Structured exercise improves calf muscle pump function in chronic venous insufficiency: A randomized trial

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Objective: **Deterioration of calf muscle pump function is associated with progression of chronic venous insufficiency (CVI). We postulated that a supervised exercise program would improve calf muscle strength and venous hemodynamics in patients with CVI.**

Methods: **We recruited 31 patients for this randomized, prospective trial. Inclusion criteria required the presence of skin changes or ulceration (CEAP 4, 5, 6), and duplex ultrasound scanning (reflux or scarring) and air plethysmographic (APG) evidence of CVI. Subjects were randomized into control (n = 13) and therapy (n = 18) groups. Class II (30-40 mm Hg) compression hosiery was given to all. The experimental group received physical therapy designed specifically to strengthen calf musculature. Dynamic strength and power were measured with a Biodex II dynamometer (Biodex Medical Systems, Shirley, NY) at slow and fast speeds. Reflux (venous filling index) and calf pump function (ejection fraction, residual volume fraction) were measured with APG. Quality-of-life questionnaires and venous severity scores were also administered. Outcomes were compared 6 months after initiation of exercise. Probability of treatment effect was tested with univariate analysis of variance, with control for baseline values.**

Results: **Demographic variables and medical comorbidities were not different between groups. After 6 months of intervention, indicators of calf pump function returned to a normal range in the therapy (experimental) group. Mean residual volume fraction was improved in the exercise group (-8.75 ± 4.6 vs 3.4 ± 2.9 in the control group; $P < .029$). Mean ejection fraction was increased in the exercise group (3.48 ± 2.7 vs -1.4 ± 2.1 in the control group; $P < .026$). Reflux, while substantially greater than the normal value of 2.0 mL/s in both groups, was unchanged. The exercise regimen improved isokinetic peak torque/body weight at both slow speed (3.1 ± 1.4 in the therapy group vs -1.0 ± 1.1 in the control group; $P < .05$) and fast speed (2.8 ± 0.9 in the therapy group vs $- 0.3 \pm 0.6$ in the control group; $P < .03$). No changes were observed in quality-of-life or severity scores.**

Conclusions: **Calf muscle pump function and dynamic calf muscle strength were improved after a 6-month program of structured exercise. Directed physical conditioning of the calf musculature may prove beneficial for patients with or without alternative management options for severe CVI. Further research on exercise for patients with CVI is warranted. (J Vasc Surg 2004;39:79-87.)**

Treatment options are limited for patients with severe chronic venous insufficiency (CVI). Limbs with advanced CVI are often perfunctorily categorized as postthrombotic, and as a result are infrequently assessed for location and cause of disease. When recognized and indicated, substantial improvement is reported after surgical intervention.[1,2] However, many patients remain chronically debilitated as a result of CVI symptoms. A mainstay of therapy, an appropriately prescribed compression garment, continues to provide substantial relief for patients with severe CVI, regardless of cause. If physiologic function can be improved with exercise, this too may provide additional therapeutic benefit.

Although commonly advocated in Europe, physical therapy for CVI has not been widely adopted in North America. Reduced ankle range of motion (ROM) and diminished calf muscle pump function are associated with progressive severity of CVI.[3-6] We reasoned that physical conditioning structured to enhance calf muscle strength and ankle mobility would improve venous hemodynamics by improving calf muscle pump function. In turn, gains in musculoskeletal function and venous hemodynamics should translate into improved functional mobility and general well-being.

METHODS

Subjects with advanced CVI were recruited for this trial from an outpatient veterans clinic population. Demo-

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graphic information and comorbidities were recorded; CEAP classifications and severity scores were assigned. Functional and quality-of-life (QOL) instruments were administered. Investigations included comprehensive venous duplex ultrasound scanning, air plethysmography (APG), and isokinetic dynamometry (Biodex Medical Systems, Shirley, NY).[7-10]

Initial evaluation included a history and clinical examination, with attention to related comorbidities, including obesity, diabetes, cardiorespiratory dysfunction, musculoskeletal impairment, and prior thrombosis. Obesity was defined as body mass index greater than 30, calculated as weight in kilograms divided by height in meters squared. Arterial insufficiency was defined as ankle-brachial index (ABI) less than 0.7.

Inclusion criteria required the presence of skin changes or ulceration (CEAP clinical classes 4, 5, 6), as well as objective evidence of CVI as determined with duplex ultrasound scanning and APG. Exclusion criteria included ulceration greater than 4 cm in diameter, painful ulceration, active local infection, recognized noncompliance, absence of objective evidence of a venous cause, uncompensated cardiorespiratory insufficiency, ABI less than 0.7, and recent venous thrombosis. In general, limbs with active ulceration or infection were stabilized, with a decrease in ulcer diameter to less than 2 cm and control of pain or local infection before screening; volunteers did not proceed to consideration until they could wear the study stocking regularly (no alternative bandages were used once recruitment and testing had begun). In lieu of therapy, superficial vein surgery was offered to those with appropriate anatomy. The experimental intervention was carried out in the vascular laboratory or clinic, and the physical therapy department, but, when necessary, supervision of therapy was extended into satellite clinics or the patient's home.

