Dose-response of compression therapy for chronic venous edema—higher pressures are associated with greater volume reduction: Two randomized clinical studies

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Background: **Two phase II clinical studies used an experimental, multi-chambered compression device with different cuff pressure combinations in subjects with leg edema and chronic venous insufficiency. The objective of each study was to evaluate the safety and the relative effects of different cuff pressure combinations to determine if edema reduction was dose-dependent.**

Methods: **Each study enrolled adults with chronic (≥6 weeks) venous edema corresponding to CEAP C_3-C_5. The test device could apply different pressures at the foot, gaiter, mid-calf, and upper-calf. In the first study, the following six sustained pneumatic compression (SPC) profiles were applied for six hours each: 20, 30, and 40-mm Hg at the gaiter with graduated SPC (ie, lower pressures at the calf); and 20, 30, and 40-mm Hg at the gaiter with nongraduated SPC (ie, the same pressures at the calf). In the second study, the following three intermittent pneumatic compression (IPC) profiles were applied for two hours each: 40, 50, and 60-mm Hg at the gaiter with graduated IPC (ie, lower pressures at the calf). Each study included a baseline profile with no compression and two-day intervals between profiles. Leg volume was measured before and after compression using the water-displacement method.**

Results: **A dose-response relationship was observed between increased SPC/IPC pressures and reduced limb edema. Limb volume was reduced most effectively with the highest pressures of 40-mm Hg nongraduated SPC and 60-mm Hg graduated IPC (136 mL and 87 mL, respectively); however, some subjects reported discomfort with these profiles. Limb volume was reduced by more than 100 mL with 30 to 40-mm Hg graduated SPC and by 69 mL with 50-mm Hg graduated IPC, and subjects rated these profiles as comfortable or very comfortable. Of the 28 study participants (12 SPC, 16 IPC), two subjects reported pain with 60-mm Hg IPC; no other adverse events were reported with SPC or IPC.**

Conclusion: **Pneumatic compression was safe and well-tolerated, with a dose-response relationship between increased SPC/IPC pressures and reduced leg edema. To our knowledge, this is the first study to demonstrate a dose-relationship in compression therapy: higher pressures are associated with greater volume reduction in subjects with chronic venous edema. (J Vasc Surg 2009;49:395-402.)**

The most important clinical consequence of chronic venous insufficiency (CVI) is venous leg ulcers,[1] which are associated with significant morbidity and cost.[2] Venous leg ulcers are the most prevalent form of chronic wounds, accounting for up to 80% of all leg ulcers in the Western world.[2] Thus, adequate management of CVI may have substantial clinical implications for chronic wound care.

Standard care of CVI includes appropriate compression therapy in patients with an ankle brachial pressure index ≥0.8 to treat edema and promote venous return.[3] Pneumatic compression reduces venous stasis by promotion of return venous blood flow.[2] Some studies suggest that pneumatic compression also enhances fibrinolytic activity,[4] although other studies have challenged this conclusion.[5]

Bandages or stockings are used for static compression therapy, but there is considerable variation in the type of compression.[6] Furthermore, it is not possible to accurately adjust the pressure gradient applied by these devices. Additionally, uncontrolled variation in applied gradient can occur over time with limb shape change; for example, as edema in the limb decreases, the pressure on the limb from the compression device subsequently decreases. Several clinical studies have reported that intermittent pneumatic compression (IPC) of the legs in addition to stockings or bandages improves healing of venous ulcers and alleviates symptoms in patients with CVI without ulcers, but a systematic review of the available evidence concluded that the data could not be relied on to inform the optimal choice of compression therapy or optimal protocol for patients with CVI or venous

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Table I. Pressure profiles studied

Pressure profile	*Pressure, mmHg*			
	Foot	*Gaiter*	*Mid-calf*	*Upper-calf*
SPC study				
No compression	NA	NA	NA	NA
20 mm Hg graduated	10	20	10	0
30 mm Hg graduated	20	30	20	10
40 mm Hg graduated	30	40	30	20
20 mm Hg nongraduated	10	20	20	20
30 mm Hg nongraduated	20	30	30	30
40 mm Hg nongraduated	30	40	40	40
IPC study				
No compression	NA	NA	NA	NA
40 mm Hg graduated	40	40	35	30
50 mm Hg graduated	50	50	45	40
60 mm Hg graduated	60	60	55	50

IPC, Intermittent pneumatic compression; *NA,* not applicable (no compression device was applied during this period); *SPC,* sustained pneumatic compression.

