

# Sequential gradient pneumatic compression enhances venous ulcer healing: A randomized trial

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*The treatment of venous ulcers has remained largely unchanged for centuries. The application of properly applied graduated compression bandages, the use of graduated compression stockings, and surgery have been shown to achieve healing. However, some ulcers persist despite appropriate management. A randomized study was undertaken to compare two regimens of treatment for such patients. Both regimens included ulcer debridement, cleaning, nonadherent dressing, and graduated compression stockings. In one regimen, sequential gradient intermittent pneumatic compression was applied for 4 hours each day. Only one of 24 patients in the control group had complete healing of all ulcers compared with 10 of 21 patients healed in the intermittent pneumatic compression group. The mediari rate of ulcer healing in the control group was 2.1% area per week compared to 19.8% area per week in the intermittent pneumatic compression group. The results indicate that sequential gradient intermittent pneumatic compression is beneficial in the treatment of venous ulcers. (SURGERY 1990;W8:871-5.)*

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VENOUS ULCERATION IS A COMMON PROBLEM in many Western countries. In the United Kingdom it is estimated that over a half million patients currently receive treatment for it.<sup>1,2</sup> In Switzerland a survey of over 4000 chemical plant workers found a prevalence of severe venous insufficiency including venous ulceration, which exceeded 1% of the population studied.<sup>3</sup> Data collected within a venous disease study of a Michigan community and extrapolated to present adult population figures of the United States indicate that approximately 800,000 Americans have or have had venous ulceration.<sup>4</sup> The management of venous ulcers presents a large problem to the community nursing services and consumes considerable health care resources.

Traditionally many approaches to the treatment of venous ulcers have focused on dressing systems that are

directed to the wound healing process itself, as opposed to the underlying hemodynamic problem associated with chronic venous hypertension. Some authors have found an advantage in a particular topical application,<sup>3</sup> others have failed to find any effect of a dressings on wound healing.<sup>6</sup> The use of elastic compression has been assessed as a treatment for chronic venous disease, and several authors have found this effective in correcting the hemodynamic abnormality in this disease.<sup>7,9</sup> In many cases, particularly in older patients, the effective level of compression required is greater than that which the patient can tolerate. Either bandages are said to be too tight or stockings of a sufficiently high compression grade cannot be applied because the patient has insufficient strength to pull them on. As a consequence, alternatives have been sought to facilitate the application of sufficient compression and yet maintain patient compliance. One alternative approach is the use of intermittent pneumatic compression (IPC). The use of IPG as a prophylactic modality for the prevention of deep venous thrombosis is well documented.<sup>10</sup> However, the application of IPC to the treatment of venous ulceration, although intriguing in concept, is supported by studies that are limited in size and lack a controlled design.<sup>10</sup> " Therapeutic application of IPC is designed to reduce

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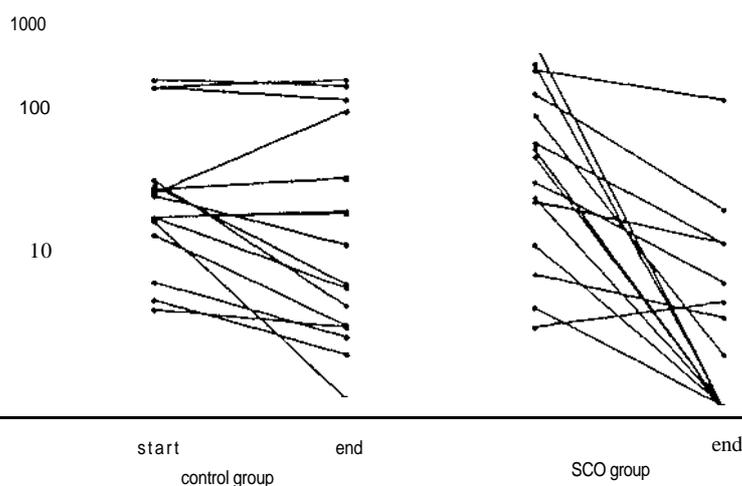


