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ORIGINAL ARTICLE

Efficacy and tolerability of an ulcer compression stocking for therapy of chronic venous ulcer compared with a below-knee compression bandage: results from a prospective, randomized, multicentre trial

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SUMMARY

Objective: To investigate the possibility of improving healing rates in ulcus cruris venosum by using an ulcer compression stocking (U-Stocking) (Venotrain* ulcertec) as compared to compression bandages.

Research design and setting: Prospective, multicentre, open-labelled, randomized, active-controlled study with blinded assessment of the primary endpoint. Sixteen phlebology outpatient clinics in Germany or the Netherlands or German medical practices specialized in phlebology.

Patients and methods: 134 patients with venous leg ulcers entered the study. Among others, patients with infected ulcer or obesity were excluded. 121 patients were eligible for primary efficacy analyses. U-Stocking or bandages applied for at least eight hours per day and for up to 12 weeks. The primary endpoint was the healing rate after 12 weeks as assessed by planimetric measures. The secondary outcome variables were time to healing, changes in ulcer size (planimetry), experience of use and patient compliance.

Main outcome measures: Therapy with the U-Stocking produced a significantly higher rate of complete healing of 47.5% (29/61) versus 31.7% (19/60) with bandages, 1-sided $p = 0.0129$ [CI: 95% for differences: 4.3% to 28.5%]. Mean time to healing was 46 days in both groups.

* Venotrain is a registered trade name of Bauerfeind Phlebologie GmbH & Co. KG, Zeulenroda, Germany

Time required for application of the U-Stocking was a mean of 5.4 min (SD 5.4) versus 8.5 minutes (SD 6.5) for bandages, $p = 0.0001$. Around three patients in each treatment group were affected by serious adverse events. All treatment-related adverse events are known for compression therapy.

Conclusions: The U-Stocking was superior to bandages in compression therapy for venous ulcer. This is of significance to new treatment standards as well as to future studies of longer term therapy (> 12 weeks) for unhealed ulcers or prevention of recurrence.

Introduction

In 45 to 60% of cases ulcerations of the lower extremities are of venous origin[1]. Open or unhealed venous leg ulcers are prevalent in approx 1% of the adult population[2]. The recurrence rate in the first year following successful compression therapy is high, at 26%[3]. The aim of therapy when treating venous leg ulcers is to reduce the pressure overload in the vascular system. Compression therapy is therefore regarded as a basic approach which is combined, if necessary, with other measures[4]. These can be further physical measures, vascular surgery, sclerotherapy to eliminate epifascial veins, adjuvant systemic pharmacotherapy, local wound therapy and the treatment of exogenic inhibitory factors such as necroses, fibrinous deposits, wound infections or local allergic reactions[5].

Study results published hitherto on the efficacy of compression stockings are of limited significance despite highly promising outcomes. A cohort study involving 20 patients achieved complete healing of the 30 tested ulcers without exception after up to 30 weeks of using compression stockings and a special locally applied wound treatment[6]. Further cohort studies involved 53 patients and 31 patients[7,8]. The first comparative study revealed ulcer healing in 10 of 14 (71%) patients given compression stockings compared with 7 of 10 (70%) patients wearing Unna's boots[9]. A further study achieved healing in 84% of cases after three months' treatment with compression stockings as compared with 52% when using compression bandages. Again, the number of patients ($n = 25$) was too small to make a statistical statement about differences between the treatment groups[10].

The aim of the present study was to compare for the first time the rate of complete healing achieved by the ulcer compression stocking (Venotrain ulcertec), with a standard therapy (phlebologic compression bandage) using a randomized design. Aside from the healing rate, comfort and handling were investigated. The ulcer compression stocking (U-Stocking), specially developed and used here to treat ulcus cruris venosum, has a special patented trellis in the knitted fabric and attained a working pressure equivalent to that of a vascular compression bandage directly after application by an experienced dressing specialist. The mean pressure of the U-Stocking at ankle level was measured, while lying, at 42.7 ± 13.0 mmHg[11]. Unlike the compression bandage, the pressure from the U-Stocking remains constant over the course of the day[12].

Methods

Patients

The patients were enrolled and treated at German medical practices specialized in phlebology, or at German as well as Dutch phlebology outpatient clinics. Inclusion and exclusion criteria are listed in Table 1. The study was approved by ethics committees at all study sites and the Dutch Central Committee for Research Studies with Humans (CCMO) and the German National Regulatory Agency (BfArM) was notified. It was conducted according to ICH–GCP and based upon the Declaration of Helsinki.

