ORIGINAL RESEARCH

Using Physical Modalities in the Treatment of Venous Leg Ulcers: A 14-year Comparative Clinical Study

Jakub Taradaj, MD, PhD;[1,2] *Andrzej Franek, MD, PhD;*[1] *Edward Blaszczak, MD, PhD;*[1] *Anna Polak, MD, PhD;*[2] *Daria Chmielewska, MD, PhD;*[2] *Piotr Krol, MD, PhD;*[2] *Patrycja Dolibog, MD, PhD*[1]

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From the [1]Department of Medical Biophysics, Medical University of Silesia, Katowice, Poland; [2]Department of Physical Therapy, Academy of Physical Education, Katowice, Poland

Address correspondence to:
Jakub Taradaj, MD, PhD
Medical University of Silesia
Medyków 18, bud. C2 40-752
Katowice, Ligota, Poland
jtaradaj@slam.katowice.pl

Abstract: Venous ulcers are prevalent, challenging wounds; their incidence is rising with the increasing age of the general population. Physical modalities often are used to help heal these chronic wounds. A prospective study was conducted to investigate the application of high-voltage stimulation (HVS), ultrasound therapy (US), low-level laser therapy (LLLT, 810 nm, 65 mW, 4 J/cm^2), and compression therapy (CT), with and without surgical intervention; along with standard of care comprising drug therapy (micronized flavonoid fraction in two 500-mg tablets once daily) and wet dressings of 0.9% sodium chloride on venous leg ulcer healing. *Methods*. The 305-patient study was conducted between 1994 and 2008 among persons with venous ulcers in 3 facilities in Poland. After surgery involving crossectomy, partial [short] stripping of the greater or short saphenous vein, local phlebectomy, and ligation of insufficient perforators, 4 groups of patients were treated with the standard of care drug/dressing therapy and HVS, US, LLLT, or CT, and 1 group received the drug/dressing therapy only. Four non-surgical groups received HVS, US, LLLT, or CT and drug/dressing therapy, and 1 group received drug/dressing therapy only. Changes in wound area and volume were compared among all the groups receiving the various treatments using the Gilman index. In all groups therapy lasted 7 weeks. The computed planimetry method for observation of healing process was used. *Results*. The Gilman index values at 4 weeks were significantly higher in the compression plus surgery compared with other groups ($P = 0.01$). After therapy for patients from the CT + surgery group, the Gilman index was 1.18 cm ($P \leq 0.001$ compared with other groups). The percentage total surface area regression analysis confirmed that compression plus surgery is the most efficient in venous leg ulcer therapy (61.89% reduction after 4 weeks of therapy and 78.19% at the end of study) compared to the other groups ($P \leq 0.001$). The HVS and US appeared useful only in conservatively treated patients ($P < 0.05$). The LLLT did not accelerate reduction of the ulceration surface.
Conclusion. Venous surgery plus compression therapy is the most efficient treatment for venous leg ulcers. Compression therapy should be provided to both surgically and conservatively non-surgically treated patients. High-voltage stimulation and ultrasound therapy are useful methods in conservative treatment of venous leg ulcers. For surgically treated patients, these physical modalities are not effective. Low-level laser therapy is not an efficient method for treating venous leg ulcers.

Venous ulcers represent the most prevalent form of difficult-to-heal wounds and require a substantial number of health care resources for their treatment. The incidence of venous ulceration is rising with the increasing age of the general population. The most common cause of lower extremity ulcers is venous insufficiency, which accounts for nearly 80% of all venous ulcers.[1]

Risk factors for development of venous ulcers include venous disease, obesity, immobility, family history of varicose veins, deep vein thrombosis, previous surgery for varicose veins, and congestive cardiac failure. Up to 50% of patients with chronic venous insufficiency have a history of leg injury.[1,2]

Physical modalities often are used to help heal chronic wounds such as venous leg ulcers. Although clinical studies have examined the effects of compression therapy on leg ulcers,[3-5] the trials evaluating electrical or electromagnetic therapy, ultrasound, and laser irradiation are small, poor-quality, and heterogeneous. According to Cochrane Register of Controlled Trials (CENTRAL) meta-analyses,[6,7] there is no reliable evidence of the benefits of these therapies in the healing of venous leg ulcers; further research is needed.

As such, the authors developed a study to address the following question: Is the application of high-voltage stimulation (HVS), ultrasound therapy (US), low-level laser therapy (LLLT), or compression therapy (CT) efficient for venous leg ulcer healing?

Keypoints

- The most common cause of lower extremity ulcers is venous insufficiency, which accounts for nearly 80% of all venous ulcers.[1]
- Risk factors for development of venous ulcers include venous disease, obesity, immobility, family history of varicose veins, deep vein thrombosis, previous surgery for varicose veins, and congestive cardiac failure.[1,2]
- Physical modalities often are used to help heal chronic wounds such as venous leg ulcers. Although clinical studies have examined the effects of compression therapy on leg ulcers,[3-5] the trials evaluating electrical or electromagnetic therapy, ultrasound, and laser irradiation are small, poor-quality, and heterogeneous.

Material and Methods

Setting. The study was conducted between 1994 and 2008 among patients (divided into groups according to setting and treatment) with venous leg ulcers treated in 3 centers: the General, Vascular, and Transplant Surgery Department at the Medical University of Silesia in Katowice, Poland (groups A, B, C, D, and E); the Dermatology Department of Hospital No. 2 in Bytom, Poland (groups F, H, I, and J); and the Dermatology Department at the Medical University of Silesia in Katowice, Poland (Group G).

Patient inclusion/exclusion criteria. To qualify for participation, patients had to be > 18 years of age, diagnosed with a venous ulcer (i.e., skin breakdown with venous insufficiency symptoms, confirmed by ultrasonography), have an ankle brachial pressure index (ABPI) of 1.0 – 1.3, and need physical therapy. Patients with ulcers of mixed etiology or other than venous, or with associated diseases such as diabetes, arteriosclerosis, and autoimmunologic disorders, were excluded from the study, as were patients who resigned from the study or were contraindicated for physical therapy (Figure 1).