ulcers.[7] Furthermore, multi-chambered compression devices and decreasing pressure gradients from ankle to thigh may be more effective than single-pressure, one-chambered models at achieving the desired "milking" pattern, but comparative data on multi- and single-chambered devices are lacking.[7]

Given the potential advantages of adding IPC to provide precise regulation of limb compression, it is important to know which compression profiles reduce edema most effectively. Hypothetically, greater compression should provide greater reduction of edema, but surprisingly up to now there have been no clinical studies to firmly establish this relationship. This report describes two phase II clinical studies of an experimental, multi-chambered compression device that used several different cuff pressure combinations. The objective of each study was to evaluate the safety and the relative effects of different cuff pressure combinations to determine if edema reduction was dose-dependent.

METHODS

Two separate phase II studies were conducted. Inclusion criteria for each study were at least 18 years of age (with an upper limit of 80 years of age in the study of sustained pneumatic compression), chronic (≥6 weeks) leg edema, CVI for at least 6 weeks (CEAP classification C_3–C_5; $E_{p,s}$; $A_{s,d}$; P_r), refluxes greater than 0.5 seconds in at least one major venous segment assessed by Duplex, and ankle-brachial pressure index ≥0.8 to treat edema. Key exclusion criteria were active leg ulcer (C_6), compression therapy during the prior 48 hours, deep vein thrombosis in the last six months, active cardiac disease or significant history of cardiac disease, edema-reducing therapy, or anticoagulant therapy. Informed consent was obtained for all subjects, and each study was approved by an Independent Ethics Committee.

The Physiological Test Device was a battery-operated experimental unit that used inflatable pneumatic cuffs to apply controlled compression to the foot and calf. It consisted of three main elements: a foot cuff, a calf cuff, and an electronic control/user-interface unit. The three elements were linked together by pneumatic tubing to form one complete functional unit. The cuffs contained four separate air bladders, one in the foot cuff and three in the calf cuff, that allowed different pressures to be applied independently to the foot, gaiter, mid-calf, and upper-calf. The user interface allowed graduated pressures to be entered into the electronic control unit. Pressure transducers in the pneumatic supply system ensured that accurate pressures were delivered and could be monitored and maintained throughout testing. The use of battery power to operate the device allowed subject mobility during testing. However, subjects were instructed to remain seated as much as possible during study treatment to reduce the potential influence of ambulation on study assessments.

During pneumatic compression therapy, the test device was applied to the more edematous leg and the contralateral leg was used as a control. The device was used in conjunction with an associated sock that was worn between the limb and the inflatable cuffs. Subjects did not wear any other compression stockings/devices except the study devices. After each profile and device removal, the subject was allowed 10 minutes rest sitting down before efficacy measurements.

Previous data on the optimal pressure profile were not available, so the test profiles were selected on the basis of clinical experience to be consistent with currently available devices. In the sustained pneumatic compression (SPC) study, subjects completed an observation-only profile and were randomized to treatment with the following seven profiles (Table I): one profile each with 20, 30, and 40 mm Hg SPC at the gaiter and the same pressures at the calf (nongraduated SPC); and one each with 20, 30, and 40 mm Hg SPC at the gaiter and lower pressures at the calf (graduated SPC). All subjects completed the non-treatment profile first; thereafter, randomization determined the order in which each subject was treated with the six

active treatment profiles. All of the SPC profiles used lower pressures at the foot than at the gaiter. Each SPC profile was administered for 6 hours with at least 48 hours between profiles.

In the IPC study, subjects completed an observation-only profile and were randomized to treatment with the following three profiles (Table I): one profile each with 40, 50, and 60 mm Hg at the gaiter, the same pressures at the foot, and lower pressures at the mid-calf and upper-calf (graduated IPC). Each IPC profile was administered for two hours with at least 46 hours between profiles.

In each study, the volumes of the test leg and untreated leg were measured at the start and end of application of each profile by the water immersion technique.[8,9] The subject stood and immersed one leg into a boot-shaped device filled with water at 30°C. The weight of water displaced was recorded with a precision scale and was converted to the volume of water displaced, and thus, the volume of the leg, using the conversion 1 g = 1 mL (ie, the Archimedes principle). This procedure was then repeated with the other leg.

At the start and end of each profile, the investigator reported whether ankle edema was present and whether skin condition was normal. At the end of study visits when the device was used (ie, all study visits except the observation-only profile), the subject categorized the profile as very comfortable, comfortable, uncomfortable, or very uncomfortable. Adverse events were recorded at each study visit.