Study Design

The study was based on a prospective, multicentre, open-labelled, randomized, active-controlled, parallel-group design with blinded assessment of the primary endpoint, which included a pre-planned adaptive interim analysis after inclusion of 120 patients. Patients were randomly assigned to receive either a compression treatment with U-Stocking or bandages. Randomization used blocks of four patients and was performed at the statistical department of a contract research organization (IMEREM GmbH, Nürnberg, Germany) prior to patient enrolment. Numbered containers were supplied to the study sites; patients were assigned by the investigators to one of the two treatments by opening a code envelope with available treatment numbers in ascending order. The maximum treatment duration was 12 weeks but could be discontinued earlier in the event of complete healing of the venous ulcer. Treatment outcome and tolerability was assessed at control visits after 2, 4, 8 and 12 weeks.

The course of healing was checked by the investigator prior to starting therapy and at each control visit: the outline of the ulcer was traced onto foil and the ulcer

Table 1. Selection criteria for study patients

Inclusion criteria
Venous ulcer (WIDMER stage III, CEAP 6) of a maximum of 1 cm to 10 cm in breadth
Period of disease of less than 12 months.
In the case of more than one ulcer the ulcer with the largest size was to be treated and analysed
Reflux (demonstrated by Doppler or Duplex sonography);
in the area of the extrafascial cutaneous saphenous veins
and/or of the deep conducting veins
and/or perforating veins
No peripheral arterial occlusive disease (ankle/arm pressure index > 0.9)
Age: 18–80 years
Readiness and ability to adhere to medical instructions and comply with the scheduled visits
Written informed consent
Exclusion criteria
Bedridden patients or those spending less than one hour per day on their feet
Clinical signs of infected ulcer
Ulcer of diabetic, arterial or combined (arterial and venous) origin
Insulin-dependent diabetes mellitus
Diabetic polyneuropathy
Deep vein thrombosis in the last three months
Uncontrollable hypertension; advanced coronary disease
Primary chronic polyarthritis
Clearly restricted ankle movement (dorsal flexion < 5°)
Vascular surgery and/or sclerotherapy of varicose veins within the last three months
Concomitant therapy with venous medication (to be discontinued four weeks prior to starting therapy), immunosuppressants and cytostatics
Obesity (BMI > 35 kg/m^2)
Further general risk and non-compliance factors

was also photographed. All the drawings of the ulcer outlines were digitalized at a central reading institute (Department of Dermatology, University Hospital, Eberhard-Karls University, Germany). The ulcer surface was then planimetrically determined by a technician who was blind with regard to the treatment applied. The planimetry was performed using a computer program (CapImage, Zeintl, Heidelberg, Germany). The degree of healing of the ulcer was determined according to Gillmann[13], who relates the difference in the areas before and at the end of therapy to the sum of the circumferences of the ulcer at both time-points. A planimetrically defined ulcer area of '0 cm^2' was required in order to achieve the evaluation predictive of the primary endpoint, namely 'complete healing'. Time until healing was determined from the difference between baseline and the first day when complete healing was diagnosed.

The patient questionnaire requested information on the occurrence of adverse concomitant symptoms (constriction, tightness, restricted freedom of movement, leg pain, burning in the leg, sweating under the bandage/stocking, heat sensation in the leg, itching of the skin on the leg, prickling of the leg, difficulties applying the U-Stockings/bandages, see Table 3) in each case in four categories (none, mild, moderate, severe). Patients also recorded the time needed for applying the compression therapy. In terms of time, the patient was given the choice between 'high' and 'appropriate'. The nursing staff evaluated the therapy with regard to the desired effect, patient compliance, discomfort to the patients, amount of support needed, personal satisfaction with the implementation of therapy and average time spent applying the test product (for criteria see Table 4). The patients' experience of use as well as the assessments made by the nursing staff were documented at the end of therapy (after 12 weeks or at the respective termination of therapy). The time spent wearing the U-Stocking or bandages was recorded every day by the patient in a diary.

Treatment (Compression Therapy)

The size of the U-Stocking (Venotrain ulcertec) was specified individually for each patient. To this aim the circumference of the leg at ankle level and at the broadest section of the calf was measured, as well as the length of the lower leg. The size of stocking suitable for the patient was selected accordingly in line with a table. The U-Stocking was available in three ready-made widths, each of two different lengths. In one case, where the circumference of the lower leg was too large, a custom-made stocking was provided by the manufacturer. Initially each patient had a set of two

under-stockings and one outer-stocking at his disposal (registration number DE/CA90/2940). The circumference of the leg was re-measured at all the control examinations and a U-Stocking which no longer fitted, or was damaged, was replaced.

The bandages comprised two short-stretch bandages each of 10.0 cm width and 5.0 m length with expansibility of 90% ± 10% (CEB – ROSELASTIC 'S' 530†). The bandages were wrapped in opposite directions from the metatarsophalangeal joint to the head of the fibula. This technique of bandaging was standardized in all centres.

