Risk factors related to the failure of venous leg ulcers to heal with compression treatment

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Background: **Compression therapy is the most widely used treatment for venous leg ulcers and it was used in different forms for more than 400 years. Published healing rates of venous ulcers obtained with compression therapy vary widely from 40-95%. According to numerous studies, it has been suggested that the application of external pressure to the calf muscle raises the interstitial pressure resulting in improved venous return and reduction in the venous hypertension. Several risk factors have been identified to be correlated with the failure of venous leg ulcers to heal with compression therapy (longer ulcer duration; large surface area; fibrinous deposition present on >50% of the wound surface and an Ankle Brachial Pressure Index (ABPI) of <0.85.**

Methods: **An open prospective single-center study was performed in order to determine possible risk factors associated with the failure of venous ulcers to heal when treated with multi-layer high compression bandaging system for 52 weeks. In the study, 189 patients (101 women, 88 men; mean age 61 years) with venous leg ulcers (ulcer surface >5 cm^2; duration >3 months) were included. The study excluded patients with arterial disease (ABPI <0.8), heart insufficiency with ejection fraction (EF) <35, pregnancy, cancer disease, rheumatoid arthritis, and diabetes. Based on clinical opinion and available literature, the following were considered as potential risk factors: sex, age, ulceration surface, time since ulcer onset, previous operations, history of deep vein thrombosis, body mass index (BMI), reduction in calf circumference >3 cm during the first 50 days of treatment, walking distance during the day <200 meters, calf:ankle circumference ratio <1.3, fixed ankle joint, history of surgical wound debridement, >50% of wound covered with fibrin, depth of the wound >2 cm.**

Results: **Within 52 weeks of limb-compression therapy, 24 (12.7%) venous ulcers had failed to heal. A small ulceration surface (<20 cm^2), the duration of the venous ulcer <12 months, a decrease in calf circumference of more than 3 cm, and emergence of new skin islets on >10% of wound surface during the first 50 days of treatment were favorable prognostic factors for ulcer healing. A large BMI (>33 kg/m^2), short walking distance during the day (<200 m), a history of wound debridement, and ulcers with deepest presentation (>2 cm) were indicators of slow healing. Calf:ankle circumference ratio <1.3, fixed ankle joint, and reduced ankle range of motion were the only independent parameters associated with non-healing ($P < .001$).**

Conclusion: **The results obtained in this study suggest that non-healing venous ulcers are related to the impairment of the calf muscle pump. (J Vasc Surg 2009;49:1242-7.)**

Chronic venous insufficiency and venous leg ulcers are a major health problem because of their high prevalence and associated high cost of care. Compression therapy is the most widely used treatment for venous leg ulcers and it was used in different forms for more than 400 years.[1] The mechanism of action of compression therapy in the treatment of venous leg ulcers is not completely understood. According to numerous studies, it has been suggested that the application of external pressure to the calf muscle raises the interstitial pressure resulting in improved venous return and reduction in the venous hypertension.[2,3] Published healing rates of venous ulcers obtained with compression therapy vary widely from 40-95%.[4-10] Several risk factors have been identified to be correlated with the failure of venous leg ulcers to heal with compression therapy (longer ulcer duration, large surface area, fibrinous deposition present on >50% of the wound surface, and an Ankle Brachial Pressure Index [ABPI] of <0.85).[11]

The purpose of this study was to identify possible risk factors related to the failure of venous leg ulcers to heal with compression treatment.

METHODS

An open prospective single-center study was performed in order to determine possible risk factors associated with the failure of venous ulcers to heal when treated with multi-layer high compression bandaging system for 52 weeks.

Patients aged at least 16-years-old with leg ulceration of venous etiology were screened for inclusion in the trial. Before inclusion in the study, all patients underwent color duplex scan examination (CDS) and ABPI measurements. CDS examinations were performed using Siemens Sonoline Sienna (Erlangen, Germany) ultrasonography scan device with a 7 MHz probe. Venous compressibility and flow characteristics were the key elements to exclude thrombosis. The direction of flow was assessed in a 20-30° reverse Trendelenburg position during Valsalva maneuver. A cuff inflation-deflation method with rapid cuff deflation in the

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Table I. Demographic and clinical characteristics of patients by outcome groups