Data that were collected only in the SPC study included leg circumference measurements at the start and end of each profile at the minimum girth of the ankle, at the maximum girth of the calf, just below the tibial tuberosity, and at the middle of the foot. Changes in toe systolic pressure and transcutaneous oxygen pressure ($TcpO_2$) were collected only in the IPC study, which used higher pressures and was designed and conducted after the SPC study.

The primary safety outcome was the incidence of all reported adverse events during the study period. The number and percentage of subjects with adverse events, serious adverse events, discontinuations due to adverse event, related adverse events, severity of adverse events, and deaths were summarized by term. The primary efficacy outcome was change in limb volume. Absolute changes and percentage changes in limb volume from the start to the end of each profile were compared between the test profiles and the observation-only profile. Relative reduction of limb volume was calculated as the change in the test leg minus the change in the untreated leg. Secondary efficacy outcomes included relative change in circumference at the ankle, at the mid-foot, below the tibial tuberosity, and at the calf; skin condition at the end of each profile; device comfort for each profile; and shift tables for the presence of ankle edema at the start and end of each profile.

Table II. Baseline demographic and clinical characteristics

	SPC study (n = 12)	*IPC study (n = 16)*
Gender, n (%)		
Male	5 (42)	5 (31)
Female	7 (58)	11 (69)
Age, years		
Mean ± SD	60.8 ± 11.31	64.4 ± 12.67
Median (min, max)	61.0 (38, 78)	64.0 (43, 79)
Duration of venous insufficiency, years		
Mean ± SD	18.9 ± 9.44	21.0 ± 7.17
Median (min, max)	20.0 (3, 30)	20.5 (5, 31)
Clinical classification, n (%)		
C_3 – Edema	3 (25)	1 (6)
C_4 – Skin changes without ulceration	7 (58)	13 (81)
C_5 – Skin changes with healed ulceration	2 (17)	2 (13)
Etiologic classification, n (%)		
E_P – Primary	12 (100)	13 (81)
E_S – Secondary	0	3 (19)
Ankle branchial pressure index, mmHg		
Mean ± SD	1.03 ± 0.08	1.05 ± 0.06
Median (min, max)	1.0 (0.9, 1.1)	1.1 (0.9, 1.1)
Anatomical distribution of reflux, n (%)		
Superficial	8 (67)	7 (44)
Deep	0	3 (19)
Both	4 (33)	6 (38)

IPC, intermittent pneumatic compression; *SPC,* sustained pneumatic compression.

RESULTS

SPC study. All 12 subjects enrolled in the SPC study were included in the safety and efficacy populations, and all subjects completed treatment. Baseline demographic and clinical characteristics are summarized in Table II.

No adverse events were reported in this study. Edema was not reported as an adverse event, but it was observed in the ankle area not covered by the sleeve for two (17%) subjects with the 40-mm Hg nongraduated SPC profile and one (8%) subject with the 30-mm Hg graduated SPC profile. One (8%) subject developed skin irritation with 20-mmHg graduated SPC. Subjects usually rated SPC as comfortable or very comfortable with each of the profiles (Fig 1), but three (25%) subjects reported discomfort at least once with the following profiles: one subject reported discomfort with 30- to 40-mm Hg nongraduated SPC and 20-mm Hg graduated SPC; and the other two subjects reported discomfort only with 40-mm Hg nongraduated SPC.

Dose-dependent reductions of leg volume were observed with SPC therapy (Fig 2). The volume of the test leg increased by 12 mL relative to the untreated leg when no compression was administered during the observation-only profile. In contrast, 20- to 40-mm Hg of SPC reduced the volume of the test leg relative to the untreated leg during each profile, with a dose-dependent range of 44 mL to 106