At the start of therapy the patients were instructed in detail, as well as provided with a written information leaflet, on how to fit the U-Stocking or the bandages. The compression therapy was to be applied for at least eight hours per day according to the instructions. In the interval between each control visit the patients could either treat themselves or ask for assistance (nursing help, physician/GP, outpatient nursing services, study centre). Videotapes were available, describing the standard method of application of both compression therapies. All persons involved in providing nursing care at the centres were given training, as far as possible.

Statistical Evaluation

The general biometrical concept aimed at showing non-inferior efficacy of U-Stocking compared to bandages, which is considered as the standard therapy in this condition. The rate of complete ulcer healing after 12 weeks was defined as primary outcome measure. The non-inferiority margin was set as 15% of the healing rate. If the hypothesis of non-inferiority could be rejected, the superiority of the U-Stocking over the bandages was then to be investigated. These hypotheses were analysed by use of one-sided 95% confidence intervals the calculation of which included the influence of centre size. In addition, chi²-tests were calculated from Lehmacher's approach[14].

The main secondary target variable was the comparison of time to complete healing. Time to complete healing was analysed with the log-rank test. Patients who dropped out of the study for reasons other than complete healing were censored in this analysis. The planimetrically defined degree of ulcer healing was presented as a percentage remission of the ulcer surface and evaluated with the Mann–Whitney U-test. Further secondary outcome criteria were defined, among others, as: (1) experience of use on the part of the patients; (2) satisfaction on the part of the nursing staff; (3) patient compliance and (4) time needed for applying the compression bandages or U-Stocking. Compliance was assessed by taking the number of days from the patient diary on which the U-Stocking or bandages were worn for at least eight hours, divided by the number of days of study participation; the rate of patients with a compliance of > 80% was compared. Comparisons were performed with 2-sample tests (Mann–Whitney U-test, chi²-test) and interpreted in an exploratory manner. Efficacy was assessed using the intention-to-treat (ITT) population which included all patients who were treated with one of the compression therapies and were evaluable for primary efficacy analyses. The last observation was carried forward in patients who dropped out of the study if at least one post-baseline assessment was available. Tolerability was evaluated by analyzing adverse events in all patients who received treatment. Due to a lack of valid empirical data for the estimation of a fixed sample size for the comparison of two active compression therapies, an adaptive interim analysis was scheduled in the study protocol after completion of therapy in 120 patients[15]. The findings of this interim analysis were used to recalculate the final sample size or to terminate the study prematurely (α was set to 0.023 for premature termination).

Results

A total of 134 Caucasian patients with venous ulcus cruris were randomized at 16 study sites between October 2000 and October 2002. In two patients, no treatment was applied; one of those refused participation when randomized to the bandages group, the other needed additional compression therapy at the thigh (Figure 1). Of 132 patients on study treatment, 11 dropped out early after baseline due to adverse events (two patients in each group), lost-to-follow-up (three patients in the bandages group) or were withdrawn because of protocol violations (body mass index > 35 kg/m², two patients in each group). Among the 121 patients of the ITT population, 12 dropped out after at least one post-baseline assessment (six in each group) for reasons other than healing. The reasons were withdrawal of consent (U-Stocking: four; bandages: two patients), poor compliance (two patients in each group) and adverse events (two patients in the bandages group).

At study enrolment 191 active concomitant diseases were documented in 60 of 65 patients of the U-Stocking group and 192 in 63 of the 67 patients of the bandages group, highlighting the multi-morbidity of