Duplex ultrasound scanning was conducted with a Sonoline Elegra or Quantum 2000 (Siemens, Iselin, NJ) scanner, with 2.5 to 7.5 mHz probes. An imaging survey evaluated standard sites in both lower extremities for patency, compressibility, wall thickness, scarring, and thrombosis of any duration. Limbs were evaluated with the patient in the standing position, and reflux was noted when retrograde flow persisted longer than 0.5 seconds after distal compression and release.[11,12] Venous anatomic scores for reflux and obstruction, both of which range from 0 to 10, were computed from these data.[8]

Severity of CVI was characterized with both the Venous Clinical Severity Scores (VCSS) and the older Venous Clinical Scores.[8,9] The VCSS has 10 items, with severity rated 0 to 3 by the examiner; it is reported as a numeric score, which ranges from 0 to 30. Increasing linearly with the clinical classification, a mean score of 14.9 ± 2.88 was reported for limbs with C6 CVI.[13] The venous clinical score has 9 items, with a range of 0 to 18.[9] The Venous Disability score was also recorded.

Hemodynamic and musculoskeletal variables were determined with APG and ankle isokinetic dynamometry (Biodex). Because extremes of human performance are demanded with these functional measures, there is a greater likelihood of variability from test to test; thus examinations were completed twice, and the baseline value was reported as the mean of the two baseline hemodynamic and isokinetic tests.

Air plethysmography. APG (APG-1000, ACI Medical, San Marcos, Calif) provides a noninvasive, easily repeatable, reliable method for determination of reflux volume, outflow, and calf pump function. Reflux measured with APG is expressed as venous filling index (VFI; venous volume in milliliters per second of refill time). Increasing values of VFI have been associated with progressive clinical symptoms of chronic venous insufficiency, including ulceration.[6] An outflow fraction less than 38% is associated with venous outflow obstruction; outflow fraction less than 28% is considered poor outflow. Calf pump function is reflected by volume changes with muscular activity; calf volumes are indexed to the total venous volume to obtain the ejection fraction (EF) and residual volume fraction (RVF). EF is the volume ejected with a single toe raise maneuver, and RVF is the volume remaining after 10 toe raises. A linear correlation between ambulatory venous pressure and RVF ($r = 0.83$) has been described.[14] Deficiencies in calf pump function have also been associated with increased occurrence of ulcers.[3,4,14] In addition, progressive severity of CVI was associated with decreased ankle ROM.[4] Examinations were performed without stockings in the morning hours on two separate days, and conducted as described by Araki et al,[3] Back et al,[4] and Christopoulous et al.[6] Testing included EF, RVF, VFI, and outflow fraction.

Ankle isokinetic dynamometer. A Biodex System 2 multi-joint testing and rehabilitation system (Biodex) with Biodex Advantage Software (version 4.0; Biodex) was used for collecting data on calf torque, work, power, and ROM. Subjects were tested for ankle plantar flexion and extension twice, 1 week apart. The anatomic ankle joint was positioned at the rotational axis of the machine, and contractions started from full dorsiflexion, with the concentric mode for slow (60 degrees per second) and fast (120 degrees per second) plantar flexion speeds. Each participant completed five repetitions for the slow speed, followed by 15 repetitions for the fast speed. Compensatory motion was prevented by a three-point seatbelt to prevent trunk and pelvic musculature from contributing to ankle plantar flexion; thus ankle isokinetic measurements were maximally isolated. Tests were conducted as described by Sisto et al[10] and Holback et al.[15]

The parameters evaluated were the average of all contractions for peak torque, peak torque per unit body weight, maximal repetition work, total work, average power, and maximal ROM. Peak torque represents the highest amount of tension a muscle can develop at one instant in the ROM at specific test speeds. Peak torque per unit body weight represents the peak torque normalized for an individual's body weight, to allow for comparisons across subjects. Maximal repetitions work represents the maximal amount of work exerted over the number of repetitions in the set. Total work is the area under the peak

torque curve. Total work may be better representative of functional ability of a joint, because it is a measure of the amount of torque that can be maintained throughout the ROM. Power is the product of force and velocity. Average power is work of one or several contractions over a specified time. Average power may be considered a true measure of work intensity. Reliability of the Biodex values is reported elsewhere, and all measured variables exceeded an intraclass correlation coefficient of 0.7.[10]

Functional and QOL assessment. Participants also completed a series of questionnaires assessing QOL and functional capacity at 0 and 6 months. Two QOL instruments specifically target venous insufficiency: the Aberdeen Varicose Vein Survey[2] and the CIVIQ.[16] The physical function items (PF10) of the SF-36 were also employed.[2] The Functional Independence Measure, Craig Handicap and Reporting Techniques, and older American resources and services questionnaire were administered to test for function in daily life as opposed to ability.[17] A separate, nonvalidated questionnaire was also administered to inquire about specific issues relevant to this particular study. These were analyzed by standard scoring techniques.