Consent was obtained from the local bioethics commission. Patients gave written consent for participation in the study with the option to resign at any time.

Randomization was based on software. Computer generated random numbers were sealed in sequentially numbered envelopes and group allocation was independent of place and person delivering the treatment. All patients were provided care by a special medical team (vascular surgeons, dermatologists, physiotherapists, and nurses).

Participating facilities provided patients a standard regimen of drug therapy including micronized flavonoid fraction 450 mg diosmin, 50 mg hesperidin, 2 tablets of 500 mg once daily, and gauze dressings saturated in 0.9% sodium chloride changed once a day. Before beginning therapy, patients in groups A, B, C, D, and E received surgery that included crossectomy, partial (short) stripping of the greater saphenous vein (GSV) or short saphenous vein (SSV), local phlebectomy, and ligation of insufficient perforators.

High-voltage stimulation. Patients in group A (5 days after surgical intervention) and group F received high-voltage stimulation (HVS) using a constant current generator (Ionoson, Physiomed Electromedizin AG, Germany). Treatment involved double-peak monophasic impulses of 100 μs at a frequency 100 Hz; voltage was 100 V. The stimulating current produced no motion effects, only a tingling sensation. Electrodes were made of conductive carbon rubber. The active electrode size was matched to the wound size and placed on saline-soaked gauze directly on the wound. The passive electrode was positioned above the knee joint, on the frontal surface of the patient's thigh. HVS was provided for 50 minutes, once a

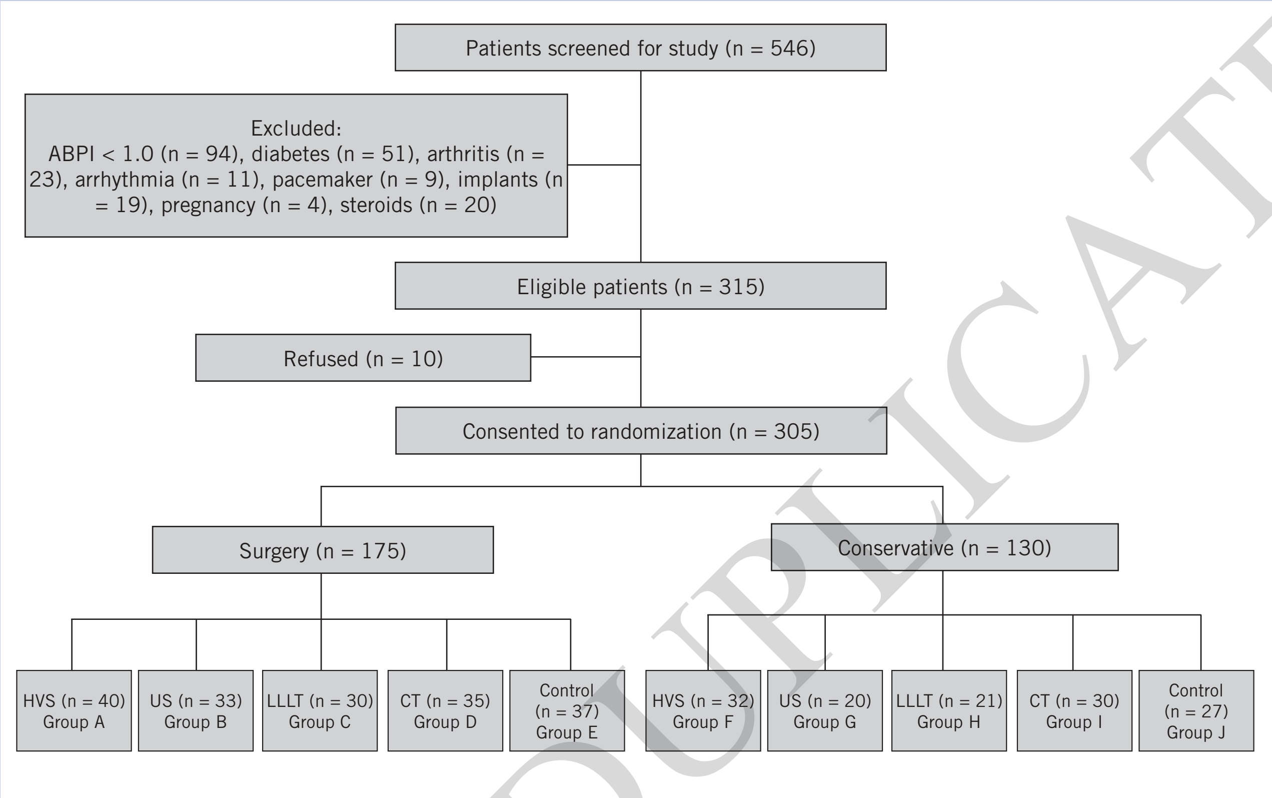

Figure 1. Patient flow through the study.

day, 6 days a week, for the 7 weeks of the study. Treatment always started with cathode stimulation to clean wound pus. After cathode stimulation was provided for 2 weeks, anode stimulation was provided for 5 weeks.

Ultrasound. In addition to drug therapy, patients in group B (5 days after vein surgery) and group G were treated with US therapy. The acoustic beam was generated by a Sonicator 730 apparatus (Mettler Electronics Corp, Anaheim, CA). The power density was 0.5 W/cm^2 (spatial average, temporal average). A pulsed wave with a duty cycle of 1/5 (impulse time = 2 ms, interval = 8 ms) and 1 mHz frequency was used. The procedures were performed in a water bath with a temperature of 34˚ C. The 10 cm^2 US probe was placed 2 cm above the wound. The time duration of a single procedure was dependent on the ulcer size — 1 minute for each 1 cm^2 of ulcer area. The procedures were repeated once daily, 6 days a week, over 7 weeks.