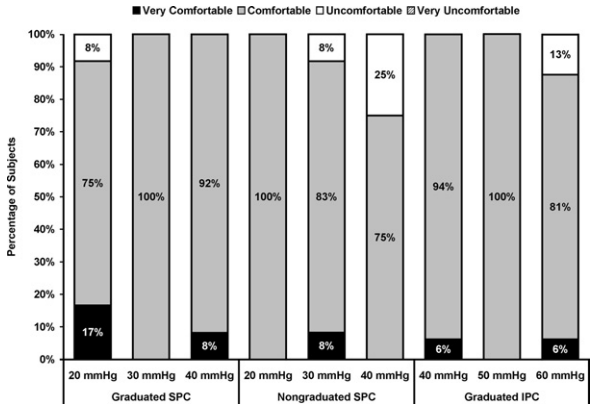

Fig 1. Device comfort ratings by pneumatic pressure profile. Most subjects reported being comfortable or very comfortable with each pressure profile, and no subject reported being very uncomfortable. Device comfort ratings were not applicable for the periods with no treatment. Pressures refer to the pressure administered at the gaiter. Twelve subjects were treated with each sustained pneumatic compression (SPC) profile for 6 hours, with at least 48 hours between each profile. Sixteen subjects were treated with each intermittent pneumatic compression (IPC) profile for two hours, with at least 46 hours between each profile.

mL and 80 mL to 136 mL with graduated SPC and nongraduated SPC, respectively. These differences were statistically significant ($P \leq .011$) for the 30 to 40 mm Hg graduated SPC profiles and the 20 to 40 mm Hg nongraduated SPC profiles compared with the observation-only profile.

Mean reductions of circumference during SPC (Table III, online only) appeared to be dose-dependent at the ankle, calf, and tibial tuberosity; circumference reduction in the treated leg relative to the untreated leg at these locations was progressively greater as the SPC pressure increased. Circumference reduction at the foot during SPC was not dose-dependent. All subjects had improvement with edema from the observation-only profile to the last treatment profile, including marked improvement in eight (67%) subjects.

IPC study. All of the 16 subjects enrolled in the IPC study were included in the safety and efficacy populations, and all subjects completed the study treatment. Baseline demographic and clinical characteristics of the study participants are summarized in Table II.

There were 15 (94%) subjects with normal skin throughout treatment and one (6%) subject with lipodermatosclerosis at baseline had "other" skin condition at every assessment. All subjects reported the 40-mm Hg and 50-mm Hg graduated IPC profiles were comfortable or very comfortable (see Fig 1). Two (13%) subjects reported discomfort with the 60-mm Hg graduated IPC profile. These two subjects also reported pain as an adverse event with this profile. Both adverse events were categorized as mild in severity, non-serious, and related to the device, and neither subject reported pain with use of the device at 40- to 50-mm Hg. No other adverse events were reported.

Evaluations of toe systolic pressure and $TcpO_2$ revealed no negative effects (Table IV). Toe systolic pressure in the test leg increased dose-dependently at 1.5 hours (ie, during graduated IPC or observation only) for every profile; at 2.5 hours (after treatment), toe systolic pressure continued to increase in the observation-only profile, but it returned to near baseline for each of the graduated IPC profiles. Values for $TcpO_2$ also increased from baseline during IPC but returned to near baseline shortly after treatment; IPC did not appear to have a dose-dependent effect on $TcpO_2$ during or after treatment.

Dose-dependent reductions of leg volume were observed with graduated IPC therapy (Fig 3). Volume of the test leg increased 19 mL relative to the untreated leg for the observation-only profile. Relative decreases with active treatment ranged from 109 mL for 40-mm Hg graduated IPC to 146 mL for 60-mm Hg graduated IPC. Significantly greater ($P < .001$) reductions in leg volume were observed with all treatment profiles than with the observation-only profile.

No subject developed new-onset ankle edema and several subjects had resolution of ankle edema during graduated IPC therapy. The resolution of baseline ankle edema after use of the device appeared to be dose-dependent, with percent resolution ranging from 27% for 40-mm Hg graduated IPC to 75% for 60-mm Hg graduated IPC.

DISCUSSION

In these two physiological phase II clinical studies, the use of SPC or IPC with a four-chamber pneumatic compression device was shown to be safe and generally well tolerated. The safety and tolerability of pneumatic compression were confirmed by the absence of reported adverse events for any of the six SPC treatment profiles and reports of an adverse event (pain with device wear) by two subjects in the IPC study only at the highest pressure profile tested (60-mm Hg at the gaiter). There were no apparent negative effects on toe systolic pressure and $TcpO_2$ during and after device wear in the IPC study. These endpoints were not evaluated in the SPC study, which was conducted before the IPC study. Additional study of these endpoints with SPC could provide valuable information about the safety of sustained compression with respect to foot health.