Randomization. Appropriately selected patients were randomized into two unblinded groups: a control group and a therapy (experimental) group. Patients in the control group were fully evaluated at baseline (0 months) and again at 6 months; monthly monitoring was scheduled to confirm and reinforce appropriate use of compression stockings. After completion of their 6-month evaluation, volunteers in the control group were offered the opportunity to participate in supervised therapy as wait-listed participants. The data for the wait-listed control subjects is not reported in this article. If CVI was present bilaterally, the more affected limb was selected as the study limb, assuming that it would have the greatest effect on function. All participants received two pairs of class II (30-40 mm Hg), below-knee, compression hosiery and instruction in their use, thus standardizing optimal medical treatment for both groups.

Exercise prescription. Subjects randomized to the experimental group received 3 months of supervised therapy followed by 3 months of unsupervised therapy. The program was designed by a physical therapist (S.A.S.) and individualized for each participant, with both written and graphic instructions. The exercises chosen were standard clinical practice and conducted by a physical therapy assistant. Clinical examinations, APG, and isokinetic dynamometry were performed at baseline, 3 months, and 6 months. While most subjects came to our clinic for all of these sessions, some were constrained by travel difficulties; when necessary, the supervised therapy was continued by the physical therapy assistant at the subject's home or a local satellite clinic. The physical training program was designed to strengthen calf musculature and enhance joint mobility. The exercise program consisted of lower limb and trunk stretching and strengthening, with active gravity strengthening and resistive weights in two sessions per week. Physical training focused on leg strengthening, primarily of the calf musculature, and progressed in repetitions, sets, and weights throughout the 3 months. Uphill treadmill walking was included in each session of the supervised component of the intervention, to further strengthen the calf, and participants were encouraged to walk uphill while maintaining their exercise program during the unsupervised component. Each session consisted of approximately 1 hour of individualized therapy. Patients were taught the principles of exercise progression, and were asked to continue the progression for an additional 3 months unsupervised. Participants submitted exercise training logs that were completed for each session in both supervised and unsupervised components of the study. Compliance was documented as the number of days attending supervised exercise, and the number of days exercises were completed or not, for example, because of illness or vacation, in the unsupervised phase.

We hypothesized that physical conditioning structured to enhance calf muscle strength and ankle mobility would improve venous hemodynamics by improving calf muscle pump function. In turn, gains in musculoskeletal function and venous hemodynamics should translate into improved functional mobility and general well-being. The primary outcome variables were APG measures of calf pump function, that is, EF and RVF; in addition, we assessed the following hemodynamic variables: venous filling index, outflow fraction, EV, and venous volume. Secondary outcome variables included the various measures of strength, endurance, and ROM from isokinetic dynamometry, and various functional and QOL instruments.

Randomization and statistics. Group assignment was based on a previously prepared confidential randomized list. Candidates completing the initial evaluation and consent were given a case number, and the study statistician (M.V.J.) reported the group assignment.

Differences in means of outcome variables between therapy and control groups were initially tested with simple uncontrolled *t* tests. Distribution shape and outliers were examined. Nonparametric analyses (Mann-Whitney *U* test, Kolmogorov-Smirnov test) are not presented, because distribution shapes were not radically non-normal, and results of these analyses did not differ appreciably. Mean baseline values were computed from the two performance measures (APG; Biodex). Then, controlling for a linear association with the baseline value, treatment effects were estimated with univariate analysis of variance (ANOVA) with SPSS version 10.0.5 (SPSS, Chicago, Ill). Statistical significance was accepted in this exploratory study at the conventional level ($P < .05$).

The institutional review board approved the protocol; each subject participated with informed consent. Funding was awarded through the Merit Review Board, Department of Veterans Affairs, Veterans Health Administration, Rehabilitation Research and Development.