† ROSELASTIC is a trade name of KOB (Karl Otto Braun), Germany

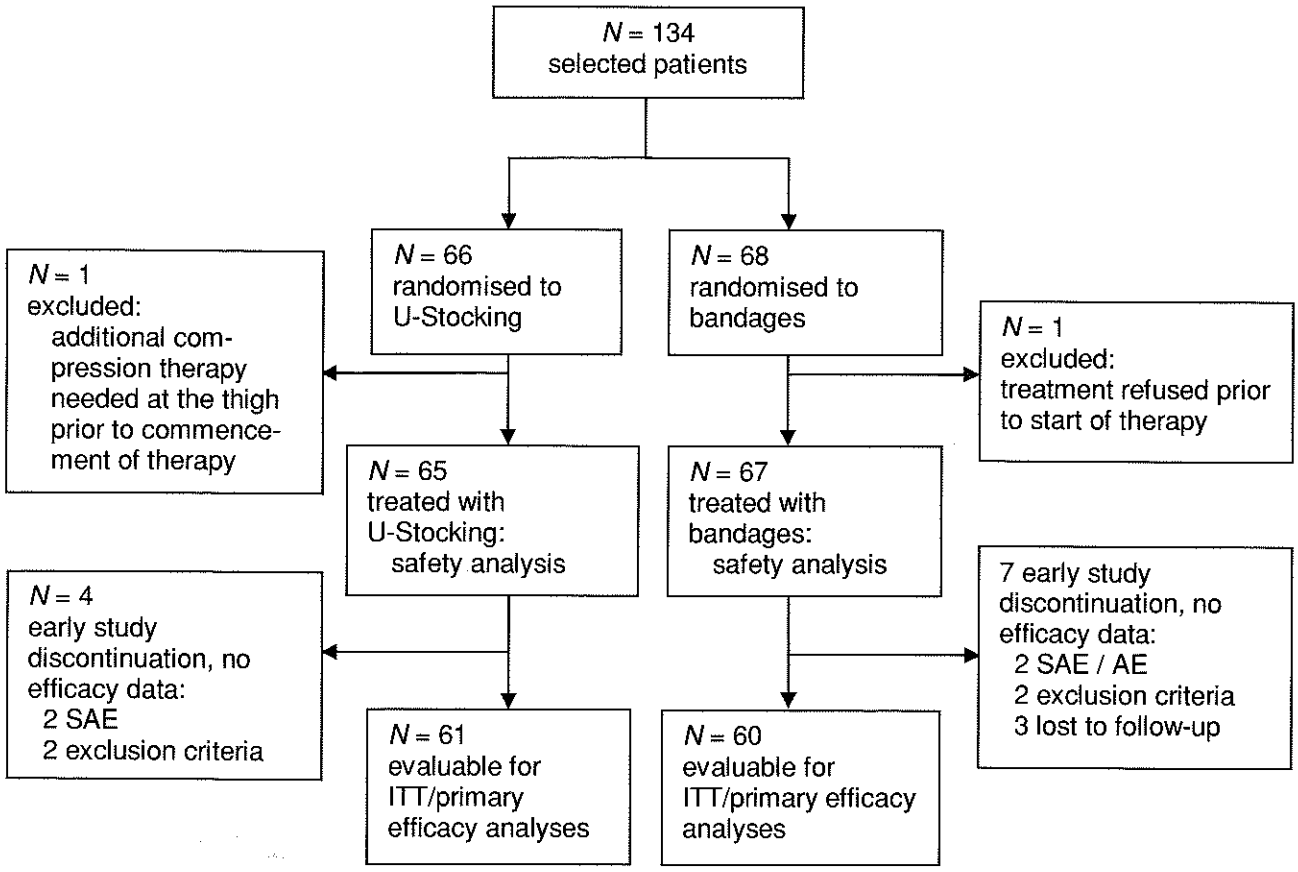

Figure 1. *Study enrolment and populations*

such patients. Further baseline characteristics (ITT population) are presented in Table 2.

Figure 2 displays the outcome of the efficacy analysis related to the primary target variable for the ITT population. Complete healing of the ulcer was achieved in 29 of 61 (47.5%) patients of the U-Stocking group and 19 of 60 (31.7%) patients of the bandages group showing 15.8% more complete healings in the U-Stocking group. The limits of the one-sided 95% confidence interval for the differences between the two treatment groups weighted by centre were +4.3% and +28.5%, respectively; the related p-value was $p = 0.0129$ (one-sided) in favour of the U-Stocking group. This confidence interval excludes both the non-inferiority area (until $\delta = -15\%$) and the identity measure of $\delta = 0$. The study was therefore stopped after the interim analysis. The mean duration until healing was 46 ± 20 days (range 10–83 days, median 47 days) in the U-Stocking group and 46 ± 22 days (range 6–80 days, median 52 days) in the bandages group, $p = 0.8165$ (Mann–Whitney U-test). Figure 3, in the form of a life-table analysis (Kaplan–Meier curves), shows the rates of completely healed ulcers over the course of therapy. A tendency towards a benefit in favour of the U-Stocking group ($p = 0.0565$, log-rank test) is illustrated here by means of a higher relative frequency of complete healing which accelerates after approximately four weeks of therapy. At the individual study end a regression of the ulcer surface by a mean of –74.8% (SD 42.4, median –98.4% [range –100 to +83.1]) in 61 U-Stocking patients and –51.4% (SD 86.7, median –82.9% [range –100 to +396.2]) in 58 evaluable bandages patients, could be ascertained ($p = 0.0679$, Mann–Whitney U-test).

