ® GloriaMed (ITA)	Ankle stocking class I – calf stocking class I Ankle stocking class II – calf stocking class I Ankle stocking class II – calf stocking class II

US: under-stocking OS: over-stocking * ankle pressure

type 2 McCS are dressed primarily wearing the understocking (non-elastic or lower-pressure stocking), and then the elastic overstocking. In some cases, the kit is provided with a tool that facilitates the sliding of the under on the overstocking, particularly in foot and heel regions. In some cases, stockings are equipped with a posterior zip for easy donning. In McCS type 3 it is recommended to wear first the higher stocking (calf), getting a flap of its caudal portion upwards to a height of 8 cm. The lower stocking (ankle) is worn immediately below the flap. Lowering the higher stocking flap you are allowing the overlapping of two stockings.

CURRENT LITERATURE EVIDENCES

Jünger and collaborators for the first time tested the efficacy of a type 1 McCS (Venotrain Ulcertec, Bauerfeind, Zeulenroda, Germany) versus a below-knee compression bandage (Roselastic 'S' 530, KOB, Wolfstein, Germany) in venous leg ulcers healing²¹. This prospective, multicenter, open-labeled, randomized trial enrolled 134 patients between 2000 and 2002 (ITT population: 121 patients) in order to highlight the healing rate of venous leg ulcers after 12 weeks of treatment. Secondary endpoints were healing time, patients and healthcare staff compliance and experiences with the two type of compression systems and the time spent for application. Subjective patients experiences were assessed using a questionnaire composed by items about adverse concomitant symptoms (constriction, pain, itching, restricted movement, ...) experienced during the daily use of McCS or bandage, evaluated by a four degrees scale (none, mild, moderate, severe). In case of multiple ulcers on the same leg, "target ulcer" was the largest. The average size of target ulcer was $562 \pm 788 \text{ mm}^2$ and $595 \pm 899 \text{ mm}^2$ in McCS and bandage group, respectively. One patient out of ten had diabetes and the mean duration of disease before enrollment was 116 ± 100 days in McCS group and 156 ± 120 days in the bandage group. In 90% of cases, patients were treated with compression therapy before the enrollment. Complete ulcer healing was achieved in 47.5% of patients with McCS and in 31.7% of patients wearing bandage (one-sided $p = .0129$ in favor of McCS). The average healing time was similar (46 ± 20 days for McCS, 46 ± 22 days for bandage), although in the McCS group the rate of healed patients increased significantly starting from the fourth week of therapy compared with the bandage. The benefits of McCS were also demonstrated by the questionnaire, in terms of decreased constriction, greater freedom of movement, decreased sweating under the dressing and itching. Health professionals (nurses) judgments on therapeutic compression effect were also in favor of the McCS (63% very satisfied with the McCS, 38% very satisfied with the bandage, $p = \text{ns}$). Finally, the time dedicated to application was significantly lower in the

McCS group than in the bandage group (5.4 ± 5.4 min vs 8.5 ± 6.5 minutes; $p < .001$).

Mariani et al. evaluated the efficacy of a type 1 McCS (Ulcer X Kit, Sigvaris Inc., Peachtree, USA) versus a SSB in 56 patients randomized into three Italian centres specialized in ulcers treatment²². This open-labelled trial excluded patients already underwent surgery and/or compression therapy for ulcers before randomization, previous acute deep thrombosis (DVT) and arterial insufficiency (considering as a rejection parameter a < 0.8 Ankle Brachial Index, ABI). Clinical endpoints were ulcer 4-months healing rate after randomization, number of outpatients' visits and their frequency during study period and time-needed to heal; subjective outcomes were assessed using a validated survey²³. After the study period, 96.2% of patients treated with McCS and 70% of those treated with the SSB had complete ulcer healing ($p = .011$), with no significant difference in healing time between groups, although the more ulcers were small ($< 6\text{-}7$ cm in diameter), the less was the healing time in McCS group than in the SSB (p not declared). The average outpatients' visits number in McCS group was lower (7.2 vs 9.1 times during the healing time, $p = \text{ns}$) and they were more delayed in time (8.2 vs 6.7 days between 2 consecutive visits, $p = .002$) compared with SSB group. Regarding the subjective survey, McCS produced less pain, less inhibition of normal daily activities and less discomfort during the day and asleep ($p < .05$). Dolibog and collaborators²⁴ randomized 147 patients in five homogeneous groups: intermittent pneumatic compression (IPC; group A), McCS type 1 (Ulcer X, Sigvaris, Gianzoni & Cie AG, Switzerland; group B), four-layers SSB (4LSSB; group C), two-layers SSB (2LSSB; group D) and Unna's boot (UB; group E). Digital planimetry using Gilman index was used to measure therapeutic improvements (ulcer surface, length and width, volume). Patient with diabetes, bilateral ulcers, cancer and peripheral nerve injury were excluded from the analysis. After two months of therapy, healing rates were 57.14%, 56.66%, 58.62%, 16.6% and 20% in group A, B, C, D and E respectively ($p = .03$ comparing A vs D, A vs E, B vs D, E vs B, C vs D and C vs E). These results were also confirmed by the analysis of the Gilman index and the percentage in ulcer size changes (48.11% A, 41.22% B, 49.02% C, 17.77% D, 20.48% E).