Characteristic	*Healed by week 26 (n = 95)*	*Healed by week 27 to 52 (n = 70)*	P	*Total healed (n = 165)*	*Not healed (n = 24)*	P
Ulceration surface >20 cm^2	24 (25)	47 (67)	<.001	71 (43)	13 (54)	.306
Wound duration >12 months	31 (33)	49 (70)	<.001	80 (48)	14 (58)	.368
Female gender	51 (54)	37 (53)	.916	88 (53)	13 (54)	.939
Age (years)	61.4 ± 9.4	61.4 ± 10.6	.995	61.4 ± 9.9	61.4 ± 9.3	.991
Previous operations	38 (40)	33 (47)	.361	71 (43)	10 (42)	.900
Deep vein thrombosis	38 (40)	21 (30)	.187	59 (36)	9 (37)	.868
BMI >35	11 (12)	19 (27)	.011	30 (18)	3 (12)	.773
Reduction in calf circumference	73 (77)	37 (53)	.001	110 (67)	12 (50)	.112
Daily walking distance <200 m	5 (5)	12 (17)	.013	17 (10)	2 (8)	.765
Calf:ankle circumference ratio <1.3	10 (10)	12 (17)	.218	22 (13)	18 (75)	<.001
Fixed ankle joint and ROM <20°	5 (5)	7 (10)	.248	12 (7)	16 (67)	<.001
Ulcer recurrence	95 (100)	70 (100)	—	165 (100)	24 (100)	—
Wound debrided surgically	11 (12)	18 (26)	.019	29 (18)	3 (12)	.771
Wound covered with fibrin >50%	11 (12)	34 (49)	<.001	45 (27)	8 (33)	.538
Lipodermatosclerosis	84 (88)	61 (87)	.804	145 (88)	24 (100)	.082
Depth of the wound >2 cm	8 (8)	20 (29)	<.001	28 (17)	5 (21)	.577
Emergence of new skin islets	29 (30)	9 (13)	.008	38 (23)	2 (8)	.100

Values are given as number (percent) or mean ± SD.
BMI, Body mass index; *ROM,* range of motion; *SD,* standard deviation.

standing position was performed to induce reflux. The presence of reflux was determined by the direction of flow (significant flow toward the feet was suggestive of reflux). A reflux time of >0.5 seconds has been used to diagnosis the presence of reflux.

The study excluded patients with an ABPI <0.8 (27 patients), patients with heart insufficiency with an ejection fraction (EF) <35 (1 patient), pregnancy (1 patient), cancer disease (3 patients), rheumatoid arthritis (2 patients), and diabetes (11 patients). Thirteen patients with unidentified cause of leg ulcer were also excluded from the study. Only patients with verified venous ulcers (ulcer surface >5 cm^2; duration >3 months) were included in the study. Wound size was determined by measurement (maximal length and width) as well as by computerized process consists of mapping the two-dimensional digital image onto the polygonal mesh. The margins of a wound were outlined on a computer screen and the enclosed wound area was automatically determined. Digital images were taken with the Sony Cyber Shot (Kohda, Japan) digital camera T10. The digital image included a 5 cm-long calibration marker positioned below the wound surface. The wound area was evaluated every 15 days.

Two hundred fifty-eight patients were considered for the study and 200 were included. Eleven patients were lost during the study and 189 patients (101 women, 88 men; mean age 61 years) with venous leg ulcers completed the study. Based on clinical opinion and available literature, the following were considered as potential risk factors: sex, age (years), ulceration surface (cm^2), time since ulcer onset (months), previous operations (stripping, superficial endoscopic perforator vein surgery [SEPS]), history of deep vein thrombosis, body mass index (BMI), reduction in calf circumference >3 cm during the first 50 days of treatment, walking distance <200 meters during the day, calf:ankle circumference (CAC) ratio <1.3, fixed ankle joint and reduced ankle range of motion (ROM) (<20°), ulcer recurrence, history of surgical wound debridement, >50% of wound covered with fibrin, depth of the wound >2 cm, and emergence of new skin islets on more than 10% of ulcer surface during the first 50 days of treatment.

Time since ulcer onset, previous operations, history of surgical wound debridement, and history of deep vein thrombosis (DVT) were determined according to medical documentation. The BMI was calculated at the beginning of the treatment. The depth of the wound was measured using a cotton-tipped applicator that was inserted into the deepest portion of the wound. The applicator was marked with the pen at skin level and the distance was measured from the tip to the mark. Calf and ankle circumference were measured in the recumbent position with the maximal (calf) and minimal (ankle) point determined visually. Calf: ankle ratio was determined at the beginning of the treatment and afterwards every 30 days. Walking distance during the day was determined according to the patient's daily activities and patients who had predominantly inactive and sessile lifestyle were considered to walk less than 200 meters per day. The wound surface covered with fibrin and surface of new skin islets were determined using a sheet of transparency film that was placed over the wound, and the boundary of the entire wound and wound surface covered with fibrin or surface of new skin islets were drawn with a marking pen on the film. The surfaces were analyzed and ratio was calculated.