The mean duration of therapy in the ITT population was 61 days (SD 26, range 10–100 days, median 70 days) in the 61 U-Stocking patients and 68 days (SD 25, range 6–92 days, median 83 days, $p = 0.0297$; Wilcoxon-U test) in the 59 evaluable patients treated with bandages. According to the patient diaries 57 (93.4%) patients wore the U-Stockings and 50 (84.8%) patients the bandages for at least eight hours on more than 80% of the study days ($p = 0.1504$, exact Fisher test). The mean duration of compression therapy per

Table 2. Baseline characteristics (ITT-population)

	U-Stocking ($n = 61$)	Bandages ($n = 60$)
Demographics		
Age (years)*	63 (11)	63 (13)
Male / Female	21 / 40	26 / 34
BMI (kg/m^2)*	28 (4)	28 (5)
Obesity	25 (41%)	19 (32%)
Clinical finding Ulcus cruris		
Localisation on the leg		
Outer ankle	16 (26%)	10 (17%)
Inner ankle	45 (74%)	50 (84%)
Multiple ulcers	18 (30%)	25 (42%)
Oedema	28 (46%)	25 (42%)
Hyperpigmentation	46 (75%)	48 (80%)
Ulcer size (mm^2) (planimetry)*		
Mean	562 (788)	595 (899)†
Median	274	370
Variceal status		
Truncal varicosis total	49 (80%)	46 (77%)
Great saphenous vein	35 (57%)	25 (42%)
Small saphenous vein	2 (3%)	10 (17%)
Great and small saphenous vein	12 (20%)	11 (18%)
Lateral branch varicosis	38 (62%)	42 (70%)
Reticular varicosis	26 (43%)	23 (38%)
Diabetes	7 (11%)	7 (12%)
History of disease		
Disease duration in days*	116 (100)	156 (120)‡
Pretreatments:		
Medicinal	9 (15%)	9 (15%)
Physiotherapy	10 (16%)	16 (27%)
Variceal surgery	3 (5%)	4 (7%)
Sclerotherapy	0	1 (2%)
Compression therapy	54 (89%)	54 (90%)

Data are presented as absolute and relative frequency
*Mean values, in parentheses: standard deviation
†$p = 0.1306$ Wilcoxon test; missing value in one patient of bandages group
‡$p = 0.08$

day was 12.7 hours (SD 2.9, median 12.2) in the U-Stocking group and 16.9 hours (SD 5.7, median 15.9) in the bandages group ($p = 0.0002$, Mann–Whitney U-Test).

Explorative analysis of the patient questionnaires revealed benefits from the U-Stocking over the bandages in terms of constriction, restricted freedom of movement, sweating under the dressing and itching of the skin on the leg (Table 3). There tended to be less pain in the U-Stocking group. Statements regarding difficulties in application were comparable between the treatment groups: of the 54 and 53 patients evaluated in this regard in the U-Stocking and bandages groups, respectively, difficulties were reported as: mild: 11 (20%) vs. 12 (23%); moderate: 4 (7%) vs. 6 (11%) and great difficulties: 2 (4%) vs. 0 patients ($p = 0.9323$). The time required for applying the U-Stocking was judged to be high by 1 in 55 patients (1.8%); 5 of 54 patients (9.3%) in the bandage group made the same statement ($p = 0.0915$).

Explorative analysis of the judgements made by the nursing staff during control assessments at the study sites revealed that statistically the group differences were remarkably favourable towards the U-Stocking group rather than the bandages group in terms of a better effect from the compression therapy, less discomfort and improved satisfaction (Table 4). With a mean of 5.4 minutes (SD 5.4; median 3) the U-Stocking was also superior to the bandages (8.5 minutes; SD 6.5; median 6) in terms of the time required for application ($p < 0.001$).

According to the diaries of all 132 treated patients, slightly more patients in the bandages group (15, 22.4%) than in the U-Stocking group (6, 9.2%) got external

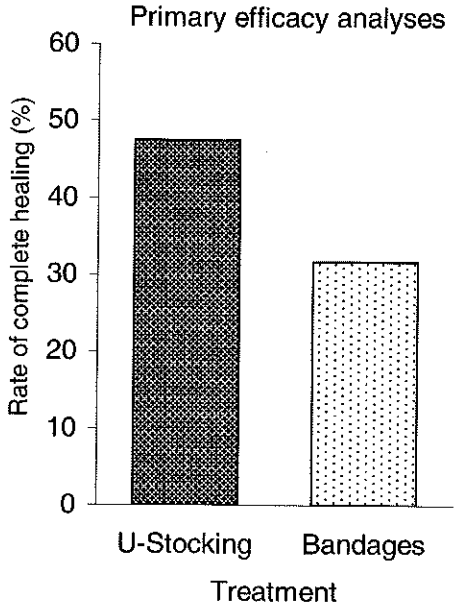

Figure 2. *Proportion of patients with completely healed ulcer after 12 weeks or at individual end of study. Comparison of the response of ulcers completely healed during the study (final visit after 12 weeks of treatment or visit at individual end of study) in both treatment groups. The boundaries of the one-sided 95% confidence interval for the difference in complete healing rate between the two groups, weighted by centres, were [+4.3%; +28.5%], the associated p-value (one-sided) was $p = 0.0129$ in favour of U-Stocking (ITT population)*

support for application of treatment ($p = 0.0654$, Fisher's exact test). One patient in the U-Stocking group and 5 patients in the bandages group received professional nursing care, while 5 and 15 patients needed help from relatives during the whole treatment period (3/8) or part-time (2/2).