RESULTS

We screened 77 patients for this prospective trial funded by the Department of Veterans Affairs between September 1999 and November 2002. All had skin changes

Table I. Flow of candidates through screening, recruitment, and participation

Patients	*No.*	*Control group*	*Experimental (therapy) group*	*Commentary*
Assessed for enrollment	77			Recruited and screened for eligibility
Excluded	46			Excluded for failure to meet criteria, refusal, inability to complete studies, other medical contraindications, nonvenous ulceration, surgical preference
Subjects	31	13	18	Refused to complete initial assessment, any intervention, or data collection; postrandomization complaint of pain
Randomized dropouts	1	0	1	
Trial subjects	30	13	17	Received allocated intervention
Lost to follow-up	1	0	1	Psychiatric decompensation; 4 mo
Discontinued intervention	1	0	1	Failed to return for 6-mo exams
Analyzed subjects	28	13	15	One incomplete
Excluded	0	0	0	None totally, but some cases were deleted from some analyses because of missing data for a key item or because recorded value was impossible or an extreme outlier (eg, >5 SD from mean of other values)

or ulceration (CEAP clinical classes 4, 5, 6), as well as objective evidence of CVI as determined with duplex ultrasound scanning (reflux or scarring) and APG. Potential candidates (n = 46) were excluded for often overlapping reasons; these included refusal (n = 10), inability to complete the exercise or testing (n = 6), painful ulcer (n = 1), failure to meet inclusion criteria (n = 12), nonvenous findings (n = 10), acute thrombosis (n = 1), arterial insufficiency (n = 3), and election of surgical intervention (n = 9). Failure to meet criteria included known noncompliant patients; nonvenous findings included 7 candidates with class III obesity, with minimal anatomic evidence of venous disease.[18] Details of patient accession and flow are summarized in Table I, as recommended by the most recent Consolidated Standards of Reporting Trials document.[19] Although initially randomized to therapy, one individual failed to receive the intervention; recurrence of painful ulceration occurred before collection of any outcome measures, which precluded participation in the exercise and testing methods, and the patient was excluded from further analyses.

Thus 30 subjects with bona fide venous insufficiency were enrolled, randomized, and analyzed in control (n = 13) and experimental (n = 17) groups (Table I, online only). In the control intervention, that is, stockings alone, no patients were lost to follow-up and all completed the 6-month analysis. In the experimental intervention, that is, therapy and stockings, follow-up was incomplete for 2 subjects. One completed 4 months of therapy before discontinuing because of unrelated psychiatric reasons; the other completed 5 months, but failed to attend for the sixth and final assessment. Beyond the painful ulceration and the unrelated psychiatric problem, no adverse events transpired.

Age, height, weight, and ABI were typical for a population of subjects with advanced venous insufficiency (Table II). Comorbid medical conditions were frequent in this group with a mean age of 70 years, and included obesity, coronary heart disease, angina, hypertension, dyspnea, asthma, and diabetes. Cardiac failure was present in 10% of our subjects, but none had renal or hepatic failure. Although arthritis and other musculoskeletal conditions may secondarily affect venous function, their incidence was distributed equally in both groups. A medical history of previous venous thrombosis was recorded in 50% of patients; however, duplex ultrasound scans demonstrated an abnormal deep venous lumen in only 30%. In either case, no difference was detected between the two groups (Tables II, III).

All volunteers had advanced CVI, with a distribution of 60% in CEAP class 4, and 40% with ulceration from CEAP classes 5 and 6 (Fig, online only). Cause was secondary in 47%, but objective evidence of a partially obstructive pathophysiologic condition was confirmed in only 27%. Statistical assessment identified no differences between the two groups (Table IV). The anatomic components of venous insufficiency are delineated in Table III; deep venous insufficiency predominates, as would be expected. Mean venous severity scores (Table IV) are consistent with the advanced CVI required by the eligibility criteria. Anatomic scores for reflux and obstruction are given in Table IV. None of the initial differences between experimental and control groups were statistically significant (Tables I-IV).

Baseline (month 0) calf pump functions (mean EF, RVF) were abnormal; mean baseline reflux (VFI) was also abnormal (Table V). Mean RVF in the experimental intervention group returned to normal after 6 months of therapy. Univariate ANOVA, controlling for baseline values,

Table II. Demographic data and coexistent medical illnesses

	Control groups (n = 13)		*Therapy groups (n = 17)*		*Both groups (n = 30)*	
	n	*%*	*n*	*%*	*n*	*%*
Mean age (y)	70		71		70	
Height (in)	69		69		69	
(m)	1.75		1.75		1.75	
Weight (lb)	239		223		230	
kg	108		101		104	
BMI (kg/m^2)	35.3		32.9		33.9	
Ankle-brachial index	1.16		1.16		1.16	
Diabetes	4	31	6	35	10	33
Dyspnea	5	39	6	35	11	37
Arterial hypertension	10	77	7	41	17	57
Angina	3	23	1	6	4	13
Heart failure	2	15	1	6	3	10
Coronary artery disease	4	31	3	18	7	23
Arthritis	5	39	8	47	13	43
Other musculo skeletal (eg, back, knee)	5	39	9	53	14	47
Prior vein operation	1	8	3	18	4	13
Prior thrombosis	8	62	7	41	15	50
IVC filters	1	8	1	6	2	7