Ankle ROM was determined with the patient in the supine position by goniometry during maximal voluntary plantar flexion and dorsiflexion of the ankle. ROM was determined as the sum of plantar flexion and dorsiflexion.

The study was approved by relevant authorities and written consent was obtained by all patients included in the study. The same treatment team comprised of three doctors and three medical nurses treated all patients. The patients

were treated at the Clinic for Vascular Surgery, Clinical Centre of Nis (Serbia) on an ambulatory basis with the primary endpoint of the study being complete ulcer healing at 26 and 52 weeks. After ulcer healing, patients were instructed to continue to wear Tubulcus elastic stockings (35 mm Hg, Laboratoires Innothera, Arcueil, France) in order to avoid recurrence. During the treatment, patients were monitored by the study team at least once a week.

Treatment regimen. The standard regimen was to debride the wound. This was a normally simple mechanical debridement with sterile gauze in order to remove slough and other dead tissue. According to the extent of the wound, exudation dressings were changed from 1 to 7 days. Extensive wound exudation was treated with crystal acidum boricum (after debridement, acidum boricum was applied over the wound in a thin layer) and in patients with no exudation, dry dressings were performed. No antibiotics were used and patients in both groups received only aspirin (100 mg). After wound debridement and dressing bandaging systems were applied, the bandaging system was applied as follows:

- First and second layer were cotton gauze without tension (50% overlap) and cotton crepe bandage.
- Third layer in the treatment group consisted of ready-made tubular compression device (Tubulcus) that exerts graduated pressure with the highest compression (30-40 mm Hg) at the ankle, diminishing up the calf, and corresponds to class III compression stockings. It is open-toed and has no heel. Because it is a tubular, knitted, ready-made device, the appropriate pressure is exerted regardless of the fitter's skill. Tubulcus can be reused and laundered at 60°C. Device size was determined for each patient according to the circumferences of the leg measured at the ankle and the largest part of the calf (5 sizes - S, M, L, XL, and XXL - were available). The circumference of the limb was measured every 4 weeks during the treatment and according to these measurements a new pair of Tubulcus was applied. If the measurements of the limb stayed in the initial size, Tubulcus was changed after 6 months.
- The fourth layer was medium-stretch elastic bandage (100% stretch) 15 cm wide and 5 m long (Niva, Novi Sad, Serbia) in a spiral with a 50% overlap. The elastic bandages were applied with the patient in the recumbent position and the foot in dorsal flexion. One pair of elastic bandages was changed regularly every 3 months. The patient was advised to walk 30 minutes after bandaging.

The bandaging systems were worn day and night. Although compliance was not formally assessed, there were no withdrawals from the study because of noncompliance.

Endpoints and statistical analyses. Primary endpoint of the study was complete ulcer healing at 26 and 52 weeks. In cases where the original ulcer closed but a new area developed on the same limb while the original ulcer was still present, the limb was considered to be open until this new area of ulceration had also closed. The definition of ulcer closure was the point at which complete epithelialization of the reference limb occurred.

After 52 weeks of treatment, statistical data were collected and analyzed. The patients were classified in 3 groups: (1) patients with unhealed ulcers, (2) patients with ulcers that healed in less than 26 weeks, and (3) patients with ulcers that healed from 26 to 52 weeks (Table I).

Analysis of potential risk factors associated with the failure of a venous leg ulcer to heal with compression treatment was performed between the patients with healed and unhealed ulcers (Table II). Also, analysis of risk factors were performed between the patients with healed ulcers taking into account time for healing (<26 weeks and 26-52 weeks) in order to define possible indicators of slow healing and favorable prognostic factors for ulcer healing (Table III).

Statistical methods. To assess the magnitude of the effects of given risk factor, single variable logistic regression was performed to estimate odds ratios (ORs) with 95% confidence intervals (CIs). The age was used as continuous, and all other factors as categorical variables.

Reported *P* values are for the Wald statistics, calculated as the estimated regression coefficient divided by its standard error. To calculate adjusted ORs, multivariate logistic regression was performed using unconditional Enter method, where all other risk factors, except the risk factor of interest, were held constant. Independent-samples *t* test was used to compare means between two groups. Mantel-Haenszel χ^2 test and Fisher exact test were performed for the frequencies comparison.