The main objective of these studies was to examine a range of pressure profiles and determine the safety and the relative effects of the different cuff pressure combinations. Reduction of leg edema was dose-dependent for both SPC and IPC. The most effective reduction of leg edema in the SPC study was observed with the highest pressure tested of 40-mm Hg nongraduated SPC (30, 40, 40, and 40-mm Hg at the foot, gaiter, mid-calf, and upper-calf, respectively), but discomfort was also reported by three subjects with this profile. Use of the highest pressure at the gaiter, but graduated SPC in the

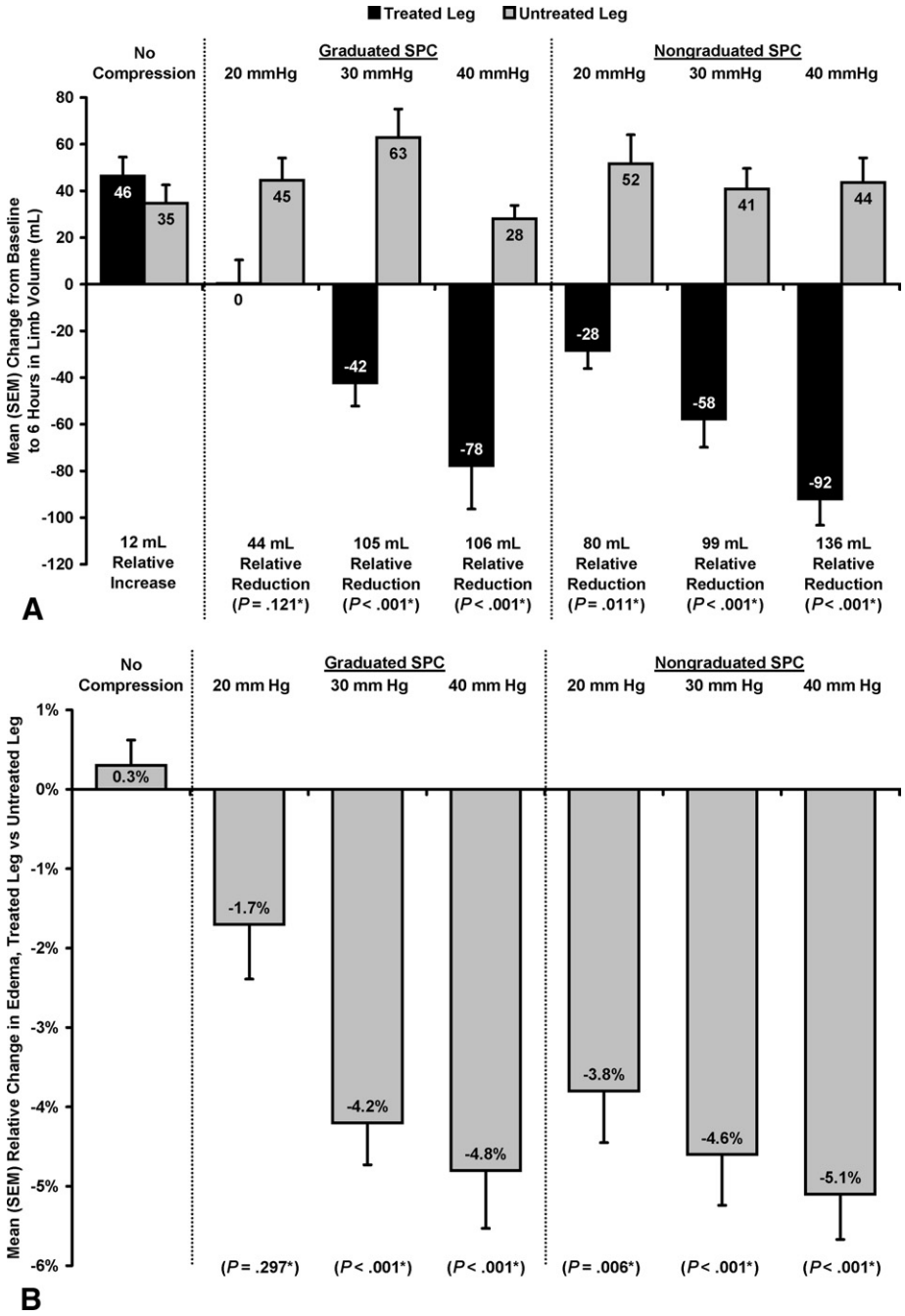

Fig 2. A, Mean (SEM) absolute change in leg volume from baseline for each sustained pneumatic compression (SPC) profile and least-squares mean for the difference between the treated and untreated legs. **B**, Mean (SEM) relative reduction in leg volume with SPC, treated leg vs untreated leg. Pressures for each graduated and nongraduated profile refer to the pressure administered at the gaiter. Treatment with SPC was associated with dose-dependent mean reductions of leg volume from the start to the end of each six-hour observation/treatment period. Twelve subjects were treated with each profile for six hours, with at least 48 hours between each profile. **P* value based on least-squares mean, pairwise comparison to no compression.