Ashby et al. published a randomized controlled trial (RCT) conducted in 34 centers in England and Northern Ireland between 2009 and 2012²⁵. 454 patients were included in the analysis, 230 allocated in the type 1 McCS group (intervention group) and 224 in the 4LB group (control group). The primary endpoint was healing time. Secondary endpoints were unmasked outcome assessment, unmasked measurement of time to healing of the reference leg, health-related quality of life, resource use, treatment modifications, adverse events and ulcer recurrence. Health-related quality of life were evaluated using the SF12 questionnaires (M and P parts), sub-

mitted every 3 months. Patients were followed for a period of 12 months. An economic analysis was conducted quarterly by compilation of the EQ-5D questionnaire. Authors did not record difference in ulcer healing rates between intervention and control group (71% vs 70%; HR 0.99, 95%CI 0.79-1.25, $p=.96$). Furthermore, no difference was seen in mental and physical component summary within 12 months of treatment, except for a higher physical component summary score in the McCS group at 3 months, suggesting better physical health. Economic analysis revealed a difference of about £300 between stocking and bandage annual cost (on average 1492.9 vs 1795.3 £ / year), mainly caused by the lower number of visits in the McCS group. Unfortunately, during the treatment period, 38% of patients in the McCS group and 28% of the bandage group ($p=.02$ between two groups) changed type in therapy into a treatment not included in the protocol trial. In most cases the change was due to uncomfortable compression (42% and 24% in the McCS and bandage group, respectively), and concerned mainly elderly patients and subjects with non-serious adverse events during treatment.

Discussion

Several meta-analyses demonstrated evidence in compression treatment for VLU: O'Meara et al. collected 48 RCTs reporting 59 comparisons between stockings/bandages and all kinds of treatment (compression or no compression) in patients with VLUs¹⁵. Table II shows main study results. Regarding the use of hosiery, selected studies included comparisons between CSs or tubular devices and bandage paste, SSB, two-component bandage systems and 4LB. Through data analysis, Authors concluded that CSs reported better results in terms of healing, reduction of painful symptoms and costs, compared to SSB. Remaining comparisons (stocking and bandages pastes, low compression stocking and SSB, stockings and two-component bandages, stockings and 4LB) did not show significant results, probably because RCTs were numerically too small. Mauck et al. showed similar results (compression over no compression, multicomponent systems over single component systems

and systems with an elastic component over those without elastic component) in a recent meta-analysis²⁶. Analyzing 12 RCTs comparing stockings and bandages, Authors demonstrated a pooled risk ratio (RR) for healing ulcer of 1.10 (95% CI, 0.94-1.28), with no difference between stocking and bandage. Also in this case CSs were demonstrated better than SSB (RR 1.33, 95% CI, 1.02-1.74) and not lower than the 4LB (RR 0.97, 95% CI 0.87-1.08) in ulcer healing rate. Low-quality evidence supported the effect of compression on ulcer recurrence, as well as Nelson and Bell-Syer demonstrated in a review²⁷. Amsler et al. collected 8 studies comparing CSs (multicomponent or non-multicomponent) and bandages²⁸, concluding that stockings were more effective than bandages in ulcer healing within 12-16 weeks of treatment (64.9% vs 46.5%, $p=.02$; OR 0.44, 95%CI 0.32-0.61, $p < .00001$). Although encouraging, the results of this systematic review were burdened by numerous limitations, most notably the frequent inadequacy of bandage application. Other methodological failures were identified by Mosti²⁹. He noted the following criticism:

- the pressure exerted by compression devices was often not declared;
- bandage usually was applied so loose, not reaching optimal under-pressure bandage;
- in some cases bandage was applied by patients or their relatives, increasing donning errors.