Statistical analyses were conducted using SPSS Version 10.0 software (SPSS Inc, Chicago, Ill).

RESULTS

One hundred eighty-nine patients treated for a venous leg ulcer completed the study. One hundred one patients (53.4%) were women, and 88 patients (46.6%) were men. The mean patient's age at the first office visit was 61.4 years (range, 17-84 years). After 52 weeks of limb compression therapy, 24 ulcers (12.7%) had failed to heal. The healing rate at 26 and 52 weeks of limb compression therapy was 50.26% and 87.3%, respectively.

The median number of previous episodes of ulceration was 4.7 (range, 2-11), the median size of the ulcer was 29.3 cm^2 (range, 5.0-112.0 cm^2), and 83.6% of ulcers were medial, 13.2% were lateral, 2.1% were circumferential, and 1.1% were a combination. The median duration of the ulcer was 6.2 years (range, 4 months-17 years). Sixty-eight patients (36%) had previous DVT.

Pain, edema, pigmentation, and lipodermatosclerosis were present in all 189 patients (100%). Eighty-one patients (42.9%) had previously undergone some surgical procedure (stripping of greater saphenous vein [GSV] was performed in 72 patients (38.1%) and 9 patients (4.8%) underwent SEPS procedure). Mean time from operation until inclusion in the study was 8.9 years (range, 20 months–29 years). During the observation period, neither

Table II. Influence of the risk factors on the failure of a venous leg ulcer to heal

Risk factor	*Unadjusted OR (95% CI)*	P	*Adjusted OR (95% CI)*	P
Ulceration surface >20 cm^2	1.56 (0.66-3.70)	.31	1.32 (0.31-5.61)	.70
Wound duration >12 months	1.49 (0.62-3.54)	.37	1.92 (0.42-8.71)	.40
Female gender	1.03 (0.44-2.44)	.94	0.41 (0.10-1.71)	.22
Age (years)	1.00 (0.96-1.04)	.98	1.05 (0.98-1.13)	.19
Previous operations	0.95 (0.40-2.25)	.90	1.38 (0.32-5.85)	.66
Deep vein thrombosis	1.08 (0.44-2.61)	.87	0.68 (0.17-2.68)	.58
BMI >35	0.64 (0.18-2.29)	.50	1.43 (0.18-11.39)	.74
Reduction in calf circumference	0.50 (0.21-1.18)	.12	0.96 (0.24-3.86)	.96
Daily walking distance <200 m	0.79 (0.17-3.66)	.76	0.89 (0.09-8.44)	.92
Calf:ankle circumference ratio <1.3	19.50 (6.98-54.47)	<.001	42.31 (8.19-218.51)	<.001
Fixed ankle joint and ROM <20°	25.50 (9.03-71.59)	<.001	60.09 (10.80-334.44)	<.001
Wound debrided surgically	0.67 (0.19-2.40)	.54	2.90 (0.42-19.84)	.28
Wound covered with fibrin >50%	1.33 (0.53-3.33)	.54	0.47 (0.09-2.51)	.38
Depth of the wound >2 cm	1.29 (0.44-3.74)	.64	1.59 (0.27-9.40)	.61
Emergence of new skin islets	0.30 (0.07-1.35)	.12	0.38 (0.04-3.43)	.39

OR, Odds ratio; *CI,* confidence interval; *BMI,* body mass index; *ROM,* range of motion.

Table III. Influence of the risk factors on the prolonged time of a venous leg ulcer to heal