All patients were men.
All *P* values nonsignificant.
BMI, Body mass index; *IVC*, inferior vena cava.

tested for differences in outcomes, and detected an effect of therapy on EF and RVF (Table V); that is, in comparing the experimental group with the control group, EF increased significantly ($P < .026$) and RVF decreased significantly ($P < .029$). While the magnitude of VFI (reflux) was consistent with severe CVI, no effects on VFI were observed or expected. No differences were observed between the two groups at baseline. Although a 6-month difference was observed between groups for outflow fraction (obstruction), mean outflow fraction values were not in the range considered abnormal. Thus, while a difference in outflow fraction was observed, it is unlikely to be of clinical significance. Similarly, no changes in VCSS were observed after 6 months.

Mean peak torque per unit body weight improved in the exercise group, but not in the control group (Table VI). Univariate ANOVA, controlling for baseline values, detected a difference for both the slow ($P < .053$) and fast ($P < .033$) test conditions. Slow and fast peak torque improved in comparison with control values in those receiving the exercise regimen. None of the other Biodex measurements demonstrated a difference between groups at 6 months. The exercise group tended to improve, at least slightly, in all other Biodex parameters, while the control group did not; trends for these other parameters, however, did not reach statistical significance.

No differences between groups were observed in the multiple QOL, functional, or perceived impairment instruments used in this protocol; thus data on these secondary outcomes are not presented. Compliance with both supervised and unsupervised exercise was good. During the supervised phase, subjects participated in a mean 18 ± 1.6 of 22 scheduled sessions. During the unsupervised phase, participants reported exercising on a mean of 63 ± 7.3 of a possible 90 days. Stocking compliance was excellent, with 89% of patients wearing the stockings for a mean of 6.24 days and 95 hr/wk at the outset; 97% compliance was achieved at month 6, with similar hours per week and days of use.

Table III. Duplex ultrasound: distribution of findings

	Control group		*Therapy group*		*Both groups*	
	n	*%*	*n*	*%*	*n*	*%*
Superficial			1	6	1	3
Deep			2	12	2	7
Perforator						
Superficial + deep	4	31	4	24	8	27
Superficial + perforator			2	12	2	7
Deep + perforator						
Super + deep + perforator	9	54	8	47	17	50
Evidence of chronic thrombosis (scarring, wall thickening, incompressibility)	5	38	4	24	9	30

No subjects had isolated perforator incompetence or deep + perforator incompetence.

DISCUSSION

The benefits of physical conditioning for patients with arterial occlusive disease (claudication), coronary disease, and musculoskeletal dysfunction have long been recognized.[20] However, to our knowledge, the efficacy of physical conditioning has never been convincingly demonstrated in patients with CVI. Calf muscle, like dermis, may

Table IV. CEAP characterization

	Control group (n = 13)		*Therapy group (n = 17)*		*Both groups (n = 30)*		
Clinical	*n*	*%*	*n*	*%*	*n*	*%*	P
Clinical class							
4	7	54	11	64	18	60	
5	3	23	3	18	6	20	
6	3	23	3	18	6	20	
Etiology							
Primary	5	38	11	65	16	53	
Secondary	8	61	6	35	14	47	
Anatomy: see Table III							
Pathophysiology							
Reflux	9	69	13	77	22	73	
Obstruction							
Reflux/obstruction	4	31	4	23	8	27	
Venous clinical scores (mean ± SEM)							
VCSS total (0-30)	9.77 ± 1.29		9.35 ± 84				.781
Clinical score (0-18)	5.23 ± .89		4.76 ± .81				.703
Disability score (0-3)	1.15 ± .27		1.24 ± .18				.799
Anatomic score							
Reflux (0-10)	4.27 ± .62		5.09 ± .333				.261
Obstruction (0-10)	1.50 ± .60		.92 ± .53				.473

There was no congenital etiology or pure obstructive pathophysiology.
Percentages represent a proportion of each group in the category.
VCSS = Venous Clinical Severity Score.