Low-level laser therapy. In addition to drug therapy, patients in group C (5 days after surgery) and H received LLLT. The authors used a 810 nm semiconductor GaAlAs laser (CTL, 1106MX, Elektronika i Elektromedycyna, Otwock, Poland), that emitted a continuous wave. The laser head was a single diode (High Power Devices Inc, North Brunswick, NJ). The cross-section of the beam emitted from the head was a rectangle measuring 2 mm x 5 mm (i.e., 10 mm^2). The laser was wired to a CTL–1202S scanner (Elektronika i Elektromedycyna, Otwock, Poland). The laser beam scanned the wound surface from a distance of 50 cm from the ulcer surface with a compound movement along the ordinate axis at a frequency of 20 Hz and along the abscissa axis at a frequency of 0.5 Hz. The average output of the radiation was 65 mW. The output power was checked every week using Mentor MA10 apparatus (ITAM, Zabrze, Poland). Scanning frequency was 0.5 Hz. The time duration of a single procedure was related to the wound size; therapy was adjusted to obtain an average dose of 4 J/cm^2. The procedures were repeated once daily, 6 days a week, for 7 weeks.

Compression. In addition to drug therapy, patients in groups D (5 days after surgery) and I were treated with medical compression stocking therapy (Sigvaris 702, Gianzoni & Cie AG, Switzerland, certified in Poland) providing 25 mmHg to 32 mmHg of pressure at the ankle. χ

Table 1. Characteristics of patients and ulcers in groups A, B, C, D, and E.

Parameter	A	B	C	D	E	*P*
Number of patients[b]	40	33	30	35	37	> 0.05
Age (years)[b] Average (years) SD (years)	41 – 75 60.03 10.20	47 – 85 61.30 9.48	43 – 82 62.37 10.68	43 – 80 61.43 7.76	40 – 79 60.93 9.67	> 0.05
Gender[a] Women Men	 25 15	 21 12	 17 13	 22 13	 22 15	> 0.05
Body weight (kg)[b] Average (kg) SD (kg)	51 – 95 75.83 11.68	56 – 96 74.52 11.55	51 – 99 72.93 14.04	54 – 111 76.77 14.43	33 – 130 80.87 21.40	> 0.05
Body height (cm)[b] Average (cm) SD (cm)	160 – 184 169.86 6.84	159 – 188 170 7.2	158 – 188 172.59 8.34	156 – 188 173 8.66	142 – 186 169.97 10.03	> 0.05
Localization of ulcers Medial ankle Lateral ankle Anterior crural surface Tibial crural surface	 22 5 10 3	 16 5 9 3	 15 6 7 2	 19 5 8 3	 20 5 9 3	> 0.05
Duration of disorder (months)[b] Average (months) SD (months)	3 - 156 36.14 39.73	4 - 120 35.04 27.19	2 – 120 35.30 28.54	6 - 180 33.50 33.91	4 – 120 35.57 34.32	> 0.05
Initial wound total area[b] (cm^2) Average (cm^2) SD (cm^2)	4.1 – 37.4 22.10 10.07	3.5 – 48.6 24.27 17.12	4.7 – 37.1 24.48 10.52	4.4 – 35.1 22.39 13.11	3.9 – 40.1 24.98 16.19	> 0.05

[a] test χ^2
[b] analysis of variance ANOVA

The stockings were put on the leg at the outpatient clinic every morning, worn for 10 to 12 hours, and removed at night for 7 weeks.

Patients in groups E and J received standard-of-care treatment (drug therapy and saline-soaked gauze bandages) only.

Data collection and analysis

Healing progress was assessed using planimetry (Kurta XGT, Altek Inc, Liberty Lake, WA). Measurements were taken at the beginning of therapy and every 7 days until the end of therapy for a total of 8 measurements. The dynamics of the healing process were assessed using a modified Gilman Index, which is a correlation between changes in surface related to the shape of the wound [8] and "dynamic" percentage changes of the total area and wound volume. These indicators were: Gilman Index (cm), per-

Keypoints

- The study was conducted between 1994 and 2008 among patients (divided into groups according to setting and treatment) with venous leg ulcers treated in 3 centers: the General, Vascular, and Transplant Surgery Department at the Medical University of Silesia in Katowice, Poland (groups A, B, C, D, and E); the Dermatology Department of Hospital No. 2 in Bytom, Poland (groups F, H, I, and J); and the Dermatology Department at the Medical University of Silesia in Katowice, Poland (Group G).
- Healing progress was assessed using planimetry (Kurta XGT, Altek Inc, Liberty Lake, WA). Measurements were taken every week until the end of therapy. The dynamics of the healing process were assessed using a modified Gilman Index, a correlation between changes in surface related to the shape of the wound[8] and "dynamic" percentage changes of the total area and wound volume.

Table 2. Characteristics of patients and ulcers in groups F, G, H, I, and J.

Parameter	F	G	H	I	J	*P*
Number of patients[b]	32	20	21	30	27	> 0.05
Age (years)[b] Average (years) SD (years)	39 – 90 68.13 4.81	44 – 85 62.12 10.02	47 – 81 61.02 8.18	40 – 78 62.63 8.71	43 - 79 61.13 8.37	> 0.05
Gender[a] Women Men	 20 12	 12 8	 13 8	 20 13	 17 10	> 0.05
Body weight (kg)[b] Average (kg) SD (kg)	51 – 112 73.92 12.61	54 – 93 74.33 12.02	55 - 92 72.01 10.83	50 – 99 74.88 16.03	50 - 94 75.44 12.43	> 0.05
Body height (cm)[b] Average (cm) SD (cm)	152 – 186 163.61 4.60	160 – 187 172.89 9.08	158 - 187 172.17 8.08	166 – 187 172.22 6.66	152 – 188 169.44 9.03	> 0.05
Localization of ulcers Medial ankle Lateral ankle Anterior crural surface Tibial crural surface	 16 6 8 2	 10 3 5 2	 10 3 5 3	 14 5 8 3	 9 4 4 3	> 0.05
Duration of disorder (months)[b] Average (months) SD (months)	2 - 216 42.19 38.13	10 - 100 30.99 20.09	6 - 100 33.84 23.09	2 - 120 34.42 25.91	4 – 136 30.57 24.12	> 0.05
Initial wound total area[b] (cm^2) Average (cm^2) SD (cm^2)	5.5 – 33.4 22.77 8.57	8.2 – 31.1 18.47 10.11	8.1 – 44.8 17.92 12.02	3.8 – 35.4 20.22 12.14	9.1 – 40.1 20.18 17.80	> 0.05