Risk factor	*Unadjusted OR (95% CI)*	P	*Adjusted OR (95% CI)*	P
Ulceration surface >20 cm^2	6.04 (3.06-11.94)	<.001	4.43 (1.73-11.34)	.002
Wound duration >12 months	4.82 (2.47-9.39)	<.001	3.49 (1.34-9.11)	.011
Female gender	0.97 (0.52-1.80)	.92	0.65 (0.26-1.65)	.36
Age (years)	0.99 (0.97-1.03)	.97	1.03 (0.98-1.08)	.27
Previous operations	1.34 (0.92-2.50)	.36	1.94 (0.77-4.91)	.16
Deep vein thrombosis	0.64 (0.33-1.24)	.19	0.61 (0.24-1.52)	.29
BMI >35	2.84 (1.25-6.46)	.012	3.85 (1.06-13.94)	.04
Reduction in calf circumference	0.34 (0.17-0.66)	.001	0.20 (0.07-0.54)	.002
Daily walking distance <200 m	3.72 (1.25-11.12)	.019	1.73 (0.31-9.50)	.53
Calf:ankle circumference ratio <1.3	1.76 (0.66-4.75)	.22	3.17 (0.82-12.27)	.09
Fixed ankle joint and ROM <20°	2.00 (0.61-6.59)	.25	4.09 (0.71-23.39)	.11
Wound debrided surgically	2.64 (1.16-6.04)	.021	1.85 (0.58-5.97)	.30
Wound covered with fibrin >50%	7.21 (3.29-15.80)	<.001	8.89 (2.96-26.73)	<.001
Depth of the wound >2 cm	4.35 (1.78-10.60)	.001	1.65 (0.46-5.95)	.44
Emergence of new skin islets	0.34 (0.15-0.77)	.01	0.18 (0.05-0.57)	.004

OR, Odds ratio; *CI,* confidence interval; *BMI,* body mass index; *ROM,* range of motion.

surgery nor sclerotherapy was performed in the patients included in the study. There were no deaths or major complications during the treatment period.

The CEAP classification was as follows:

(a) Clinical-all included limbs had active ulceration (C6);
(b) Etiologic: 58.7% of the patients had primary chronic venous insufficiency (CVI) while 41.3% of the patients were classified as secondary CVI. Secondary etiology was based on ultrasound scan findings.
(c) Anatomic: perforating vein reflux was documented at duplex scanning in 90 patients (47.6%). Association of perforating vein reflux with superficial venous reflux was noted in 32 patients (16.9%). The combination of both superficial and deep reflux with perforating vein reflux was observed in 17 (9%). Deep vein reflux was noted in 50 patients (26.5%).
(d) Pathophysiologic: the pathophysiology identified was reflux in all 189 limbs (100%).

Risk factors associated with prolonged healing time and non-healing of venous ulcers using compression treatment and statistical analysis. To assess the magnitude of the effects of given risk factor on prolonged time of a venous leg ulcer to heal, only data for healed patients were included in logistic regression models and healed within 26 weeks/healed by week 27 to 52 was set as dichotomous dependent variable. Unadjusted analyses revealed several significant associations between failure of wounds to heal within 26 weeks and the measured risk factors. Ulceration area greater than 20 cm^2,wound duration longer than 12 months, BMI value higher than 33 kg/m^2, daily walking distance shorter than 200 meters, history of surgical wound debridement, >50% of wound surface covered with fibrin, and depth of the wound greater than 2 cm significantly increased the odds of not healing within 26 weeks. In contrast, reduction in calf circumference for more than 3 cm during the first 50 days of treatment and emergence of new skin islets on more than 10% of wound surface signif-

icantly reduced the risk of not healing within 26 weeks. Sex, age, previous operations, DVT, CAC ratio less than 1.3, and fixed ankle joint with reduced ankle ROM were not associated with prolonged time of a venous leg ulcer to heal. The association between the failure of wounds to heal within 26 weeks and daily walking distance shorter than 200 meters, surgical wound debridement, and depth of the wound greater than 2 cm became attenuated after adjustment for other risk factors (Table III).

Unadjusted and adjusted analysis revealed significant associations between failure of wounds to heal within 1 year and the CAC ratio less than 1.3 and fixed ankle joint with reduced ankle ROM. All other risk factors were not associated with the failure of wounds to heal (Table II).

According to statistical analysis, all examined risk factors could be classified in four groups:

1. **Factors with no influence on ulcer healing** (sex, age, previous operations, ulcer recurrence).
2. **Favorable prognostic factors for ulcer healing** (ulceration surface <20 cm^2, time since ulcer onset <12 months, reduction in calf circumference >3 cm during the first 50 days of treatment, and emergence of new skin islets on more than 10% of ulcer surface).
3. **Indicators of slow healing** (ulceration surface >20 cm^2, time since ulcer onset >12 months, BMI >33 kg/m^2, walking distance shorter than 200 meters during the day, history of surgical wound debridement, $>50\%$ of wound covered with fibrin, depth of the wound >2 cm).
4. **Risk factors associated with non-healing** (CAC ratio <1.3, fixed ankle joint, and reduced ROM).