A total of 29 adverse events (AE) occurred in 20 of 65 (31%) patients treated with the U-Stocking and 42 AEs in 26 of 67 (39%) patients treated with the bandages. Six events were classified as serious, two of which were in the U-Stocking group: one 40 year-old female patient on oral anticoagulation experienced bleeding in the marginal area of the ulcer with therapy-resistant pain, resulting in discontinuation of therapy after 15 days, although the U-Stocking had been used only for four days. A relationship with the test product was suspected. Following severe gastrointestinal bleeding in a 71 year-old female patient on oral anticoagulants, therapy with the U-Stocking was discontinued on day 13, although no relationship to the test product was established, as was the case with four serious AEs of the bandages group: bleeding at the ulcer margin, severe lymph secretion from the ulcer, fractured neck of femur after a fall (study treatment discontinued on day 2), superficial thrombophlebitis (study treatment discontinued after 9 weeks). A causal relationship to the study treatment was postulated in four non-serious AEs: increased pain from the ulcer

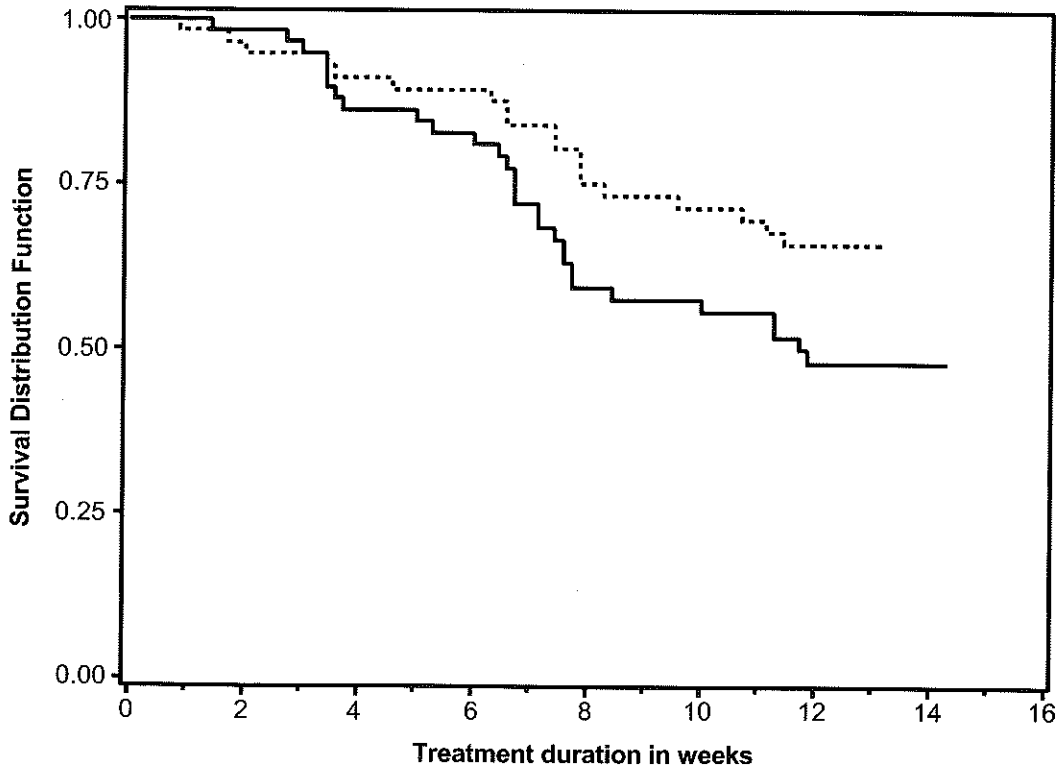

Figure 3. *Kaplan–Meier curves related to the primary study endpoint 'complete healing' for both treatment groups (ITT population). Particularly between week 6 and 8 healing occurred more frequently in the U-Stocking group*