[a] test χ^2
[b] analysis of variance ANOVA

centage change of the total surface area (%), and percentage change of the volume and linear dimensions of ulcers — ie, percentage change of the length and width.[9]

Study results were described using statistical methods. In comparing individual parameters characterizing study groups, the analysis of variance ANOVA for countable variables and Pearson's chi-squared test (χ^2) for quality variables were used. To compare healing dynamics between groups, analysis of variance ANOVA (level of significance $P < 0.05$) was implemented. The correlation between surface area, volume, and linear dimensions was determined using the Spearman correlation rank index (level of significance $P < 0.05$).

Results

The 305 participants included 175 surgical patients in groups A, B, C, D, and E treated at the General, Vascular, and Transplant Surgery Department at the Medical University of Silesia in Katowice, Poland; 110 patients from groups F, H, I, and J treated at the Dermatology Department of the Hospital No. 2 in Bytom, Poland; and 20 patients from group G at the Dermatology Department at the Medical University of Silesia in Katowice, Poland. The analyzed groups were homogeneous in terms of all patient characteristics (Tables 1 – 3). The groups were well matched for age, weight, height, gender, ulcer localization, ulcer chronicity, ulcer size, CEAP classification, and number of smokers.

The Gilman index values at 4 weeks were significantly higher (demonstrating progress toward healing) in the compression plus surgery group compared with other groups ($P = 0.01$). After therapy for patients from group D (CT + surgery), Gilman index was 1.18 cm ($P \leq 0.001$) compared with other groups. For sur-

Table 3. Classification of CVI in all groups.

CEAP	A	B	C	D	E	F	G	H	I	J	*P*
$C_6E_PA_{S2,3}P_R$	12	11	10	12	12	8	9	9	9	10	> 0.05
$C_6E_PA_{S4}P_R$	6	5	5	6	7	5	3	3	5	4	> 0.05
$C_6E_PA_{S2D13}P_R$	7	5	5	5	5	4	3	3	5	4	> 0.05
$C_6E_PA_{S3D13}P_R$	6	4	4	4	5	6	2	2	4	4	> 0.05
$C_6E_PA_{S2,3D13,14}P_{18}P_R$	6	6	4	5	5	6	2	3	4	4	> 0.05
$C_6E_SA_{S2,3D13,14}P_{18}P_R$	3	2	2	3	3	3	1	1	3	1	> 0.05
Test: χ^2											

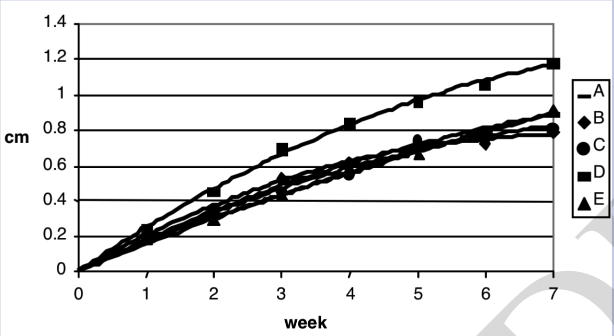

Figure 2. Dynamics of change of the Gilman index in groups A, B, C, D, and E.

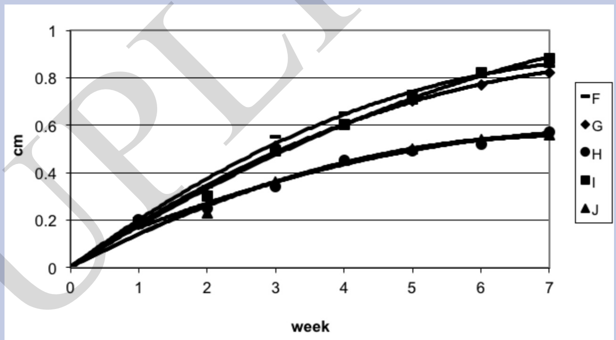

Figure 3. Dynamics of change of the Gilman index in groups F, G, H, I, and J.

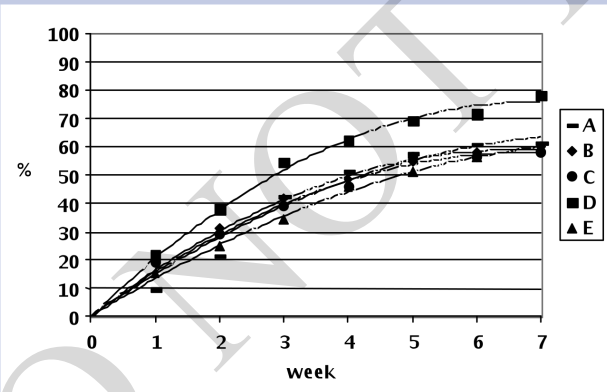

Figure 4. Dynamics of change of the percentage of total surface area in groups A, B, C, D, and E.