other chambers (30, 40, 30, and 20-mm Hg at the foot, gaiter, mid-calf, and upper-calf, respectively), also reduced leg edema and leg circumference substantially but was not associated with any reports of discomfort. A lower pressure of 30-mm Hg at the gaiter (and graduated or nongraduated SPC) also performed well, with only one report of discomfort for nongraduated SPC. The lowest pressure of 20-mm Hg graduated or non-

Table IV. Change in toe systolic pressure and transcutaneous oxygen pressure with intermittent pneumatic compression for two hours

	Mean (SEM) change from baseline, mm Hg			
		IPC profile		
	No IPC	*40 mm Hg*	*50 mm Hg*	*60 mm Hg*
Toe systolic pressure				
Change at 1.5 hours*	17.3 (4.9)	24.0 (11.3)	25.9 (8.5)	33.8 (8.9)
Change at 2.5 hours†	30.1 (12.1)	6.3 (4.1)	2.1 (5.8)	6.4 (4.1)
$TcpO_2$				
Change at 1.5 hours*	−2.13 (−1.62)	2.88 (1.06)	3.31 (0.97)	2.94 (0.70)
Change at 2.5 hours†	−1.06 (−1.35)	0.88 (1.41)	0.00 (0.83)	0.19 (1.05)

IPC, intermittent pneumatic compression; *$TcpO_2$,* transcutaneous oxygen pressure.
*During treatment.
†30 minutes after IPC.

graduated SPC was not as effective as the other pressures for limb volume or circumference reduction. Therefore, 30- to 40-mm Hg graduated SPC or 30-mm Hg non-graduated SPC seem to be the most promising variants and deserve further clinical evaluation in the management of chronic venous disorders.

In the IPC study, 40-mm Hg graduated IPC was the most effective profile but was associated with two reports of discomfort and pain, which were the only reported adverse events for pneumatic compression in either study. The 30-mm Hg graduated IPC profile performed well without any reports of discomfort. Resolution of ankle edema from the start to the end of IPC treatment revealed a pressure-dependent response, with a rank order of 40-mm Hg >30-mm Hg > 20-mm Hg > no compression. No IPC test profile was associated with new-onset ankle edema during wear.

Treatment with IPC in the management of CVI and venous ulcers has been examined for more than 25 years,[7] but to our knowledge, no prior study compared different pressure profiles and reported their relative safety, tolerability, and effectiveness for edema reduction. This study supports the hypothesis that higher pressures reduce edema more effectively than lower pressures. However, the optimal pressure profile may vary between different devices and should be evaluated for each device individually, particularly since some pressure profiles may be associated with discomfort or pain. In these studies, adverse events were only reported for two subjects, both of whom had pain with IPC at the highest pressure tested of 60 mm Hg. It is notable that recently developed consensus guidelines for compression bandages, not pneumatic compression devices, would place this pressure between the high pressure range of 40 to 60 mm Hg and the very high pressure range of 60 to 80 mm Hg. A typical range of pressures for compression bandages and stockings is closer to the medium range of 20 to 40 mm Hg.[10] Therefore, although pneumatic compression devices make it possible to exert greater pressures, as observed in this study, it is important not to simply maximize the pressure but to identify the cuff pressure that achieves the best balance of effectiveness and tolerability. Additionally, it remains to be determined whether the different pneumatic compression devices have the same optimal pressure profiles, because pressures in the cuffs may not be the same as those measured on the skin.[11]

In addition to comfort, other considerations that might influence the choice of one treatment over the other include the mobility of the patient and the therapeutic aim. Patients who are ambulatory will have some degree of cyclic vein compression from the surrounding muscles as they walk, whereas immobile patients may benefit more from stimulation of a similar process with IPC. The therapeutic aim may also influence the strength of compression that is required. For example, patients who need compression of leg veins in a standing position may require higher pressures,[12] whereas patients who receive pneumatic compression for the treatment of edema may respond to lower pressures.