Fig. 1. Comparison of ulcer areas in the two groups at the start and end of the study period plotted by use of a logarithmic vertical axis to facilitate comparison. *Ulcer area* refers to the total area of ulceration per patient. The *horizontal bars* mark the group median values.

venous stasis by promoting venous blood flow and has been shown to enhance systemic fibrinolytic activity.<sup>12</sup> As chronic venous hypertension and fibrin deposition are known to contribute to the pathogenesis of venous ulceration,<sup>13,14</sup> the application of IPC has been suggested as an appropriate modality of treatment for this condition.

A randomized controlled study to assess the effect of IPC on the healing of venous ulcers as compared with a standard treatment regimen has not been reported. It was the purpose of this study to evaluate objectively the role to IPC as an additional treatment for venous ulceration.

#### PATIENTS AND METHODS

Patients attending the venous outpatient clinic for the management of their venous ulcers were assessed for admission to the study. Only patients in whom ulceration had been present for a minimum of 12 weeks were considered. Informed consent was obtained. All patients were formally assessed for evidence of venous insufficiency with photoplethysmography, Doppler ultrasonography, strain gauge plethysmography, and duplex ultrasonic imaging. The patients in this study were all shown to have deep venous insufficiency as the cause of the ulceration. Patients with significant peripheral vascular disease, defined as an ankle/brachial systolic index of less than 0.9 were excluded. In addition, patients with evidence of congestive cardiac failure resulting in dyspnea on effort (New York Heart Association 2A or greater) were excluded. Those patients whose ulcer was

attributable to causes other than deep venous insufficiency were excluded from the study.

Patients were randomly allocated into two groups, a control group and a pneumatic compression group according to the toss of a coin. In both groups the ulcers were debrided, cleaned, and nonadherent dressings were applied. In cases of heavy exudate absorbent padding was applied, and the dressing was held in place with adhesive tape. In addition, both groups received graduated compression stockings, which exerted 30 to 40 mm Hg compression at the ankle, applied directly over the dressing. This means of treatment reflects the current practice in our clinic and has been found effective in the management of venous ulceration.

The pneumatic compression group was provided with a sequential compression device (SCD) (The Kendall Healthcare Products Company, Mansfield, Mass.), which they used on a daily basis in their homes. Full verbal and written instructions on the proper application of the device were given. The SCD was applied over the stockings. Both groups received standard advice in which they were instructed to elevate their legs whenever they were sitting as part of the standard regimen.

Patients were studied until the ulcer healed or for a total period of 3 months. The patients were reviewed weekly, and the wound was measured. Ulcer areas were traced onto a celluloid sheet and then measured. The sheet was held firmly in place on the leg, and the ulceration was traced with a fine pen. At the end of the study the tracings were measured by use of a sonic digitizer (Scientific Accessories Corporation Southport, Conn.)

Table I. Distribution of ages and duration of ulceration in the study groups

Group	No. of patients	Mean age (yr) and range	Mean duration of ulcer (yr) and range
Control	24	58 (42-76)	3.5 (0.5-22)
SCD	21	53 (50-78)	3.9 (0.5-15)

connected to a BBC microcomputer (Acorn Computer, Cambridge, England) with software designed for that purpose. The traced ulcer area was digitized with a pen-type stylus and displayed on the computer screen, providing a check that the tracing had been correctly digitized. The computer calculated the area and circumference of the tracing. This technique has been shown to agree with other established methods of measuring venous ulcer areas.<sup>15</sup>

Treatment protocol. The initial visit included history and vascular laboratory examination, randomization to control or experimental group, measurement of ulcer area, stocking sizing with instruction, and SCD application with instruction for home use for those randomized to experimental group.

Subsequent visits included weekly dressing changes with recording of additional dressings by district nurse, and ulcer measurement at 2, 4, 8, and 12 weeks then at 4 weekly intervals until the ulcer healed or to 3 months. Reinforcement of standard instructions to avoid periods of standing and elevate limbs when sitting.