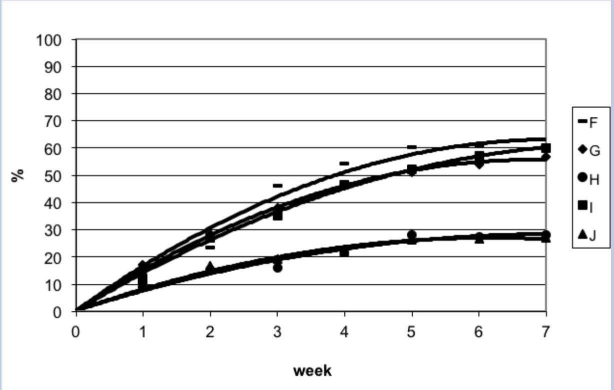

Figure 5. Dynamics of change of the percentage of total surface area in groups F, G, H, I, and J.

gically treated patients, the Gilman indices were: 0.89 cm in group A (HVS); 0.79 cm in group B (US); 0.81 cm in group C (LLLT); and 0.92 cm in group E (control). For non-surgically treated patients, Gilman indices were: 0.85 cm in group F (HVS); 0.82 cm in group G (US); 0.57 cm in group H (LLLT); 0.88 cm in group I (CT); and 0.92 cm in group J (control). Analysis for Gilman index showed laser treatment after surgery had the least effect on groups C and H compared with other physical factors both in surgically and non-surgically treated patients (groups A, B, C, E, F, G, and I versus groups H and J, $P = 0.01$). There were no statistically significant differences in weekly changes of the Gilman index ($P > 0.05$) between groups A, B, C, E, F, G, and I. The dynamics of change of the Gilman indices in all groups are presented in Figures 2 and 3.

Table 4. Dynamics of change of the Gilman index.

Parameter	Group	1 week	2 wks.	3 wks.	4 wks.	5 wks.	6 wks.	7 wks.
Average change of the Gilman index [cm]	A	0.19	0.31	0.51	0.61	0.71	0.80	0.89
	B	0.22	0.36	0.53	0.63	0.69	0.72	0.79
	C	0.20	0.32	0.45	0.55	0.74	0.76	0.81
	D	0.23	0.45	0.69	0.84	0.96	1.06	1.18
	E	0.18	0.29	0.43	0.59	0.66	0.75	0.92
	F	0.18	0.34	0.55	0.65	0.74	0.81	0.85
	G	0.20	0.30	0.51	0.60	0.70	0.77	0.82
	H	0.20	0.25	0.34	0.45	0.49	0.52	0.57
	I	0.19	0.30	0.49	0.60	0.71	0.82	0.88
	J	0.19	0.23	0.36	0.45	0.50	0.54	0.56
Analysis of varaince ANOVA *post hoc* Tukey's test	*P* (A)	0.001	0.03	0.002	> 0.05	> 0.05	> 0.05	> 0.05
	P (B)	≤ 0.001	0.03	0.01	> 0.05	> 0.05	> 0.05	> 0.05
	P (C)	≤ 0.001	0.03	0.03	> 0.05	0.004	> 0.05	> 0.05
	P (D)	≤ 0.001	≤ 0.001	≤ 0.001	0.01	0.04	0.05	0.04
	P (E)	≤ 0.001	0.03	0.02	0.01	> 0.05	> 0.05	0.04
	P (F)	≤ 0.001	0.03	0.002	> 0.05	> 0.05	> 0.05	> 0.05
	P (G)	≤ 0.001	0.03	0.002	> 0.05	> 0.05	> 0.05	> 0.05
	P (H)	≤ 0.001	> 0.05	0.04	> 0.05	> 0.05	> 0.05	> 0.05
	P (I)	≤ 0.001	0.03	0.002	> 0.05	> 0.05	> 0.05	> 0.05
	P (J)	≤ 0.001	> 0.05	0.01	> 0.05	> 0.05	> 0.05	> 0.05

Table 5. Dynamics of change of the percentage total surface area.

Parameter	Group	1 week	2 wks.	3 wks.	4 wks.	5 wks.	6 wks.	7 wks.
Average change of total surface area [%]	A	9.41	21.08	42.32	51.23	57.88	60.23	60.99
	B	18.96	30.79	41.92	48.40	54.33	57.77	60.01
	C	18.80	28.65	38.89	45.63	56.19	56.63	57.85
	D	21.47	37.87	54.30	61.89	68.98	71.22	78.19
	E	14.92	24.35	34.31	45.51	51.00	56.14	60.06
	F	10.20	23.39	46.02	54.11	60.03	60.89	61.02
	G	16.89	28.44	38.02	45.88	50.87	53.66	56.67
	H	8.89	15.00	18.88	21.44	26.05	27.04	27.85
	I	12.00	26.88	35.04	46.44	52.03	57.02	59.66
	J	8.99	16.72	19.01	21.88	26.00	26.49	26.88
Analysis of varaince ANOVA *post hoc* Tukey's test	*P* (A)	0.04	0.02	0.001	0.04	> 0.05	> 0.05	> 0.05
	P (B)	0.01	0.02	0.03	0.05	> 0.05	> 0.05	> 0.05
	P (C)	0.01	0.02	0.03	0.05	0.04	> 0.05	> 0.05
	P (D)	0.001	0.01	0.01	0.04	0.04	> 0.05	0.04
	P (E)	0.02	0.04	0.04	0.03	0.04	> 0.05	> 0.05
	P (F)	0.04	0.02	0.001	0.04	> 0.05	> 0.05	> 0.05
	P (G)	0.01	0.02	0.03	0.05	> 0.05	> 0.05	> 0.05
	P (H)	0.04	0.04	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05
	P (I)	0.02	0.04	0.04	0.03	0.04	> 0.05	> 0.05
	P (J)	0.04	0.04	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

Table 4 shows the most dynamic increase of Gilman index was in group D ($P \leq 0.001$ during the first 3 weeks of therapy; $P = 0.01$ after the fourth week; $P = 0.04$ after the fifth week; $P = 0.05$ after the sixth; and $P = 0.04$ at the end of treatment). In other groups, the healing process was not as dynamic. The percentage of total surface area regression analysis confirmed that compression plus surgery is the most efficient in venous leg ulcer therapy (61.89% reduction after 1 month of therapy and 78.19% at the end of the study) compared to other groups ($P \leq 0.01$). The HVS and US appeared useful only in conservatively treated patients. The LLLT did not accelerate reduc-

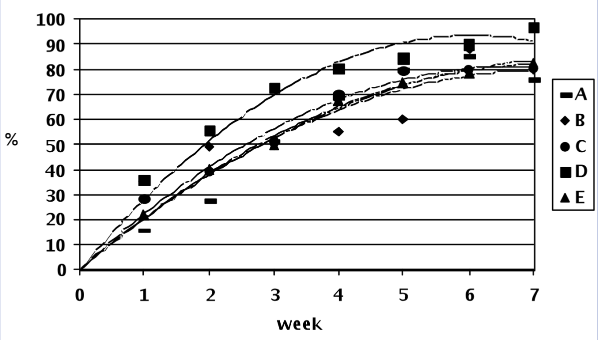

Figure 6. Dynamics of change of the volume in groups A, B, C, D, and E.