It is known that the optimal sub-pressure is achieved in approximately 40% of the bandage applications^{29,30} and that also a trained healthcare staff can apply bandage in a not adequate modality³⁰. Moreover, a not correctly bandage positioned is more prone to pressure drops over time, particularly in subjects with poor compliance and which maintain ankle and leg movements. Consequently, it is certain that pressure exerted by a CS is more effective than a low pressure exerted by a bandage donned in a wrong way, always keeping in mind that "any compression is always more effective than no compression"^{28,29}. Since compression bandages require specialized skills and a long period of practical learning, they must be applied in an optimal manner in order to be compared with other methods (CSs or McCS) and parameters (sub-bandage pressure). Regarding the articles proposed in this

TABLE II - Results by O'Meara et al.¹⁰

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- Healing outcomes (including time to healing) are better when patients receive compression compared with no compression
 - Single-component compression bandage systems are less effective than multi-component compression
 - A two-component system containing an elastic bandage healed more ulcers at one year than one without an elastic component
 - Three-component systems containing an elastic component healed more ulcers than those without elastic
 - There is a significantly faster healing with 4LB than SSB
 - High-compression stockings are associated with better healing outcomes than SSB
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4LB: four-layer bandage SSB: short stretch bandage

review, they maintain the same limits already highlighted. Only two articles possess data about pressure exerted by the applied bandage^{23,24}, and only in one²⁴ it is explained that it was measured. It is not possible to compare these studies because types of patients, type of McCS, ulcer size and protocols of treatment are too heterogeneous. Results obtained by Ashby et al.²⁵ concerning treatment exchange suggest that CSs may be less comfortable than bandage. No other study investigates this particular item although other Authors highlighted less pain, less discomfort and less inhibition of everyday activities in McCS group²². Also in this case, questionnaires used for subjective evaluation are too different.

Conclusions

McCSs are a viable alternative in compression therapy of venous leg ulcers in selected patients. Their effectiveness was evaluated similar or better to the multi-layer bandaging in healing rate and healing time. However, few studies with excessive limitations and bias investigated this comparison. It is recommended that future studies may show homogeneous methods and better clinical and subjective outcomes than current literature.

Riassunto

Le ulcere flebopatiche degli arti inferiori (VLUs) sono una grave complicanza della malattia venosa cronica. La loro presenza non solo aumenta la mortalità, ma diminuisce drasticamente la qualità della vita. Il bendaggio multistrato (SSB) si è dimostrato ad oggi la tecnica terapeutica migliore, benché sia gravato da diversi limiti, come la graduale diminuzione della sua forza elastica e la bassa compliance del paziente. Le calze terapeutiche a pressione graduata hanno raggiunto un ruolo importante negli stadi minori della malattia venosa cronica (CEAP 1-3), sebbene il loro ruolo in presenza di VLUs sia ancora marginale. Negli ultimi anni sono state proposte per la cura delle ulcere flebostatiche, sistemi di calza multistrato (McCS). Queste sono composte da 2 o più calze a pressione differente che vengono sovrapposte tra loro in maniera completa (Tipo 1 e 2) o parziale (Tipo 3). Sebbene già sul mercato da diversi anni, sono pochi gli studi in letteratura che comparano le McCS alle altre metodiche terapeutiche, prime fra tutte il SSB. Una ricerca condotta sulle maggiori banche dati scientifiche internazionali, ha selezionato solamente 4 articoli riguardanti il confronto accennato in precedenza. Questi, nella maggior parte dei casi, dimostrano una non inferiorità delle McCS rispetto al SSB. Nel valutare la compliance e la qualità di vita del paziente durante la terapia, i risultati, sebbene talvolta contraddittori, documentano una maggiore vestibilità e un minor fastidio nei pazienti portatori di McCS. Malgrado i risultati incoraggianti, gli

studi selezionati posseggono diversi limiti, che rendono il confronto e l'analisi molto difficoltosa. Le McCS rimangono una valida alternativa nella terapia compressiva delle ulcere venose degli arti inferiori in pazienti selezionati, benché sia necessario confermare i risultati ottenuti con studi randomizzati controllati futuri, che facciano riferimento a standard clinici e terapeutici omogenei e riproducibili.

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