Statistical analysis of data was undertaken by means of the Mann-Whitney U test to investigate the differences between subject groups and Fisher's exact probability test to assess distributions. Neither test assumes Gaussian distribution of data.

## RESULTS

The mean ages in the control group and the SCD group were 58 and 53 years, respectively. The mean duration of ulceration was 3.5 and 3.9 years, respectively, for the two groups. There were no significant differences in age or duration of ulceration between the two groups (Table I). Vascular laboratory assessment demonstrated that all patients in the control group and the SCD group had reflux in the popliteal vein (Table II). Five patients in the control and seven in the SCD group had reflux in the femoral vein. Three patients in the control and none in the SCD had incompetence at the saphena-femoral junction, whereas one in the control and two in the SCD group had reflux in the short saphenous vein. Eleven percent of the total ulcers in the

Table II. Vascular laboratory findings in the study-groups

Group	Median PPG refilling time (sec) and range			Location of reflux		
	no cuffs	With cuffs	LSV	SSV	CFV	Pop
Control	5 (1-16)	1 (1-15)	3-30	1	5	24
SCD	(1-11)	8 (4)		2	7	21

NOTE: Photographs were taken of PPG) with patient sitting with venous emptying produced by 10 dorsiflexions at the ankle. Measurements were made before ('no cuffs') and after ('with cuffs') the application of a 2.5 cm wide above-knee cuff inflated to 100 mm Hg to assess the contribution of superficial venous reflux. Doppler ultrasound and duplex ultrasound imaging were used to assess the competence of the valves in the long saphenous vein (LSV), short saphenous vein (SSV), common femoral vein (CFV), and popliteal vein (Pop) with the patient standing.

Table III. Outcome at the end of the 3-month study-period

Total Group	Healed	Unhealed	patients	per patient
Control	1	23	24	1.5
SCD	10	1	21	1.0

NOTE: Patients were included in the 'healed' group only if all ulcers had achieved complete healing. Significantly more ulcers healed in the SCD group than the control group. Thirty-seven ulcers were treated in the control group patients, compared with 21 in the SCD group. \* $p > 0.009$ , Fisher's exact probability test.

control group, were found to have healed by week 12, whereas 48% in the SGD group were found to have healed over the same period. By chance, patients in the control group tended to have smaller ulcers than those in the SCD group. In addition, there was a tendency to have more ulcers per patient in the control than the SCD group. Neither of these differences reach statistical significance (Table III). Complete healing of all ulcers occurred in only one patient in the control group compared with 10 in the SCD group. The median healing rate for the control group was 2.1% area per week, whereas that for the SCD group was 19.8% area per week. This difference is significant at  $p = 0.046$  (Mann-Whitney). Although there was some disparity in initial ulcer size between the two groups, the difference was not statistically significant.

The treatment regimen was well tolerated by the patients. Stockings were accepted and in general preferred to the use of compressive bandaging, in keeping with our previous experience of this technique. No specific problems were encountered in using the SCD unit in the home setting. Inquiries during follow-up visits revealed that many patients attempted to use the device for a full 4 hours per day, although a few reported that their work

Table IV. Comparison of the total ulcer area treated in each patient group, median values with interquartile (IQ) range

	<i>Median initial ulcer area in cm (IQ_range)</i>	<i>Median final ulcer area in cm (IQ_range)</i>	<i>Median healing rate in % area per week (IQ range)</i>
Group Control SCD	17.3 (13.0-31.0) 49.8 (12.7-135)	11.1 (3.1-88.6) 2.2 (0-12.5)	2.1* (-0.07-19.7) 19.8* (5.5-40.2)

Ulcers tended to be larger in the SCD group, however this was not statistically significant. \* $p = 0.046$  (Mann-Whitney).

and other circumstances precluded use for more than 3 hours daily. Patients confirmed that they were following the standard advice to elevate the limbs when possible and to avoid standing or sitting with the legs dependent.