Table V. Air plethysmography and VCSS values in each group at baseline and 6 months later

		Baseline (mean ± SEM)			*6 Months (mean ± SEM)*			*Baseline to 6-month Change (mean ± SEM)*		
Parameter APG	*Normal values*	*Control group n = 13*	*Therapy group n = 17*	P*	*Control group n = 13*	*Therapy group n = 15*†	P*	*Control group n = 15*	*Therapy group n = 15*†	P *treatment effect*‡
EF (%)	>60%; <40% poor	33.1 ± 2.6	41.7 ± 3.3	.06	31.7 ± 2.9	46.6 ± 3.1	.002	−1.4 ± 2.1	3.48 ± 2.7	.03
RVF (%)	5%-35%	36.2 ± 4.4	38.0 ± 3.7	.76	39.6 ± 4.9	29.5 ± 2.9	.08	3.4 ± 2.9	−8.75 ± 4.6	.03
VFI (ml/min)	<2.0§	7.28 ± 0.9	6.30 ± .07	.39	7.3 ± 0.97	6.6 ± 0.90	.65	.01 ± 0.6	.58 ± 0.5	.64
OF (%)	>38%; <28% poor	51.6 ± 3.0	55.0 ± 2.3	.36	45.7 ± 2.9	60.1 ± 2.7	.001	−5.9 ± 1.8	4.4 ± 2.8	.001
VV (mL)	80-150 mL	141 ± 12	120 ± 7.5	.15	158.9 ± 22	135.9 ± 12	.35	17.8 ± 12.8	15.2 ± 6.8	.69
EV (mL)		44.5 ± 3.6	48.9 ± 4.2	.46	46.1 ± 5.2	63.1 ± 6.7	.06	1.6 ± 3.2	12.4 ± 4.7	.06
VCSS		n = 14	n = 18		n = 13	n = 15		n = 13	n = 15	
Total		9.8 ± 1.29	9.4 ± 0.8	.76	9.8 ± 1.2	8.7 ± 0.8	.388	.08 ± 1.0	−.3 ± 0.9	.51

EF, Ejection fraction; *RVF*, residual volume fraction; *VFI*, venous filling index; *OF*, outflow fraction; *VV*, venous volume; *EV*, ejected volume; *VCSS*, Venous Clinical Severity Scores.
*t-test of group differences at given point in time.
†Two subjects did not return for 6-month follow-up evaluation.
‡Probability of difference in residualized outcomes (stochastic estimate of change) between therapy and control groups based on F test from hierarchical ANOVA (controlling for initial baseline values of same measure). All baseline values (covariates) affected APG outcomes, with $P < .004$; $r = .539$-$.850$ between pretest and posttest air plethysmography values.
§VFI > 9 mL/min associated with high incidence of ulcer.

also exhibit pathologic changes consistent with atrophy, necrosis, and inflammation in limbs with venous insufficiency.[21] Although many patients with CVI are elderly, physical therapy can still be effective, and supervision of the exercise provides a superior response.[20,22] The beneficial effects of muscle stretch and strengthening are rapidly induced, and are sustainable with minimal additional therapeutic encounters.[23,24]

Significant venous dysfunction is present within 5 days of acute, stabilized ankle fractures, but recovers by 18 weeks.[25] Unlike reversible musculoskeletal injury, limbs with severe CVI are subjected to prolonged venous hypertension.[3,5] Short-term (6 weeks) exercise with pedal ergometry significantly improved ankle joint motion and symptoms of pain and limb swelling in an observational study from Germany.[26] Yang et al,[27] who conducted a single-arm pilot study evaluating calf strengthening in relationship to calf pump function, also used multiple baseline studies to reduce variability in APG and Biodex measurements. After a limited exercise program consisting predom-