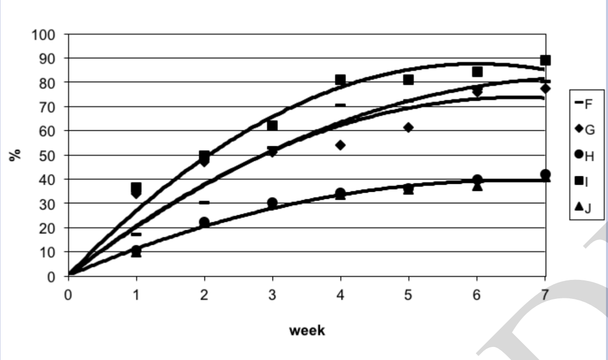

Figure 7. Dynamics of change of the volume in groups F, G, H, I, and J.

tion of the ulceration surface (Figures 4, 5). At the end of the study, the comparison in terms of percentage of wound surface area change indicated a significant difference between groups.

Table 5 shows that the most dynamic decrease of wound surface was in group D.

A less intensive process was observed in groups A, B, C, E, F, G, and I. The least favorable results were in groups H and J.

The analysis of changes of the percentage of volume confirmed compression stockings are efficient both in surgically and conservatively treated patients. Other interventions in surgically treated patients appeared to have little effect, but HVS and US appeared as effective as compression stockings in groups not having surgery. The LLLT did not accelerate the reduction of the ulceration volume (Figures 7, 8). At the end of the treatment, the comparison in terms of percentage volume indicated a significant difference between group D and the other groups (Table 6).

The most rapid wound volume reduction was in group D ($P \leq 0.001$), which healed after nearly 3 weeks of ther-

Table 6. Comparison in terms of percentage wound surface area change and volume[b].

Parameter	Comparisons
Total surface area	• A and D (60.99% vs. 78.19% $P = 0.002$) • B and D (60.01% vs. 78.19% $P = 0.002$) • C and D (57.85% vs. 78.19% $P \leq 0.001$) • D and E (78.19% vs. 60.06% $P = 0.002$) • D and F (78.19% vs. 61.02% $P = 0.002$) • D and G (78.19 vs. 56.67% $P \leq 0.001$) • D and H (78.19 vs. 27.85% $P \leq 0.001$) • D and I (78.19% vs. 59.66% $P = 0.002$) • D and J (78.19% vs. 26.88% $P \leq 0.001$) • A and H (60.99% vs. 27.85% $P \leq 0.001$) • A and J (60.99% vs. 26.88% $P \leq 0.001$) • B and H (60.01% vs. 27.85% $P = 0.01$) • B and J (60.01 vs. 26.88% $P = 0.01$) • C and H (57.85% vs. 27.85% $P = 0.01$) • C and J (57.85% vs. 26.88% $P \leq 0.001$) • E and H (60.06% vs. 27.85% $P \leq 0.001$) • E and J (60.06% vs. 26.88% $P \leq 0.001$) • F and H (61.02% vs. 27.85% $P \leq 0.001$) • F and J (61.02% vs. 26.88% $P \leq 0.001$) • G and H (56.67% vs. 27.85% $P \leq 0.001$) • G and J (56.67% vs. 26.88% $P \leq 0.001$) • H and I (27.85% vs. 59.66% $P \leq 0.001$) • J and I (26.88% vs. 59.66% $P \leq 0.001$)
Total volume	• A and D (76.11% vs. 97.03% $P = 0.003$) • B and D (80.33% vs. 97.03% $P = 0.004$) • C and D (80.12% vs. 97.03% $P = 0.004$) • D and E (97.03% vs. 82.41% $P = 0.003$) • D and F (97.03% vs. 80.22% $P = 0.003$) • D and G (97.03 vs. 77.22% $P = 0.003$) • D and H (97.03 vs. 41.85% $P \leq 0.001$) • D and I (97.03% vs. 81.33% $P = 0.03$) • D and J (97.03% vs. 40.88% $P \leq 0.001$)

Table 7. Dynamics of change of the percentage volume.

Parameter	Group	1 week	2 wks.	3 wks.	4 wks.	5 wks.	6 wks.	7 wks.
Average change of the volume [%]	A	15.84	27.62	51.62	68.47	69.73	75.58	76.11
	B	35.48	48.72	50.01	55.09	60.02	78.00	80.33
	C	28.12	47.42	64.04	77.22	78.89	80.01	80.12
	D	35.77	66.77	72.32	80.30	90.23	94.22	97.03
	E	22.03	39.74	49.72	67.53	74.60	78.58	82.41
	F	17.03	30.03	52.88	70.33	72.00	77.04	80.22
	G	33.66	47.03	50.99	53.77	61.01	75.89	77.22
	H	10.33	22.05	30.19	34.24	35.99	39.63	41.85
	I	36.44	49.66	62.04	80.74	80.89	81.01	81.33
	J	9.57	21.97	29.32	33.33	35.78	36.92	40.88
Analysis of varaince ANOVA *post hoc* Tukey's test	*P* (A)	0.01	0.02	0.001	0.001	> 0.05	> 0.05	> 0.05
	P (B)	≤ 0.001	0.002	> 0.05	> 0.05	> 0.05	0.03	> 0.05
	P (C)	≤ 0.001	≤ 0.001	≤ 0.001	0.002	> 0.05	> 0.05	> 0.05
	P (D)	≤ 0.001	≤ 0.001	≤ 0.001	> 0.05	> 0.05	> 0.05	> 0.05
	P (E)	≤ 0.001	≤ 0.001	0.04	≤ 0.001	> 0.05	> 0.05	> 0.05
	P (F)	0.01	0.02	≤ 0.001	≤ 0.001	> 0.05	> 0.05	> 0.05
	P (G)	≤ 0.001	0.002	> 0.05	> 0.05	> 0.05	0.03	> 0.05
	P (H)	0.03	0.03	0.03	> 0.05	> 0.05	> 0.05	> 0.05
	P (I)	≤ 0.001	0.03	0.03	0.03	> 0.05	> 0.05	> 0.05
	P (J)	0.03	0.03	0.03	> 0.05	> 0.05	> 0.05	> 0.05