Previous studies evaluated the effect of pneumatic compression on the rate and extent of healing for venous ulcers.[7] Because that was not a goal of these studies, patients with open wounds (C_6 on the CEAP classification[13]) were excluded. Additional study would be valuable to determine the relative safety and performance of different SPC/IPC pressure profiles for edema reduction in patients with open wounds. Another potential limitation of this study was the short treatment and follow-up period for each compression profile. Information about the return of edema after device removal was not collected and the safety and effects of ongoing treatment were not evaluated. Additional study of leg volume during and after 2 to 4 weeks of pneumatic compression therapy would be welcome.

In summary, SPC and IPC with a pneumatic compression test device were safe and well-tolerated, with a dose-response relationship between increased compression and reduced leg edema. Based on the combination of tolerabil-

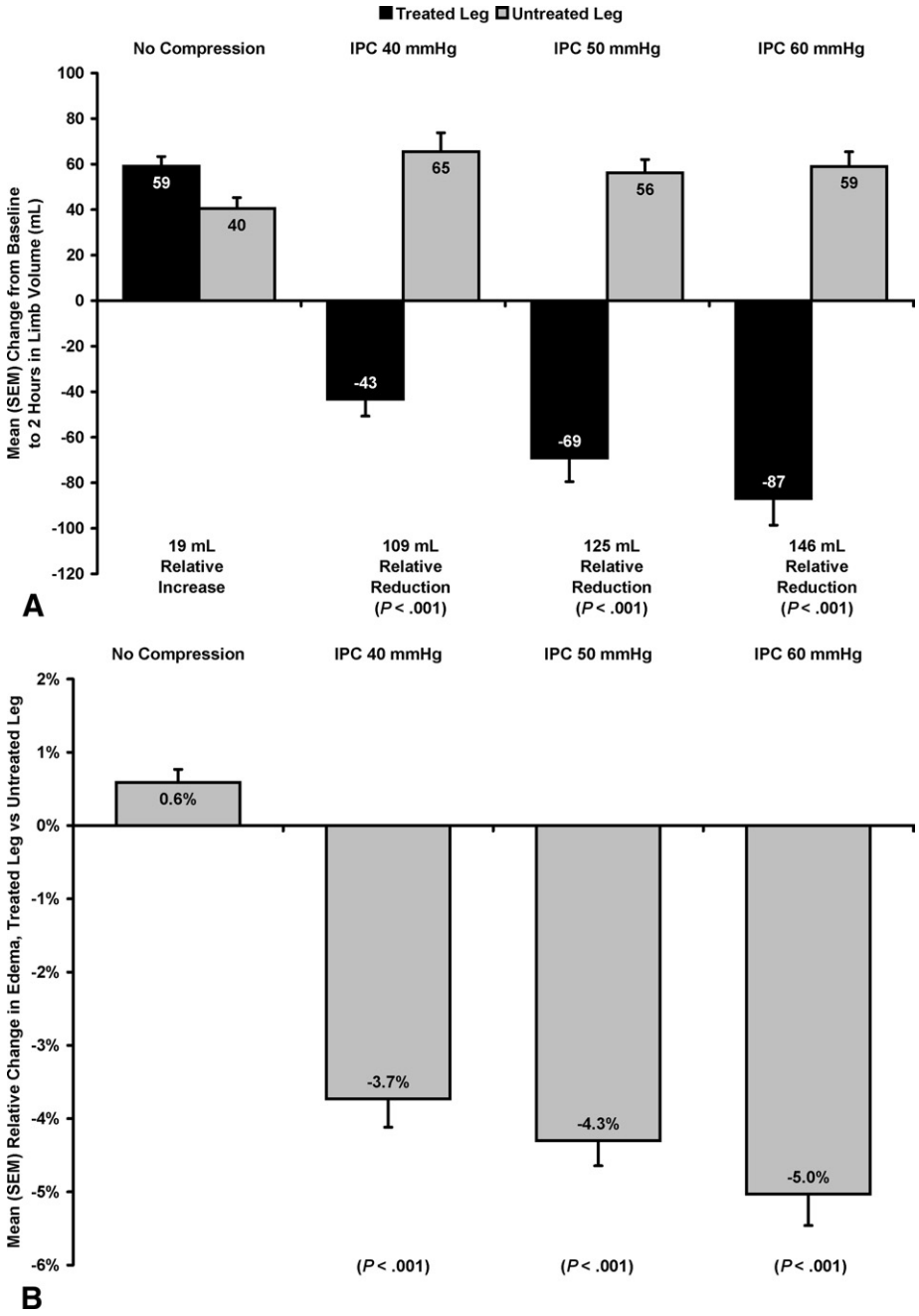

Fig 3. A, Mean (SEM) absolute change in leg volume from baseline for each intermittent pneumatic compression (IPC) profile and least-squares mean for the difference between the treated and untreated legs. **B**, Mean (SEM) relative reduction in leg volume with IPC, treated leg vs untreated leg. Reported reduction or increase for each profile is the least-squares mean for the difference between the treated and untreated legs. Treatment with IPC was associated with dose-dependent mean (SEM) reductions of leg volume from the start to the end of each treatment period. Sixteen subjects were treated with each profile for 2 hours, with at least 46 hours between each profile. **P* value based on least-squares mean, pairwise comparison to no compression.

ity, comfort, and efficacy, 30- to 40-mm Hg graduated SPC, 30-mm Hg nongraduated SPC, and 50-mm Hg graduated IPC deserve further evaluation in the management of severe venous disease.

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AUTHOR CONTRIBUTIONS