## DISCUSSION

The results demonstrate that both the healing rate, number of ulcers healed, and number of limbs in which ulceration healed completely was significantly better in the SCD group than the control group. The area of ulceration tended to be greater in the SCD group initially although this did not reach statistical significance (Table IV). Despite this, healing progressed and resulted in significantly smaller areas of ulceration at the end of the study period in the SCD group. The relatively slow healing rate and small proportion of healed ulcers in the control group can be attributed to the fact that all patients had a clinical history of wounds that were particularly resistant to healing with standard treatment regimens.

The ulcer wound management used in this study was in keeping with the usual practices in the United Kingdom. The use of hydrocolloid dressings was considered since these may permit dressings to remain for greater periods; however, our experience has been that not all ulcers are suitable for these dressings, and leakage of fluid may cause skin excoriation at the ulcer edge. In a properly constructed study it was not possible to show that such dressings improved the venous ulcer healing rate.<sup>6</sup> The use of higher compression stockings (U.K. class III, 40 to 60 mm Hg at the ankle) was considered since greater compression may be beneficial to venous ulcer healing.<sup>16</sup> Unfortunately many elderly patients find difficulty in applying stockings of this compression, and to ensure compliance we elected to use the most generally acceptable garments.

Sequential gradient pneumatic compression was used as opposed to uniform (one-cell) compression for a number of reasons. In a model of the limb uniform

compression was found to collapse the proximal veins first with the wave of vessel collapse moving in the distal direction. Sequential gradient compression was demonstrated to milk blood from the compressed vessel, beginning distally, with the wave of vessel collapse moving in the proximal direction.<sup>17,18</sup> Nicolaides et al.<sup>19</sup> have confirmed these observations in patients with venous 'disease using Doppler ultrasonography. Uniform compression produced "trapping" of venous blood in the distal veins, whereas sequential gradient compression resulted in more complete emptying of the deep veins. In addition, it has been demonstrated that sequential gradient compression induces a greater increase in fibrinolytic activity than uniform compression.<sup>20</sup> Previous work by our group and others suggests venous distension is a key factor in the underlying pathologic progression of venous disease.<sup>21,22</sup> We concluded that optimum compression would best be applied using a sequential gradient approach.

We had no means of assessing the actual usage of the SCD devices, so the study was carried out on an 'intention to treat' basis. This attempts to assess the situation in the real world where a device might be supplied to patients attending a clinic. There would not usually be any means of checking the patients' use of the device in such a situation, so this study reflects what might be expected in real clinical use. Similar arguments apply to the wearing of stockings and elevation of the legs, which might also be crucial determinants of ulcer healing. Although devices are available that might give information on these activities, the complexities of such monitors were considered too great for use in this study. We could not be certain that patients in either group would wear their stockings or elevate their legs, but we repeated our advice at each follow-up appointment.

It would have been desirable to supply the control group subjects with a device that provided no compression of the limb. We were not certain that the patients would tolerate such an obviously inoperable machine. In any case we had insufficient compression devices for this

to be feasible. We must accept the possibility that some of the effect may have been due to the patients in the SCD group elevating their limbs for longer than the control group subjects. It is debatable whether this difference would have had such a marked influence on ulcer healing. It therefore seems more likely that the SCD had a specific effect on the healing process or the venous abnormality producing it.

It seems remarkable that the improvement in healing could be achieved by a treatment that lasted for not more than 4 hours per day. The mechanism may be due to effects on the hemodynamics of flow, alterations in fibrinolysis, or white cell adhesion,<sup>23</sup> factors that are currently under investigation in our laboratory. It is also possible that the mechanism of action might involve the reduction of tissue edema. Evidence in support of this mechanism has been provided by Pekanmaki et al.<sup>24</sup> who reported a significant increase in transcutaneous oxygen after the application of sequential gradient compression to legs with ulcers of venous origin.

The results of this study suggest that sequential gradient pneumatic compression may be used safely and effectively as part of treatment for venous ulceration.

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