DISCUSSION

The goals of compression therapy in the treatment of venous leg ulcerations are ulcer healing, reduction of pain and edema, and prevention of recurrence.[12] Published healing rates of venous ulcers obtained with compression therapy vary widely from 40-95%.[4-10] Unfortunately, a significant number of venous ulcers remain refractory to compression treatment. A possible way to predict non-healing venous leg ulcers is to examine prognostic risk factors that are consistently found in a number of published studies (large wound area and wound of long duration). Patients who possess either or both of these factors are at risk for not healing.[4,13,14] The results of our study do not support these findings. Large and long lasting ulcers could be healed although more time is needed. A decrease in wound size during the first 50 days of treatment is a favorable prognostic factor for healing. According to some studies, approximately 50-70% of patients with venous ulcers and a decrease in wound size during the first month of compression therapy will be healed after 6 months of treatment.[4]

Although some studies[15] have shown that younger age is a favorable prognostic factor for ulcer healing, we could not prove such a relation.

Margolis et al[14] found that venous stripping and the presence of fibrin on more than 50% of the wound surface were the factors associated with the failure of a venous leg ulcer to heal. Our study didn't find any correlation between surgical procedures and ulcer healing while fibrin on more than 50% of the wound surface was an indicator of slow healing.

The most difficult ulcers to treat with compression therapy showing non-healing tendency in our study were the ulcers with deepest presentation (>2 cm in depth) and ulcers with history of surgical debridement. The reason for this is, in our opinion, complete destruction of skin structures and lack of growth factors present in dermis making the healing process more difficult. The emergence of new skin islets on the wound surface, a favorable factor for ulcer healing in our study, never happened in these patients.

A reduction in calf circumference for more than 3 cm during the first 50 days of compression treatment was a favorable factor for fast ulcer healing (<26 weeks). This was especially notable for the patients with calf circumference larger than 40 cm at the beginning of the treatment.

In obese patients, more time is needed for ulcer closure and high BMI (>33 kg/m^2) was an indicator of slow healing. Short walking distance during the day (<200 meters) was also an indicator of slow healing. We think that main reason for this is immobility of these patients and inactivity of their muscle pump. It may be prudent to introduce intermittent pneumatic compression in the treatment of these patients in order to stimulate muscle pump and to improve ulcer healing.

Our study of 1 year of compression treatment is longer than many other studies and this may be the reason in the discrepancy of risk factors. If the analysis had been carried out with non-healing at 6 months of compression treatment, then some risk factors do align with other studies.[4,13,14]

The only independent parameters associated with non-healing of venous ulcers when treated with compression therapy were CAC ratio <1.3 and fixed ankle joint with reduced ankle ROM ($P < .001$).

Fixed ankle joint and reduced ankle ROM is well described as a significant factor in venous ulceration development. Limited ROM was significantly correlated to EF and residual volume fraction measured by air plethysmographic measurement indicating the importance of calf pump function in the development of venous ulceration.[16] Our study strongly supports these findings. One of the main contributors to decreased ankle ROM in patients with CVI is probably inactivity. Bed rest and prolonged inactivity may lead to muscle atrophy, contracture, and degenerative joint disease. Pain with ankle motion could also cause a decrease in voluntary ankle flexion and extension.[16]

CAC ratio <1.3 was also an indicator of non-healing venous ulcers. The vast majority of patients included in our study ($>60\%$) had CAC ratio between the values of 1.6 and 1.9 and over 80% of patients had CAC ratio between the values of 1.4 and 2.2.

In our study, patients with the lowest CAC ratio (1.1-1.2) were the most difficult to treat.

It is interesting that the healing process was more difficult also in those patients who developed a low CAC ratio during the compression treatment (<1.2). This could be an indicator of the patient's inactivity during the treatment. Also, this could mean that too excessive pressure was implemented for too long a time leading to calf muscle atrophy. We think that in this case, compression system with lower interface pressure values should be implemented.

Our results emphasize the importance of the calf muscle pump in the development of venous ulcers, which is in concordance with many published studies indicating the importance of calf muscle pump dysfunction.[17-19]

CONCLUSION

The results obtained in this study suggest that non-healing venous ulcers are related to the impairment of the calf muscle pump. Further trials are necessary to identify the best treatment options especially for non-healing ulcers.

AUTHOR CONTRIBUTIONS

Conception and design: MD, ZS, ZG
Analysis and interpretation: MD, ZS, DB, ZG
Data collection: MD, ZS
Writing the article: MD, DB
Critical revision of the article: MD, ZS, DB, NK, ZG
Final approval of the article: MD, ZS, DB, NK, ZG
Statistical analysis: DB
Obtained funding: NK, ZG
Overall responsibility: MD

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