Table VI. Physical performance (Biodex) outcomes in each group at 6 months

	Baseline (mean ± SEM)			*6 months (mean ± SEM)*			*Baseline to 6-month changes (mean ± SEM)*		
Parameter	*Control group n = 13*	*Therapy group n = 17*	P*	*Control group n = 13*	*Therapy group n = 16*	P*	*Control group n = 16*	*Therapy group* * *n = 16*†	P *treatment effect*‡
Slow speed (60 rpm)									
Peak torque (ft-lb)	31.2 ± 3.9	22.2 ± 2.7	.06	28.1 ± 2.8	30.5 ± 3.2	.59	−3.1 ± 3.0	7.3 ± 3.2	.14
Peak torque/body weight	12.9 ± 1.2	10.7 ± 1.7	.33	11.9 ± 1.0	14.3 ± 1.7	.27	−1.0 ± 1.1	3.1 ± 1.4	.05
Maximum repetitions work (ft-lb)	13.8 ± 2.2	8.4 ± 1.3	.04	11.6 ± 1.7	11.0 ± 1.4	.79	−2.1 ± 1.9	2.2 ± 1.2	.38
Total work (ft-lb)	54.1 ± 8.1	33.8 ± 5.5	.04	51.8 ± 7.4	48.1 ± 6.3	.70	−2.3 ± 4.2	12.4 ± 5.6	.21
Average power (W)	20.0 ± 3.1	12.4 ± 1.7	.05	19.1 ± 2.3	19.8 ± 2.5	.83	−.9 ± 2.5	6.7 ± 2.5	.23
Maximum active ROM (°)	34.2 ± 1.5	33.8 ± 2.1	.88	35.5 ± 2.3	34.1 ± 2.3	.68	1.3 ± 1.3	.1 ± 1.1	.48
Fast speed (120 rpm)									
Peak torque (ft-lb)	26.3 ± 1.9	18.9 ± 1.8	.01	25.2 ± 2.2	25.7 ± 2.2	.90	−1.0 ± 1.7	6.4 ± 2.1	.096
Peak torque/body weight	11.0 ± 0.5	9.1 ± 1.2	.17	10.7 ± .82	12.0 ± 1.2	.41	−.3 ± 0.6	2.8 ± 0.9	.03
Maximum repetitions work (ft-lb)	10.7 ± 1.6	7.1 ± .96	.02	10.5 ± 1.4	9.28 ± .92	.47	−.2 ± 0.9	2.2 ± 0.8	.18
Total work (ft-lb)	117 ± 13.2	81.4 ± 11.9	.05	122.3 ± 15	107.3 ± 12	.43	4.7 ± 6.5	27.7 ± 11.7	.42
Average power (Ws)	19.1 ± 3.3	13.7 ± 2.1	.16	19.5 ± 2.5	17.9 ± 2.0	.62	.4 ± 1.7	3.3 ± 1.6	.51
Maximum active ROM (°)	31.7 ± 1.7	29.8 ± 1.8	.43	34 ± 2.4	30.3 ± 2.0	.25	2.3 ± 1.4	.9 ± 1.0	.48

rpm, Revolutions per minute; *ROM*, range of motion; °, degrees of rotation. Physical performance measures are described in the text.
*Based on *t* test comparing control with therapy groups at each point in time.
†One therapy case did not return for 6 month follow-up Biodex evaluation.
‡Probability of difference in residualized outcomes based on F test from hierarchical ANOVA controlling for baseline values. Baseline Biodex covariates affected Biodex outcomes with $P < .007$; $r = .494$ to $.775$ between pretest and posttest values.

inantly of toe raises in a 6-week, home-based program, they too found significant differences in both EF and RVF; although strength and power demonstrated a trend toward improvement, it did not achieve statistical significance.[27,28] More recently Kan and Delis[29] randomized 10 patients with C_6 disease to an 8-day program of supervised calf muscle exercise, with age-matched control subjects. They also demonstrated improvement in calf pump function; however, they also reported an increase in endurance manifested by doubling of the repetitions of the exercise.[29] Although acute thromboses were excluded from our investigation, Partsch et al[30] also reported improved outcomes in pain, edema, and clinical scores in a randomized trial of early ambulation (with compression and low molecular weight heparin therapy) compared with bed rest (with heparin therapy) in patients with acute proximal venous thrombosis.

Thus our findings confirm the hypothesis that a structured program of calf muscle exercise can improve hemodynamic performance. Both calf pump function (EF, RVF) and strength (peak torque per unit body weight) were improved after participation in the supervised exercise program. These data do not assess whether this benefit could be achieved in a shorter time or with exercise regimens that differ in intensity from those used in the current study. They do indicate that benefit can be sustained for at least 3 months after termination of supervised exercise. To determine the appropriate intensity of exercise, its supervision, its duration, and the need for interval reinforcement would require a larger, multicenter study. Since adjunctive therapy would appear to be complementary for limbs with CVI, further investigation into its role is warranted.

Since APG is completely noninvasive, frequent, repeated measurements are well-accepted by the subjects. This is in contrast to the reluctance expressed by patients asked to participate in studies that require repetitive venous puncture.[5,14] Consistent with previous reports, no changes in reflux as measured with VFI were observed.[27,29] While superficial venous ablation has a dramatic effect on reflux, calf pump function, and improved QOL, many of the subjects in this protocol had prior deep venous thromboses and would not have been ideal candidates for saphenous vein surgery.[1,2]. Thus therapy may offer an additional adjunctive therapy for individuals who are not candidates for traditional venous surgery. Since class II (30-40 mm Hg) stockings were provided and monitored, with excellent compliance in both groups, the treatment benefit accrued from therapy cannot be attributed to compression hosiery or variations in its use.

Although outflow fraction was determined to be different between control and experimental groups, this finding is unlikely to be of clinical significance. The mean values were all in the normal physiologic range. It is not known whether patients with severely restricted outflow fraction would have responded to this therapeutic intervention.