Keypoints

- The most rapid wound volume reduction was in group D ($P \leq 0.001$), which healed after nearly 3 weeks of therapy. In other groups, the healing process took longer, lasting mainly 4 weeks to 5 weeks.
- In all comparative groups, the change of wound area occurred simultaneously with changes in volume and linear dimensions. This was beneficial for wound healing, which progressed steadily after all examined physical factors.

apy. In other groups, the healing process took longer, lasting mainly 4 weeks to 5 weeks. Details connected with the dynamics of the healing process appear in Table 7.

In all comparative groups, the change of wound area occurred simultaneously with changes in volume and linear dimensions. This was beneficial for wound healing, which progressed steadily after all examined physical factors (Table 8).

Discussion

The authors' results indicated medical compression stockings (25 mm H to 32 mm Hg at the ankle) applied in patients with venous leg ulcers provide effective physical modality for wound healing. In the authors previous study,[9] medical compression stockings (group A) were compared with 2-layer short-stretch bandaging (group B). Of the 40 patients in group A and the 40 patients in group B, 15 (37.50%) and 5 (12.50%), respectively, healed completely ($P = 0.01$). For patients with isolated superficial reflux, the healing rates at 2 months were 10/22 healed (45.45%) in group A and 4/22 healed (18.18%) in group B ($P = 0.01$). For patients with superficial plus deep reflux, the healing rates were 5/18 healed (27.77%) in group A and only 1/18 healed (5.55%) in group B ($P = 0.002$). The authors concluded medical compression stockings are useful therapy to enhancing venous leg ulcer healing for patients either with superficial, or superficial plus deep reflux. Bandages are less effective, especially for patients with superficial plus deep reflux, where the efficiency of applied compression appeared dramatically low.

Other authors confirm the effectiveness of compression therapy of various types. In a single-centered observational study,[10] patients with venous leg ulcers on 1 or both legs were treated with a 2-component compression system for up to 12 months or until the ulcer healed. The only exclusion criteria were an ABPI < 0.8, immobilization, and limited ankle joint flexibility. Study assessment parameters included ulcer size on entry into the study, the presence of skin irritations, occurrence of adverse events, and ulcer recurrence. The primary outcome measure was the mean time to healing. In total, 136 patients were included. Baseline median ulcer duration was 7.5 months and the baseline median size was 4.3 cm^2. The

Table 8. Correlation between total surface area, volume and linear dimensions of ulcers.

Parameter	Group	1 week	2 wks.	3 wks.
Change of total surface area	Change of length	A	0.983	$P \leq 0.001$
		B	0.962	$P \leq 0.001$
		C	0.878	$P \leq 0.001$
		D	0.984	$P \leq 0.001$
		E	0.981	$P \leq 0.001$
		F	0.877	$P \leq 0.001$
		G	0.822	$P \leq 0.001$
		H	0.679	$P = 0.002$
		I	0.834	$P \leq 0.001$
		J	0.664	$P = 0.002$
Change of total surface area	Change of width	A	0.898	$P \leq 0.001$
		B	0.965	$P \leq 0.001$
		C	0.861	$P \leq 0.001$
		D	0.994	$P \leq 0.001$
		E	0.972	$P \leq 0.001$
		F	0.855	$P \leq 0.001$
		G	0.812	$P \leq 0.001$
		H	0.701	$P \leq 0.001$
		I	0.799	$P \leq 0.001$
		J	0.634	$P = 0.002$
Change of total surface area	Change of volume	A	0.743	$P \leq 0.001$
		B	0.781	$P \leq 0.001$
		C	0.545	$P = 0.003$
		D	0.878	$P \leq 0.001$
		E	0.832	$P \leq 0.001$
		F	0.676	$P = 0.002$
		G	0.597	$P = 0.002$
		H	0.544	$P = 0.003$
		I	0.622	$P = 0.002$
		J	0.533	$P = 0.003$

average reduction in total ulcer surface was 2.9 cm^2 per month. In these patients, 90.4% wounds healed after 12 months; the mean healing time was 3 months.

Milic et al[11] conducted a clinical trial with 131 patients (72 women, 59 men) with venous leg ulcers (ulcer surface > 3 cm^2; duration > 3 months) who were randomized into 3 groups: group A, 42 patients who were treated using an open-toed, elastic, class III compression device knitted in tubular form (Tubulcus); group B, 46 patients treated with a multi-component bandaging system comprised of Tubulcus and 1 elastic bandage (15 cm wide and 5 cm long with 200% stretch); and group C, 43 patients treated with the multi-component bandaging system comprised of Tubulcus and 2 elastic bandages. The healing rate during the 26-week treatment period was 13/42 (25%) in group A; 31/46 (67.4%) in group B; and 32/43 (74.4%) in group C.