Conception and design: WV
Analysis and interpretation: WV, AU, HP
Data collection: WV, AU
Writing the article: WV, AU, HP
Critical revision of the article: WV, AU, HP
Final approval of the article: WV, AU, HP
Statistical analysis: WV
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Overall responsibility: WV

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Table III (online only). Change in leg circumference with sustained pneumatic compression for six hours

	Mean (SEM) change in circumference, mm						
		Graduated SPC profile			*Nongraduated SPC profile*		
Location	*No SPC*	*20 mm Hg**	*30 mm Hg**	*40 mm Hg**	*20 mm Hg**	*30 mm Hg**	*40 mm Hg**
Ankle							
Treated leg	1.5 (1.49)	−5.2 (1.81)	−7.5 (1.57)	−14.8 (3.13)	−6.9 (1.51)	−10.8 (1.80)	−14.4 (1.80)
Untreated leg	1.9 (1.72)	2.9 (1.19)	4.6 (1.59)	4.0 (1.70)	1.3 (0.78)	1.5 (1.17)	0.4 (1.40)
Relative change†	−0.4 (1.92)	−8.1 (1.77)	−12.1 (2.13)	−18.8 (2.86)	−8.1 (1.88)	−12.3 (2.21)	−14.8 (1.91)
Calf							
Treated leg	1.3 (10)	−1.5 (1.36)	−4.0 (1.21)	−12.9 (2.66)	−8.5 (1.13)	−15.6 (2.11)	−20.6 (1.60)
Untreated leg	2.7 (1.36)	1.9 (1.27)	4.4 (1.07)	1.9 (1.51)	1.9 (0.63)	2.5 (1.51)	2.5 (1.38)
Relative change†	−1.5 (2.56)	−3.3 (1.95)	−8.3 (1.85)	−14.8 (2.88)	−10.4 (1.34)	−18.1 (2.61)	−23.1 (1.92)
Tibial Tuberosity							
Treated leg	3.5 (1.58)	1.5 (1.64)	−0.4 (1.34)	−1.3 (1.32)	−2.5 (1.63)	−2.9 (1.87)	−5.4 (2.01)
Untreated leg	0.2 (0.95)	2.5 (1.38)	4.0 (1.39)	1.7 (1.32)	1.5 (1.61)	4.0 (1.21)	3.1 (1.16)
Relative change†	3.3 (1.83)	−1.0 (2.49)	−4.4 (0.98)	−2.9 (0.96)	−4.0 (2.29)	−6.9 (2.43)	−8.5 (1.75)
Mid-Foot							
Treated leg	3.5 (1.09)	−0.6 (1.54)	−3.1 (1.38)	−2.1 (0.91)	1.3 (0.84)	1.0 (1.52)	0.4 (1.22)
Untreated leg	−0.2 (0.95)	4.2 (1.49)	4.2 (1.42)	2.5 (0.97)	3.3 (1.52)	2.5 (1.60)	3.5 (0.95)
Relative change†	3.8 (1.17)	−4.8 (1.75)	−7.3 (2.14)	−4.6 (1.40)	−2.1 (1.79)	−1.5 (1.75)	−3.1 (1.82)

SPC, sustained pneumatic compression.

*Pressure applied at the gaiter; some profiles used different profiles at the foot, mid-calf, and upper calf (see Table I).

†Relative change, treated vs untreated leg.