Table 3. Results from analysis of patient questionnaire on comfort and symptoms

Patient assessment	U-Stocking‡	Bandages‡	*p*-value§
Constriction			
'none'	35/56 (63%)	20/54 (37%)	
all categories* (quartiles)†	0 (0–1)	1 (0–2)	0.0032
Tightness			
'none'	31/56 (55%)	25/52 (48%)	
all categories* (quartiles)†	0 (0–1)	1 (0–1.5)	0.2313
Restricted freedom of movement			
'none'	40/56 (71%)	22/53 (42%)	
all categories* (quartiles)†	0 (0–1)	1 (0–1)	0.0009
Pain in the leg			
'none'	31/56 (55%)	21/54 (39%)	
all categories* (quartiles)†	0 (0–1)	1 (0–2)	0.0700
Burning in the leg:			
'none'	40/55 (73%)	32/54 (59%)	
all categories* (quartiles)†	0 (0–1)	0 (0–1)	0.1463
Sweating under the dressing:			
'none'	41/56 (73%)	28/54 (52%)	
all categories* (quartiles)†	0 (0–1)	0 (0–1)	0.0405
Heat sensation in the leg			
'none'	29/55 (53%)	25/53 (47%)	
all categories* (quartiles)†	0 (0–1)	1 (0–2)	0.4770
Itching of the skin on the leg			
'none'	32/56 (57%)	16/54 (30%)	
all categories* (quartiles)†	0 (0–1)	1 (0–2)	0.0063
Prickling of the leg			
'none'	43/56 (77%)	34/54 (63%)	
all categories* (quartiles)†	0 (0–0)	0 (0–1)	0.1180

*Median calculated from the score of the categories: 'none' with 0, 'mild' with 1, 'moderate' with 2 and 'severe' with 3 points
†In parentheses: lower quartile–upper quartile
‡ITT population
§Wilcoxon test

(U-Stocking); enlarged ulcer due to poor wrapping of the bandage; restricted flexibility of the upper ankle caused by pain (bandages); intolerance reaction to the compression material with suspected delayed allergic reaction, hence discontinuation of bandage therapy. The study treatment was discontinued in a further two patients due to a non-serious adverse event with no causal relationship (increase in calf circumference and several open sites around the ulcer in a U-Stocking patient as well as phlegmon on the lower leg in a bandages patient).

Discussion

This study of treatments for venous leg ulcers demonstrates the superior efficacy of a compression stocking over established phlebological compression bandages, using randomized comparison for the first time. The newly developed Venotrain ulcertec (U-Stocking) was used as the compression stocking. Both treatment methods proved to be safe in terms of adverse events. There were no statistically remarkable differences between the treatment groups regarding the demographic parameters and clinical findings at baseline.

The analysis of the primary endpoint, 'complete ulcer healing', revealed the U-Stocking to be significantly superior to the bandages, with a healing rate of 47.5% as opposed to 31.7%. Although both treatment groups differ in the primary outcome measure, it should be noted that the healing rates are low in general (see below). Since therapy could be prematurely ended in the event of complete healing, the shorter duration of therapy in the U-Stocking group (median 70 days versus 83 days, $p = 0.0297$) reflects the higher rate of healing. The mean time periods in this study until the desired healing was reached were comparable in both groups, at 46 days in each case. The better efficacy of the U-Stocking is possibly achieved by its maintenance of the desired pressure (high working pressure and low resting pressure) over at least eight hours. In contrast a loss of resting and working pressure is seen from the

Table 4. Assessment of compression therapy by the nursing staff

Assessment	U-Stocking* (n = 59)	Bandages* (n = 58)	p-value†
Effect of therapy			
very good	31 (53%)	16 (28%)	
good	20 (34%)	30 (52%)	0.0132
moderate	5 (8%)	9 (16%)	
poor	3 (5%)	3 (5%)	
Discomfort			
none	44 (75%)	34 (59%)	
mild	11 (19%)	14 (24%)	
moderate	2 (3%)	3 (5%)	0.0488
severe	1 (2%)	6 (10%)	
extreme	1 (2%)	1 (2%)	
Support required at study site			
none at all	22 (37%)	17 (29%)	
some	24 (41%)	24 (41%)	
moderate	10 (17%)	13 (22%)	0.2853
high	3 (5%)	4 (7%)	
Compliance			
very good	42 (71%)	38 (66%)	
good	15 (25%)	11 (19%)	
moderate	1 (2%)	7 (12%)	0.3142
poor	1 (2%)	1 (2%)	
very poor	0	1 (2%)	
Satisfaction of nursing staff with treatment			
very satisfied	37 (63%)	22 (38%)	
satisfied	17 (29%)	28 (48%)	
neither/nor	2 (3%)	6 (10%)	0.0123
dissatisfied	3 (5%)	2 (3%)	
Nursing time (minutes)			
mean ± standard deviation	5.4 ± 5.4	8.5 ± 6.5	< 0.001
median	3	6	
25%/75% quartiles	2–5	5–10	

*ITT population
†Wilcoxon test

compression bandages after just two to three hours, whether applied by experienced or inexperienced dressing specialists[16].