Brizzio et al[12] compared the proportion and rate of healing, pain, and quality of life between using Sigvaris prototype medical compression stockings (MCS) (Sigvaris Management AG, Winterthur, Switzerland) providing 15-25 mm Hg at the ankle and multi-layer short-stretch bandages. In both groups, pads were placed above incompetent perforating veins in the ulcer area. The initial static pressure between the dressing-covered ulcer and the pad was 29 mm Hg and 49 mm Hg with MCS and bandages, respectively. No difference was noted in dynamic pressure measurements. Compression was maintained daily and nightly and wraps were changed every week. The primary endpoint was healing within 90 days. Secondary endpoints were healing within 180 days, time to healing, pain (on a Likert scale, assessed weekly), and monthly quality-of-life scores (Chronic Venous Insufficiency Quality of Life questionnaire). Of the 55 patients who completed the study, 28 used MCS and 27 used bandages. Ulcers were recurrent (48%), of long duration (mean, 27 months), and large (mean, 13 cm^2). All but 1 patient had deep venous reflux and/or incompetent perforating veins in addition to trunk varices. Characteristics of patients and ulcers were evenly distributed (exception: more edema in the MCS group; $P = 0.019$). Healing within 90 days was observed in 36% of patients using MCS and in 48% using bandages ($P = 0.35$). Healing within 180 days was documented in 50% of MCS patients and in 67% with bandages ($P = 0.21$). Time to healing was identical. Initially, pain scored 44 and 46, respectively (on a scale where 100 = maximum and 0 = no pain) and decreased within the first week to 20 and 28, respectively, in the MCS and bandage groups. No difference in quality of life was noted between the treatment groups. In both groups, pain at 90 days had decreased by half, independent of completion of healing. Physical, social, and psychic impairment improved significantly only in patients with healed ulcers. The authors concluded the effect of compression with MCS was not different from that of compression with bandages. Both treatments alleviated pain promptly. Quality of life improved only in patients whose ulcers had healed.

In the present study, the HVS and US appeared to be efficient methods to aid healing progress, but only in non-surgical treatment of venous leg ulcers. Results from the authors' previous studies[13] demonstrated that electrical stimulation is an efficient method to help heal non-surgically treated venous leg ulcers and that electrical therapy has little healing value in venous leg ulcer patients after surgical treatment.

Junger et al[14] investigated 39 patients in a prospective, placebo-controlled, double-blind study on the effect of low-frequency pulsed current (Dermapulse, Gerromed, Hamburg, Germany) on healing in chronic venous ulcers during a 4-month course of treatment. The following criteria were recorded: ulcer size, pain, capillary density, and transcutaneous oxygen partial pressure. In the stimulated group, the ulcers healed. In the placebo group, 2 ulcers healed. Ulcer size was reduced significantly (P = 0.04) in each group; the difference of ulcer area reduction between the stimulated and the placebo group was not significant. Capillary density in the ulcer increased in both groups. In the stimulated group, electrical stimulation led to rapid and lasting reduction of pain (P = 0.049). By calculating for just the subgroup of outpatients (n = 13), this treatment method was economically effective. In Junger et al's[14] opinion, electrical stimulation seems to be a viable treatment option for therapy-resistant venous leg ulcers.

Kavros and Schenck[15] analyzed the medical records of 51 patients with 1 or more of the following conditions: diabetes mellitus, neuropathy, limb ischemia, chronic renal insufficiency, venous disease, and/or inflammatory connective tissue disease. All of the patients had lower-extremity ulcers, 20% had a history of amputation, and 65% had diabetes. Of all the wounds, 63% had a multifactorial etiology and 65% had associated transcutaneous oximetry levels < 30 mm Hg. The mean treatment time of wounds during the baseline standard of care (phlebotropic therapy) control period versus the noncontact low-frequency US therapy period was 9.8 weeks versus 5.5 weeks (P < 0.001). Initial and end measurements were recorded, and percent of volume reduction of the wound was calculated. The mean percent volume reduction in the baseline standard of care control period versus the noncontact (water medium) low-frequency ultrasound therapy period was 37.3% versus 94.9% (P < 0.001). The authors concluded that using low-frequency ultrasound improved the rate of healing and closure in recalcitrant lower-extremity ulcerations.

In this study, LLLT (810 nm, 65 mW, 4 J/cm^2) did not have any stimulatory effect on healing of venous leg ulcers either in surgically or non-surgically treated patients. The findings are consistent with several critical randomized controlled trials. In a placebo-controlled study using a GaAs laser, Malm and Lundeberg[16] reported no differences in results between the 2 groups investigated. After 1 month, they observed 1 completely healed ulcer in the LLLT group and none in control. After 2 months they noted 2 completely healed ulcer in the LLLT group and 2 in control. After 3 months they observed 4 completely healed ulcers in the LLLT group and 4 in control. Kokol et al[17] conducted controlled work using a 685 nm laser. They measured venous leg ulcers planimetrically at baseline (day 1), at the end of therapy (day 28), and 2 months later (day 90). There were no statistically significant differences in reduction of wound size between the examined groups.

Keypoints

- The authors' results indicated that medical compression stockings (25 mm H to 32 mm Hg at the ankle) applied in patients with venous leg ulcers provide effective physical modality for wound healing.
- The HVS and US appeared to be efficient methods to aid healing progress, but only in non-surgical treatment of venous leg ulcers.

Limitations

The study length (14 years) could have introduced some variability in methods and procedures. At the same time, the authors were unable to follow patients for a sufficient amount of time to observe healing. Although study outcomes were consistent in each treatment group, the absence of blinding and use of placebo in the control groups is a limitation of this study that may affect the generalizability of the findings.

Conclusion

Venous surgery plus compression therapy is the most efficient treatment of venous leg ulcers. The compression therapy should be provided to both surgically and conservatively treated patients. High-voltage stimulation and ultrasound therapy are useful methods in conservative treatment of venous leg ulcers. For surgically treated patients, these physical therapies are not effective. Low-level laser therapy (810 nm, 65 mW, 4 J/cm²) is not an efficient physical method in treatment of venous leg ulcers.

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