Isokinetic dynamometers are designed to allow for testing to be constrained to a variety of angular velocities, from 2 to more than 300 degrees per second. The fast speed (120 degrees per second) is considered a functional velocity for fast walking. Activities of daily living require that high-

demand tasks, such as avoiding a sudden fall or walking, can be accomplished quickly. The slower speed (60 degrees per second) would be required for more strength-related activities, such as stair climbing. Participants were asked to exert maximal effort as fast as possible throughout the available ROM. Biodex-generated maximal ROM values were consistent with those previously reported for active ROM.[4] The absence of a change with intervention suggests that a contracted tendon may not respond to the duration of therapy used. Variability is common in measures of human performance, including Biodex dynamometry.

An extension of benefits into generalized QOL and improved functional mobility was not demonstrated, despite the use of multiple survey instruments, including two specifically targeted for venous insufficiency. The subjects selected all had advanced CVI; although these questionnaires were intended to evaluate the widely varied complete spectrum of CVI, they have been most frequently used for evaluation of less severe forms of venous insufficiency.

The frequency of ineligibility was surprising. Common reasons were refusal to consider the exercise option, preference for surgery, and clinical findings without anatomic evidence of venous disease. In fact, many of the 20 morbidly obese patients described in 2002 were identified during screening for this protocol.[18] Since most had no anatomic evidence of CVI, we thought it best to exclude these individuals, because their performance may not accurately reflect experimental therapy for CVI. If, however, obesity were itself a cause of CVI, exercise would serve the dual roles of calf strengthening and encouraging increased energy utilization. Unfortunately, these patients are often too ill to consider more than minimal activity.

The primary limitation of the present study is the sample size. A sample size of 60 patients was calculated to achieve at least a 9.9% difference in RVF, with a priori analysis, but we did not attain this sample size. A nonsignificant trend toward greater medical comorbidity was noted in the control group, and slightly greater musculoskeletal problems were observed in the experimental group. Generalizability of results of any study is usually unclear without a substantial sample size and replication at various sites. A larger randomized study with multiple sites could attain greater comparability of experimental and control groups and provide a more precise picture of the benefits of structured exercise on CVI. Therefore we recommend consideration of a larger, multicenter study to confirm and clarify the effects of physical therapy on CVI, the effects on QOL, and the degree of benefit to patients.

Exercise improved calf pump hemodynamics, specifically, EF and RVF. Calf muscle strength improved at both slow and fast speeds when normalized to body weight. These data support further consideration of structured exercise as additional treatment for management of severe CVI.

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DISCUSSION

Dr Kevin G. Burnand (London, England). You obviously had more people who were excluded from the study than actually took part. What you didn't tell us was the age of these patients. You visited the ulcer clinic at St. Thomas's, and I wondered how many of our 80-year-old female patients would be appropriate for your exercise program?

Dr Frank T. Padberg. Some of the patients I saw in your clinic would indeed not have been any more eligible than some of those we excluded from ours.

The average age was a uniform 70.

Some of the patients excluded were reported at this meeting last year. The morbidly obese group was excluded because they had no anatomic evidence of venous disease; although they exhibited skin changes and ulceration, duplex scans and results of air plethysmography were normal.

Dr Thomas W. Wakefield (Ann Arbor, Mich). Frank, this was a very nice study. I have one question.

When you did the APG studies, were the patients wearing stockings or not wearing stockings? We have seen differences in APG results whether or not the patients are wearing their stockings at the time of the study.

Dr Padberg. We uniformly requested that they remove their stockings for these studies; that way we could compare the baseline values that were achieved before they received stockings with those that we achieved with the therapeutic intervals.

Dr Paul Perkowski (Phoenix, Ariz). I have two questions.

Number one, do you have any information on the clinical significance of this? What percentage of patients healed their ulcers or had freedom from recurrence of ulcers?

And the second question is, what do you think is the pathophysiology of this exercise program? Since we know the primary pathology is valvular incompetence, how do you think this exercise helps with that?

Dr Padberg. Let me take the second one first. There is evidence of direct muscle damage in patients with CVI, which is referenced in the text. Even though the muscle is damaged, we presume that it can still be conditioned to improve strength and that the calf muscle pump may compensate to some extent for reflux. We reported several years ago a sensory deficit, which was also associated with chronic venous insufficiency in these patients.

As regards the clinical significance, we didn't ask that question specifically. Our outcome variables were hemodynamic changes or muscle strengthening. We assess healing of ulceration as a primary outcome variable and did not expect to achieve healing as a result of this treatment option. We were really only looking for whether or not we could make a difference in terms of either hemodynamics or exercise strengthening. There is obviously potential for further study, and long-term follow-up will be required to determine the value of therapy as an adjunctive mechanism to maintain limbs in the healed state.