It is relevant for the interpretation of the rather low healing rate in our study that compression therapies had already been used prior to enrolment into this study in about 90% of cases in the total population, as a result of which lower rates of healing were to be anticipated than in patients who had not previously been treated. In addition, the greater percentage reduction in ulcer size at the final assessment in the U-Stocking group emphasizes the improved efficacy demonstrated on the basis of the healing rates as compared with the bandages. It also indicates that longer treatment duration might have markedly increased the healing rate. Among other influential factors on the assessment of healing rate, compliance has to be mentioned. This was high in both treatment groups, tending towards better results with the U-Stocking. The nursing staff judged compliance as 'good' or 'very good' in 97% of patients with the U-Stocking, as compared with 85% of bandage patients; the patient diaries revealed that 93.4% versus 84.8% of the patients used the compression therapy for at least eight hours on more than 80% of the treatment days. The relevance of compliance to the therapeutic outcome was demonstrated in an earlier study[17]. Aside from 'non-compliance', further influential factors are described in the literature which reduce the rate of healing or increase the risk of recurrence:

- Old age.
- Larger initially affected ulcerous area[18,19,20].
- Popliteal venous reflux[21].
- Long pre-treatment period (≥ 9 months)[17].

There were no significant differences between the treatment groups of our study with respect to these risk factors.

One point of discussion in our study is the lack of stratification of the ulcer by surface area or duration of disease. When planning the study, we did not expect an influence of ulcer size or disease duration on treatment outcome within the pre-specified surface area of less than 10 cm^2. Randomization stratified by both variables is recommended for future trials in venous ulcer patients. The percentage reduction in the size of the ulcer is possibly influenced less by varying baseline ulcer sizes than the healing rate.

Some evidence can be found in the literature of the efficacy of compression bandages in venous leg ulcers[18,22,23], hence the direct comparison made here with the bandages gives strong support to the high efficacy of the U-Stocking. The applicability of the data to other compression stockings is limited since they have been found to have varying properties, e.g. in the difference between resting and working pressure, which in turn will affect the desired haemodynamic improvement[24]. The efficacy of each compression stocking therefore needs to be tested in a controlled study.

The randomized study design and involvement of nursing staff and patients in the assessment of the therapies during our study provided further important information with regard to the use of the U-Stocking. The shorter mean period per day wearing the U-Stocking, of 12.7 hours as opposed to 16.9 hours with bandages, is explained by the possibility of continuing to wear the under-stocking overnight without the outer-stocking. Bandages are mostly also worn at night for reasons of practicality. The shorter daytime period of wearing the U-Stocking was possibly also relevant to the more favourable patient assessment regarding sweating under the dressing and itching. Furthermore, constriction and restricted freedom of movement were reported less often when wearing the U-Stocking than the bandages. The lower occurrence of the four unpleasant concomitant symptoms of compression therapy from the U-Stocking, while reported at a relative frequency of 48% (sweating) to 70% (itching) compared with bandages, enhances comfort.

The nursing staff at the study sites claimed to be 'very satisfied with therapy' in 63% of the U-Stocking patients and 38% of the bandages patients ($p = 0.0123$). This difference is understandable since at the same time the nursing staff estimated the effect of the U-Stocking as better and the therapy-related discomfort as less than with the bandages. Furthermore, both the patients and nursing staff reported that less time was needed to apply the U-Stocking than the bandages. Three minutes (mean value) were saved when applying the stocking. Economically the use of stockings seems to be of advantage: less patients in the U-Stocking group needed external support from professional care givers or from relatives. A further benefit when applying the U-Stocking is the fact that the ulcer dressing can first be fixed into place by the under-stocking before pulling on the outer-stocking. The simple handling of the U-Stocking demonstrated by this study is of clinical relevance, since in a previous study of class II compression stockings 68 of 166 (41%) patients could not pull on the stocking, or could only do so with great difficulty[3]. As a result of the beneficial application properties of the U-Stocking, this new treatment option should also be considered in the development of new concepts for prevention of recurrent ulcers.

Overall the study we performed revealed compression therapy with the U-Stocking to be superior to standard compression therapy with bandages for venous ulcers. In addition to an improved healing rate, further clinically relevant benefits were revealed with regard to comfort and handling, as reflected by the high rate of patient compliance and the greater satisfaction of the nursing staff with the compression therapy. Future studies shall investigate continuation of treatment with the U-Stocking following healing, potentially reducing the high recurrence rates. A clinically relevant question is the extent to which therapy with the U-Stocking over more than 12 weeks will produce additional benefits with regard to the healing rate in unhealed ulcers.

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